GASLINI

IRCCS - Istituto Giannina Gaslini

Scientific Report 2011
Ongoing Research 2012

SCIENTIFIC REPORT 2011
ONGOING RESEARCH 2012

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Some pictures of the Istituto Giannina Gaslini

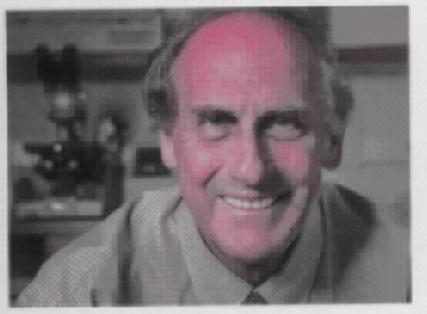
Gerolamo e Lorenza Gaslini

Giannina e Germana Gaslini

Pope Giovanni Paolo II visiting Gaslini

Pope Benedict XVI visiting Gaslini





Nobel laureates at Gaslini: Renato Dulbecco, Rolf Zinkernagel e Ralph Steinman




Some moments of the visit of the International Scientific Committee
(Professors Alain Fischer, Max Cooper, Sergio Romagnani and Anthony Fauci)

Gaslini Research Day - April 2011

The Germana Gaslini International Centre for Studies and Training (CISEF) is launched: a centre of excellence that will carry out educational activities in the fields of scientific research, pediatrics, organization and quality of health care services.

Congress on Translational Research in Pediatric Rheumatology

The 2nd Training Course on Blood and Marrow Transplantation: a course for paediatricians and pediatric nurses on HSCT in children and adolescents

Professor Alberto Marmont, Professor Luisa Massimo, Doctor Giorgio Dini and Professor Lorenzo Moretta

FOREWORD

2011 marked another year of excellence for research at Gaslini. The number of indexed international publications exceeded 300, while the Impact Factor (IF), a bibliometric index weighing the value of scientific articles, surpassed 1,700 and the "normalized" IF, i.e., the IF calculated according to ministerial indications (see table), peaked at over 1,360.

These are the highest values ever achieved at Gaslini and, considering the size of the Institute and the limited number of researchers and space available for laboratories, this result is truly exceptional. I remember that, in 2000, Gaslini's IF was below 600 and the considerable progress since then has been made despite the lower number of researchers and the difficulties stemming from the reduction of ministerial research funding. Many studies have been published in prestigeous international journals, and the mean IF of publications has increased considerably to over 5.

Via Academy has recently published a list of Italian researchers worldwide, identifying the Top Italian Scientists (TIS), i.e., researchers with a Hirsch index (h-index) over 30. The h-index is considered the most accurate scientometric index to measure both the number of international publications and their impact on scientific communities (number of bibliographic citations). Gaslini counts 17 TIS and, according to Via Academy, ranks third among Ministry of Health-funded research institutes (IRCCS). Therefore, Gaslini has the potential to retain its standing and to provide optimal training to young researchers, involving them in important translational and clinical research projects. However, we must make no secret of the difficulties and bureaucratic obstacles that the Gaslini has to face given its public status and the poor awareness in our country of scientific research, which is actually the prime engine of progress. Nonetheless, the excellence of Gaslini's researchers and the high caliber of their projects have always made it possible to raise the necessary funds for research. However, to guarantee Gaslini's scientific excellence also in the future, an appropriate generational turnover is needed. We must be able to keep and also to attract the best young researchers by offering them permanent positions or at least appropriate long-term contracts. Furthermore, investment in advanced technologies and in projects/activities projected towards the medicine of tomorrow is mandatory. In this context, beyond upgrades in advanced equipment, the Gaslini is strengthening collaboration with the Italian Institute of Technology (IIT). The extraordinary innovative talents and facilities of IIT researchers in the field of neuroscience nanotechnologies, robotics, and advanced imaging techniques find important medical applications thanks to collaboration with Gaslini's researchers and clinicians. Research on postnatal stem cells and advanced cell therapies will be given a new boost by the recent recruitment at Gaslini of Francesco Frassoni, an experimental hematologist and clinician of considerable international stature. Frassoni has literally invented the new technique of intrabone transplantation of umbilical cord-derived hemopoietic stem cells that is revolutionizing the approach to the treatment of high-risk leukemias.

To sum up, research at Gaslini is looking towards the future with conscious confidence. Gaslini possesses a truly rich legacy of expertise and devotion to science that must not be squandered. Let us support research with conviction!

Prof. Lorenzo Moretta
Scientific Director

ANNUAL REPORT 2011

INDEX

SCIENTIFIC PRODUCTION AND RESULTS

CONTRIBUTION OF UNITS TO SCIENTIFIC PRODUCTION

Table 1 - Publications assigned to each unit (first author, last author, or intermediate author)

Unit	N.	IF	Normalized IF
Pediatric Rheumatology	32	230.045	168.5
Oncology and Hematology	29	203.378	126
Muscular and Neurodegenerative Diseases	40	162.682	148
Lab Clinical and Experimental Immunology	19	138.207	105.5
Lab Oncology	23	136.272	132
Nephrology, Dialysis and Transplantation	14	104.38	62.1
Lab Pre/Postnatal Diagn Metabolic Diseases	9	96.299	39
Molecular Genetics	17	81.225	78
Pneumology	23	56.646	55
Lab Cytogenetics	4	55.268	19.5
Lab Pathophysiology of Uremia	15	53.084	70
Pediatric Clinic	12	47.447	29.4
Neurosurgery	11	43.305	47
Child Neuropsychiatry	7	42.149	37
Lab Molecular Biology	6	40.932	40
Lab Clinical Chemical Analysis and Microbiology	12	36.584	42
Infectious Diseases	12	31.82	29.2
Epidemiology and Biostatistics	3	27.383	22
Pediatric Gastroenterology	6	25.97	16.6
Radiology	4	18.268	13
Neuroradiology	5	12.965	14
Lab Hematology and Hemophilia	5	12.055	8.8
Physical Therapy	2	10.263	10
Pediatric Surgery	7	10.018	20
Pathologic Anatomy	2	9.286	8
Ophthalmology	3	8.931	6.2
Intensive Care	2	4.346	8
Neonatal Intensive Care	1	2.389	6
Cardiology	1	1.948	4
Emergency	1	1.904	2
Total	**327**	**1705.449**	**1366.8**

N.: Number of publications *in extenso* listed in the Journal of Citation Reports*

IF: Impact Factor reported in the Journal of Citation Reports

Normalized IF: Impact Factor normalized according to ministerial indications

* In case of collaborative papers of one or more units, the paper is assigned (in this order) to the first author, to the last author, or to the author appearing in the first intermediate position in order to calculate the IF of a single publication only once.

Table 2 - Total publications and related IF assigned to units in 2011

Unit	N.	IF	Normalized IF
Pediatric Rheumatology	41	278.768	215.5
Oncology and Hematology	43	247.94	183
Muscular and Neurodegenerative Diseases	47	206.365	190
Lab of Clinical and Experimental Immunology	27	169.409	145.5
Lab of Oncology	27	169.031	152.5
Nephrology, Dialysis and Transplantation	22	133.646	102.1
Epidemiology and Biostatistics	28	129.441	142
Molecular Genetics	24	116.435	118
Lab Pre/Postnatal Diagn Metabolic Diseases	10	107.979	43
Lab Pathophysiology of Uremia	23	94.658	118
Pneumology	26	71.86	73
Child Neuropsychiatry	12	66.002	65
Pediatric Clinic	16	65.668	45.4
Neurosurgery	18	65.65	75
Lab of Cytogenetics	6	65.62	29.5
Neuroradiology	15	61.283	63
Lab Clinical Chemical Analysis and Microbiology	20	59.493	78
Lab of Molecular Biology	7	49.898	48
Infectious Diseases	15	47.294	43.2
Pathologic Anatomy	11	42.22	52
Radiology	8	33.315	33
Pediatric Gastroenterology	10	33.244	27.4
Pediatric Surgery	11	18.808	36
Intensive Care	7	13.576	24
Lab of Hematology and Hemophilia	5	12.055	8.8
Ophthalmology	4	11.171	10.2
Physical Therapy	2	10.263	10
Emergency	3	6.577	8
Neonatal Intensive Care	2	4.46	10
Immunohematology and Transfusion Centre	1	2.685	4
Orthopedics	1	2.505	4
Cardiology	1	1.948	4
Medical Direction	1	1.587	4
Pharmacy	1	1.587	4
Obstetrics and Gynecology	1	1.314	4

N.: Total number of publications *in extenso* (including collaborative articles) listed in the Journal of Citation Reports

IF: Impact Factor reported in the Journal of Citation Reports

Normalized IF: Impact Factor normalized according to ministerial indications

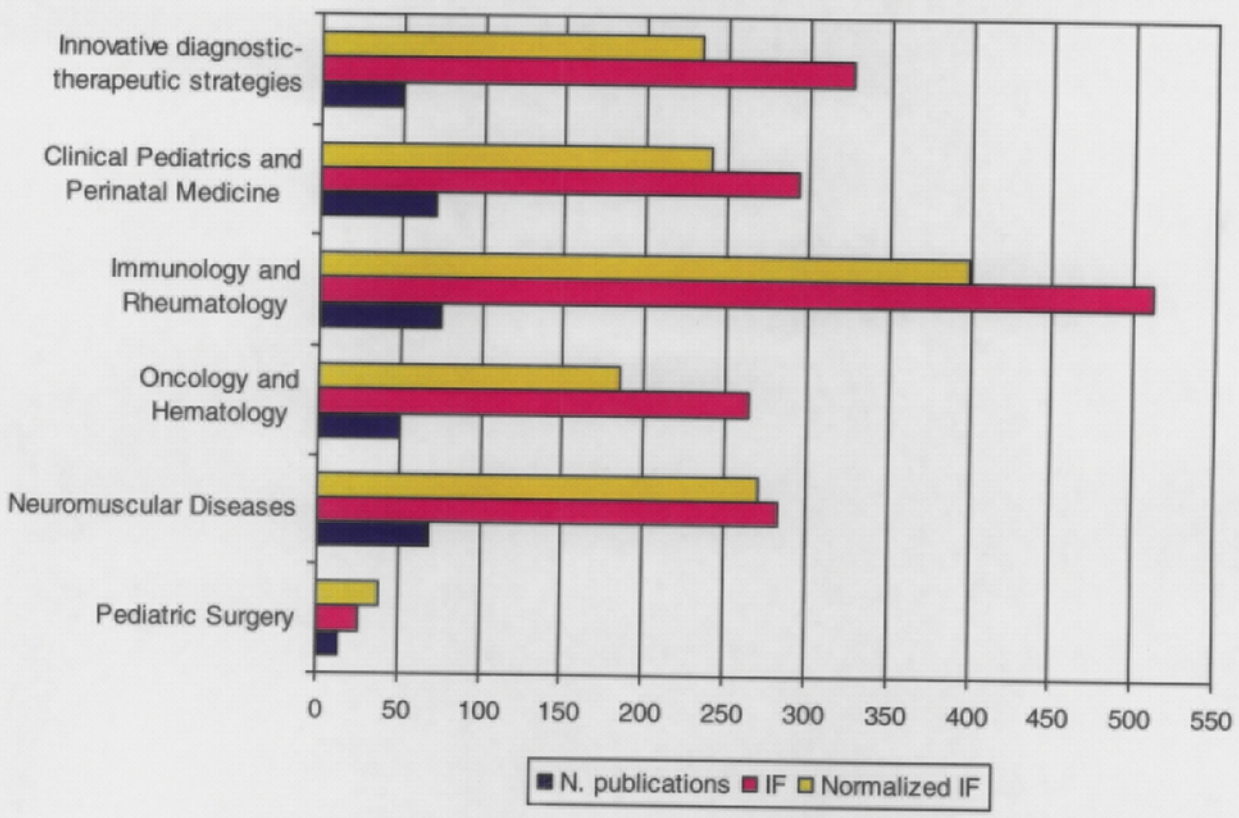
Table 3 – Impact Factor-related data in the period 1999-2011

Year	N. Publications	Impact Factor	Impact Factor normalized according to ministerial indications	IF/ Publication	Normalized IF/ Publication
1999	193	**441.6**	N.D.	2.29	N.D.
2000	170	**583**	**679.3**	3.43	4.00
2001	214	**755.8**	**892.9**	3.53	4.17
2002	218	**807.9**	**930.1**	3.71	4.27
2003	231	**924.9**	**1094.5**	4.00	4.74
2004	248	**1067.5**	**1083**	4.30	4.37
2005	280	**1154**	**1197.2**	4.12	4.28
2006	297	**1187.4**	**1293.5**	4.00	4.36
2007	274	**1244.8**	**1152.7**	4.54	4.21
2008	261	**1247.8**	**1105**	4.78	4.23
2009	311	**1420.6**	**1239.8**	4.57	3.99
2010	227	**1155.6**	**929**	5.09	4.09
2011	327	**1705.449**	**1366.8**	5.22	4.18

RESEARCH LINES

Number	Title
1	INNOVATIVE DIAGNOSTIC-THERAPEUTIC STRATEGIES
2	CLINICAL PEDIATRICS AND PERINATAL MEDICINE
3	IMMUNOLOGY AND RHEUMATOLOGY
4	ONCOLOGY AND HEMATOLOGY
5	NEUROMUSCULAR DISEASES
6	PEDIATRIC SURGERY

Figure 1 - Impact Factor for main research lines 2011



H-index of the Top Italian Scientists (TIS)*
of the Giannina Gaslini Institute

	Area	H-index **
Lorenzo Moretta	Immunologia/Ematologia	109
Cristina Bottino	Immunologia	64
Francesco Frassoni	Terapie cellulari/Ematologia	52
Roberto Biassoni	Biol. Mol/Immunologia	52
Alberto Martini	Reumatologia	47
Luigi Varesio	Biologia Molecolare	42
Claudia Cantoni	Immunologia	40
Vito Pistoia	Oncologia	36
Michela Falco	Immunologia	34
Giovanni Rossi	Pneumologia	34
Claudio Bruno	Malattie Neuromuscolari	34
Isabella Ceccherini	Genetica Med.	32
Luis Vicente Galietta	Genetica Med.	32
G. Marco Ghiggeri	Nefrologia	32
Carlo Minetti	Malattie Neuromuscolari	32
Angelo Ravelli	Reumatologia	32
Claudio Gambini	Anatomia Patologica	31

* **H-index ≥ 30**
****ISI o Via Academy**

STUDIES AND CLINICAL TRIALS APPROVED IN 2011

Unit	Title and protocol number	Ethics Committee meeting (day/month)
Oncology/ Hematology	A phase I-II dose schedule finding study of ch14.18/CHO continuous infusion combined with subcutaneous aldesleukin (IL-2) in patients with primary refractory or relapsed neuroblastoma. A SIOPEN study - 012010.	29/03
Cardiology	A randomized, open label study comparing safety and efficacy parameters for a high and a low dose of ambrisentan (aduste for body weight) for treatment of pulmonary arterial hypertension in paediatric patients aged 8 years up to 18 years - AMB112529.	29/03
Cardiology	An open label, long term extension study for treatment of pulmonary arterial hypertension in paediatric patients aged 8 years up to 18 years who have participated in AMB112529 and in whom continued treatment with ambrisentan is desidered - AMB114588.	29/03
Neuromuscular diseases	Placebo-controlled, double blind, adaptive, randomized, multicentric phase II study to evaluate the safety and efficacy of olesoxime (TRO19622) in patients affected by spinal muscular atrophy (SMA) between 3 and 25 years - TRO19622 CL E Q 1275-1.	29/03
Pediatric Clinic	Use of metformin in obese pediatric patients - FARM87JEA3.	29/03
Pediatric Rheumatology	A retrospective natural history study of patients with Lysosomal Acid Lipase Deficiency/Wolman Phenotype - LAL-1-NH01.	29/03
Oncology/ Hematology	Multicentre pharmacokinetic open label study on oral nilotinib in pediatric patients with chronic phase (CP) or accelerated phase (AP) of Ph+ LMC resistant/intolerant to Gleevec (imatinib) or refractory/relapsing Ph+ LLA - CAMN107A2120.	29/03
Oncology/ Hematology	Multicentre pediatric registry on essential thrombocythemia (ET) - SPD422-404.	29/03
Neonatal Intensive Care	Treatment of arterial hypotension in very preterm newborns: multicentre randomized controlled study - FARM73452X.	29/03
Pediatric Clinic	Recombinant human insulin-like Growth Factor (rhIGF-1) and Growth Hormone (rhGH) combination therapy of pre-pubertal children with idiopathic growth hormone deficiency and poor response to first year of growth hormone therapy: a phase II, prospective, randomized, open-label, multi-centre, parallel group add-on study comparing a flexible rhIGF-1 dose and fixed rhGH dose vs. fixed rhGH dose therapy - COGROW-8-79-52800-011.	29/03
Pediatric Rheumatology	An observational study of the clinical characteristics and disease progression of patients with lysosomal acid lipase deficiency/cholesteryl ester storage disease phenotype - LAL-2-NH01.	19/04
Child Neuropsychiatry	Open-label, expanded access multicentre study with RAD001 in patients with giant cell subependymal astrocytoma associated with tuberous sclerosis (TSC) - CRAD001MIC02.	19/04

Oncology/ Hematology	International Collaborative Protocol for the treatment of children and adolescents with Acute Lymphoblastic Leukemia - AIEOP_BFM ALL 2009.	17/05
Pediatric Clinic	A randomized double-blind, placebo-controlled parallel group dose-finding study of linagliptin (1mg or 5 mg administered orally once daily) over 12 weeks in children and adolescents, from 10 to 17 years of age, with type 2 diabetes and insufficient glycaemic control despite with diet and exercise alone - BI 1218.56.	17/05
Oncology/ Hematology	An Open-label, Multicenter Evaluation of the Safety, Pharmacokinetics, and Efficacy of Recombinant Factor VIII Fc Fusion Protein (rFVIIIFc) in the Prevention and Treatment of Bleeding in Previously Treated Subject With Severe Hemophilia A - 997HA301	17/05
Child Neuropsychiatry	A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of AFQ056 in adolescent patients with Fragile X Syndrome - CAFQ056B2214.	17/05
Pediatric Clinic	Evaluation of the effect of the diagnosis of cystic fibrosis for neonatal screening on mother-child communication relationship and possible impact on nutritional behaviour and/or growth in the first five years of life - IGG-FC-Pescini-2011.	17/05
Neurosurgery	Study on the needs and health care conditions of patients with spina bifida entrusted to hospital and/or district health care services - SBOT.	17/05
Pediatric Clinic	"European Increlex®" (mecasermin [rdna origin] injection) growth forum database: a European subject registry for monitoring long-term safety and efficacy of Increlex® - 2 79 52800 002.	17/05
Pediatric Clinic	Evaluation of long-term risk-benefit profile of levothyroxine therapy in children with congenital hypothyroidism: impact of initial levothyroxine dose on neurological development, growth, cardiovascular and skeletal systems - FARM8AFHP.	17/05
Oncology/ Hematology	Evaluation of metabolomic profile in serum and urine of patients with Fanconi anemia.	17/05
Pediatric Rheumatology	Pharmacovigilance in patients affected by juvenile idiopathic arthritis (Pharmachild). A registry of PRINTO (Paediatric Rheumatology International Trials Organisation) and PRES (Pediatric Rheumatology European Society.	14/06
Oncology/ Hematology	Long-term psychosocial consequences and analysis of needs in off-therapy patients: psychological assessment and intervention. A pilot study - QOL Padova-Genova.	14/06
Oncology/ Hematology	Follow-up of patients at risk for bronchiolitis obliterans after hematopoietic stem cell transplantation - HSCT-PNEUMO.	14/06
Laboratory of Oncology	Validation, characterization and selective targeting of new tumor markers in patients with neuroblastoma.	14/06
Neuromuscular diseases	Epinet registry: international pilot study to activate an internet platform for clinical investigations in the field of epilepsy.	14/06
Neonatal Intensive Care	SIi study: assisted respiration in delivery room with sustained lung inflation in very preterm newborns at risk for rds. A randomized controlled study	19/07
Ophthalmology	Study on long-term safety of Xalatan® in pediatric populations: a non-interventional, longitudinal, prospective cohort study to evaluate the long-term safety of treatment with Xalatan® for pediatric populations - A6111143.	19/07

Oncology/ Hematology	Expression of ABCB1/P-glycoprotein as factor for biological stratification of non-metastatic osteosarcoma of extremities: a prospective study.	19/07
Laboratory Pre- and Postnatal Diagnosis of Metabolic Diseases	Therapeutic challenge in Leukodystrophies: translational and ethical research towards clinical trials - FP7-HEALTH-2009.	19/07
Oncology/ Hematology	A phase III, randomized, double blind, active comparator-controlled clinical trial, conducted under in-house blinding conditions, to examine the efficacy and safety of Aprepitant for the prevention of chemotherapy-induced nausea and vomiting (CINV) in pediatric patients - MK-0869-208.	19/07
Pediatric Clinic	Participation of Cystic Fibrosis Centre of Genova in the Italian Registry of Cystic Fibrosis.	19/07
Pediatric Clinic	Evaluation of adherence to aerosol antibiotic therapy with Promixin and I-neb in patients with cystic fibrosis: Italian multicentre observational study - PROIBITO.	19/07
Pediatric Clinic	One answer to two questions: use of Next Generation Sequencing in neonatal screening for the simultaneous identification of patients and carriers for CFTR gene mutations - A pilot study - CFTR-NGS-IGG.	19/07
Pediatric Clinic	Radiological study of anomalies of the male reproductive system in cystic fibrosis - RAD 001.	19/07
Pediatric Clinic	Severe hypoglycemias and ketoacidosis in children and adolescents with diabetes type I: a survey by health care providers in pediatric diabetology - SHIP-D.	19/07
Pediatric Rheumatology	Registry for patients with Niemann-Pick Type C Disease - AC-056C501 NP-C Registry.	19/07
Oncology/ Hematology	Burnout among BMT staff: a survey in G.I.T.M.O. centres	19/07
Pediatric Clinic	Descriptive epidemiologic study on the identification of genomic methylation status in children with idiopathic short stature	19/07
Pediatric Clinic	Open-label phase IV study for the validation of genetic markers associated with response in terms of growth during the first year of treatment in prepuberal aged children affected by growth hormone deficiency or Turner syndrome: a pharmacogenetic validation study PREDICT - EMR 200104_010.	19/07
Emergency	Headache management in pediatric emergency.	19/07
Pediatric Rheumatology	Long-term multicentre observational study on Hunter syndrome- HOS-HUNTER OUTCOME SURVEY.	19/07
Child Neuropsychiatry	Open-label study to evaluate the long-term safety, tolerability and efficacy of AFQ056 in adult patients with fragile X syndrome- CAFQ056B2279.	20/09
Nephrology, Dialysis and Transplantation	Controlled randomized open-label multicentre 12-month study to evaluate the efficacy, tolerability and safety of early administration of everolimus in association with reduced dose of calcineurin inhibitor (CNI) and early steroid elimination compared to therapy with standard dose of CNI, mycophenolate mofetil and steroid in pediatric patients undergoing renal transplantation, with additional safety follow-up at 24 months - CRAD001A2314.	20/09

Epidemiology and Biostatistics	PanCare Childhood and Adolescent Cancer Survivor Care and Follow-up Studies - G31J11000100006.	20/09
Psychology	Multidisciplinary approach to recurrent abdominal disorders in pediatric age.	20/09
Pneumology	A phase III, 12-week, multicentre, multinational, randomised, double-blind, double-dummy, 3 arm-parallel group study to test the efficacy of CHF 1535 50/6 µg (fixed combination of beclomethasone dipropionate plus formoterol fumarate) versus a free combination of beclomethasone dipropionate 50 µg plus formoterol fumarate 6 µg and versus a monotherapy of beclomethasone dipropionate 50 µg in partly controlled asthmatic children - CCD-0807-PR-0024.	20/10
Emergency	Surveillance of the safety of drugs and vaccines and evaluation of the efficacy of antinfluenza vaccination in children.	20/10
ICU	Regional multicentric study on the risk of hospitalization for lower airway infections due to respiratory syncytial virus (RSV) in preterms: incidence and risk factors	29/11
Neurosurgery	Multicentre, randomized, open-label, phase II comparative study on therapy with bevacizumab in pediatric patients with a new diagnosis of glioma at high supratentorial risk - BO25041C.	29/11
Pediatric Clinic	National, multicentre, observational study to evaluate adherence to and long-term outcome of therapy in children using EasypodTM, an electromechanical device for growth hormone administration - EMR 200104_529.	29/11
Neuromuscular Diseases	Pharmacogenetic study on focal and generalized epilepsies: predictive criteria of clinical pharmacoresistence and search for predisposing genetic factors.	29/11
Oncology/ Hematology	International multicentre randomized phase II study on the combination of Vincristine and Irinotecan, with or without Temozolomide, in patients with refractory or relapsed rhabdomyosarcoma - VIT-0910.	29/11
Laboratory of Molecular Genetics	Molecular study of genetic disorders associated with RET gene alterations.	29/11
Pediatric Clinic	Validation study of PKU-Q0L questionnaire- EMR700733_005.	22/12
Neonatal Intensive Care	Validation of "champs" tool for the evaluation of the risk of fall of pediatric patients in a children's hospital	22/12

Research projects funded in 2011

EU-funded research projects

"PanCare Childhood and Adolescent Cancer Survivor Care and Follow-up Studies" PanCareSurFup.
Principal investigator: Riccardo Haupt, Epidemiology and Biostatistics
Grant: € 250,780.00

"Long-term PHARMAcovigilance for Adverse Effects in Childhood Artritis Focusing on Immune Modulatory Drugs"
Principal investigator: Alberto Martini/ Nicola Ruperto, Pediatric Rheumatology
Grant: € 1,241,550.00

"Global Reaserch in Paediatrics – GRIP"
Principal investigators: Alberto Martini, Nicola Ruperto, Pediatric Rheumatology
Grant: € 40,000.00

"European Network for Cancer Research in Children and Adolescents" – ENCCA
Principal investigator: Riccardo Haupt, Epidemiology and Biostatistics; Luigi Varesio, Laboratory of Molecular Biology
Grant: € 478,014.00

Research projects funded by public institutions

MINISTRY OF HEALTH

"Hirschsprung disease as a model of neuro-immune dysfunctions in the gut: role of the ret proto-oncogene in the correct development and maintenance of microbial homeostasis"
Principal investigators: Paola Griseri, Alessio Pini Prato
Grant assigned to Istituto Gaslini: € 160,000.00, of which € 80,000.00 to the Laboratory of Molecular Geneticsi and € 80,000.00 to the Surgery unit.

"The primary and metastatic cancer stem cell in microenvirnment in neuroectodermal tumors: studies in human neuroblastoma and melanoma"
Principal investigator: Vito Pistoia, Laboratory of Oncology
Grant: € 211,200.00
Share assigned to Istituto Gaslini: € 77,200.00

"New Therapeutical approaches to RANKL-dependent Autosomal Recessive Osteopetrosis"
Principal investigator: Francesca Schena, Pediatric Rheumatology
Grant assigned to Istituto Gaslini: € 125,777.96

MINISTRY OF UNIVERSITY AND RESEARCH – FIRB

"P2 purigenic receptors and ectonucleotidases: new targets for the development of innovative antitumoral drugs"
Principal investigator: Vito Pistoia
Grant assigned to Istituto Gaslini: € 241,547.00

UNIVERSITY OF SASSARI, DEPARTMENT OF NEUROSCIENCES

"Evaluation of neuroprotective activity of ceftriaxone in Alexander disease"
Principal investigator: Isabella Ceccherini, Laboratory of Molecular Genetics
Grant assigned to Istituto Gaslini: € 0.00

Research projects funded by private institutions

TRUSTEES OF COLUMBIA UNIVERSITY

"Genetics of renal hypoplasia"
Principal investigator: Gian Marco Ghiggeri, Nephrology, Dialysis and Transplantation
Grant: € 30,850.02

ASSOCIATION FOR THE RESEARCH ON BRAIN TUMORS IN THE CHILD

"Correlation between genotype and phenotype of pediatric tumors of glial origin"
Principal investigator: Maria Luisa Garrè, Neurosurgery
Grant: € 30,000.00

"Characterization of cells with *cancer stem cells* phenotype and their possible clinical correlation in pediatric brain tumors"
Principal investigator: Valeria Capra, Neurosurgery
Grant: € 30,000.00

ITALIAN ASSOCIATION FOR CANCER RESEARCH
(Associazione Italiana per la Ricerca sul Cancro - A.I.R.C.)

"Biology-driven integrated approach for risk factor discovery in Neuroblastoma"
Principal investigator: Luigi Varesio
Grant: € 62,000.00

"PH0X2B overexpression and pathogenetic interactions as targets for a pharmacological approach to Neuroblastoma"
Principal investigator: Tiziana Bachetti
Grant: € 50,000.00

ITALIAN FOUNDATION FOR CANCER RESEARCH
(Fondazione Italiana per la Ricerca sul Cancro - F.I.R.C.)

Three-year fellowship (2010-2012)
Giovanna Bianchi, Laboratory of Oncology
Grant: € 60,000.00

Three-year fellowship (2010-2012)
Paolo Carrega, Laboratory of Clinical and Experimental Immunology
Grant: € 60,000.00

Three-year fellowship (2010-2012)
Carola Prato, Laboratory of Clinical and Experimental Immunology
Grant: € 60,000.00

Three-year fellowship (2010-2012)
Elisa Prato, Laboratory of Oncology
Grant: € 60,000.00

Two-year fellowship (2011-2012)
Federica Raggi, Laboratory of Molecular Biology
Grant: € 40,000.00

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS INC.

"Functional evaluation of CFTR pharmacological modulators"
Principal investigator: Luis Galietta, Laboratory of Molecular Genetics
Grant: € 26,121.72

EUROPEAN FOUNDATION AGAINST LEUCODYSTROPHIES (ELA)

"Identification of genes involved in hypomyelinating white matter disorders", seconda annualità.
Principal investigator: Federico Zara, Neuromuscular Diseases
Grant: € 44,750.00

CARIPLO FOUNDATION

"Pathogenetic mechanisms and therapeutic strategies in congenital central hypoventilation syndrome (CCHS)"
Principal investigator: Isabella Ceccherini, Laboratory of Molecular Genetics
Grant: € 70,000.00

CASSA DI RISPARMIO DI PARMA FOUNDATION

Research project for patients with fibrodysplasia ossificans progressiva
Principal investigator: Roberto Ravazzolo, Laboratory of Molecular Genetics
Grant: € 5,000.00

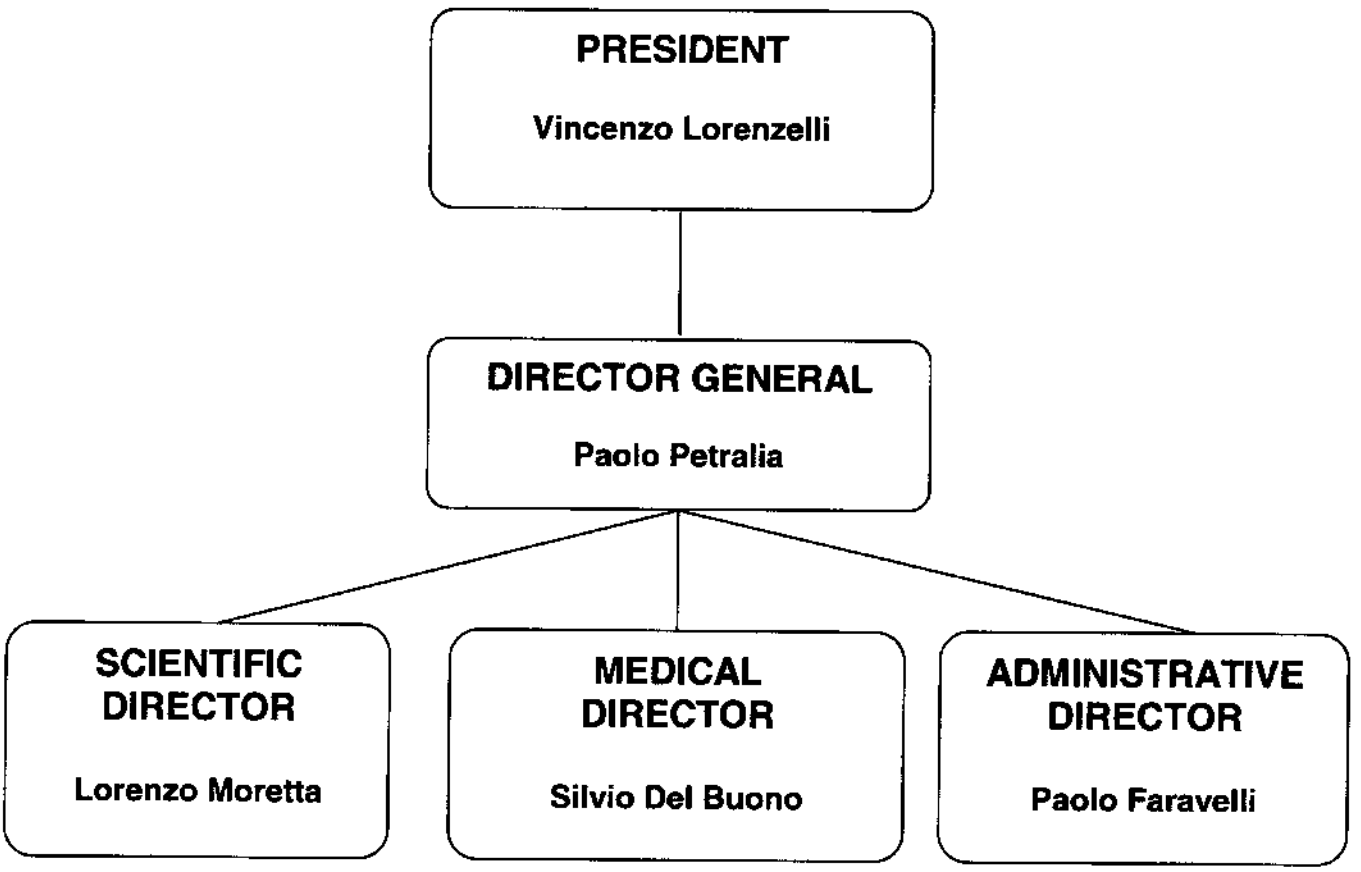
GENZYME EUROPE B.V.

"Characterization of key pathogenetic pathways leading to bone abnormalities in Type 1 Gaucher patients through a biosensor fish model"
Principal investigator: Mirella Filocamo, Laboratory of Pre- and Postnatal Diagnosis of Metabolic Diseases.
Grant: € 141,250.00

Research activity in the field of lisosomal diseases
Principal investigator: Mirella Filocamo, Laboratory of Pre- and Postnatal Diagnosis of Metabolic Diseases
Grant: € 15,000.00

ERG S.P.A.

"Continuation in 2011-2012 of laboratory genotype-phenotype analysis of patients with Fanconi anemia and in-depth study of hematopoietic damage mechanisms"
Principal investigator: Carlo Dufour, Oncology and Hematology
Grant: € 35,000.00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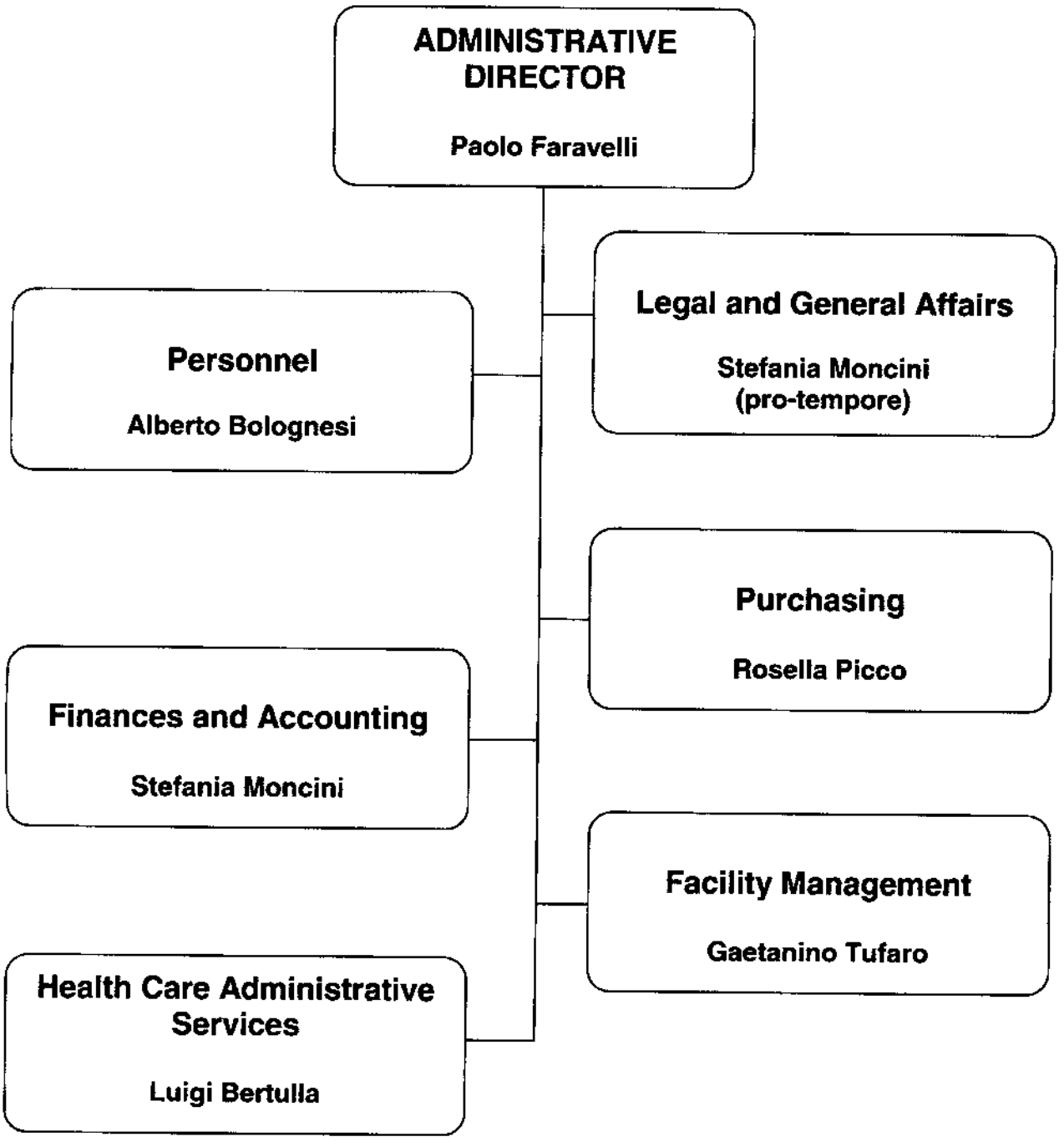
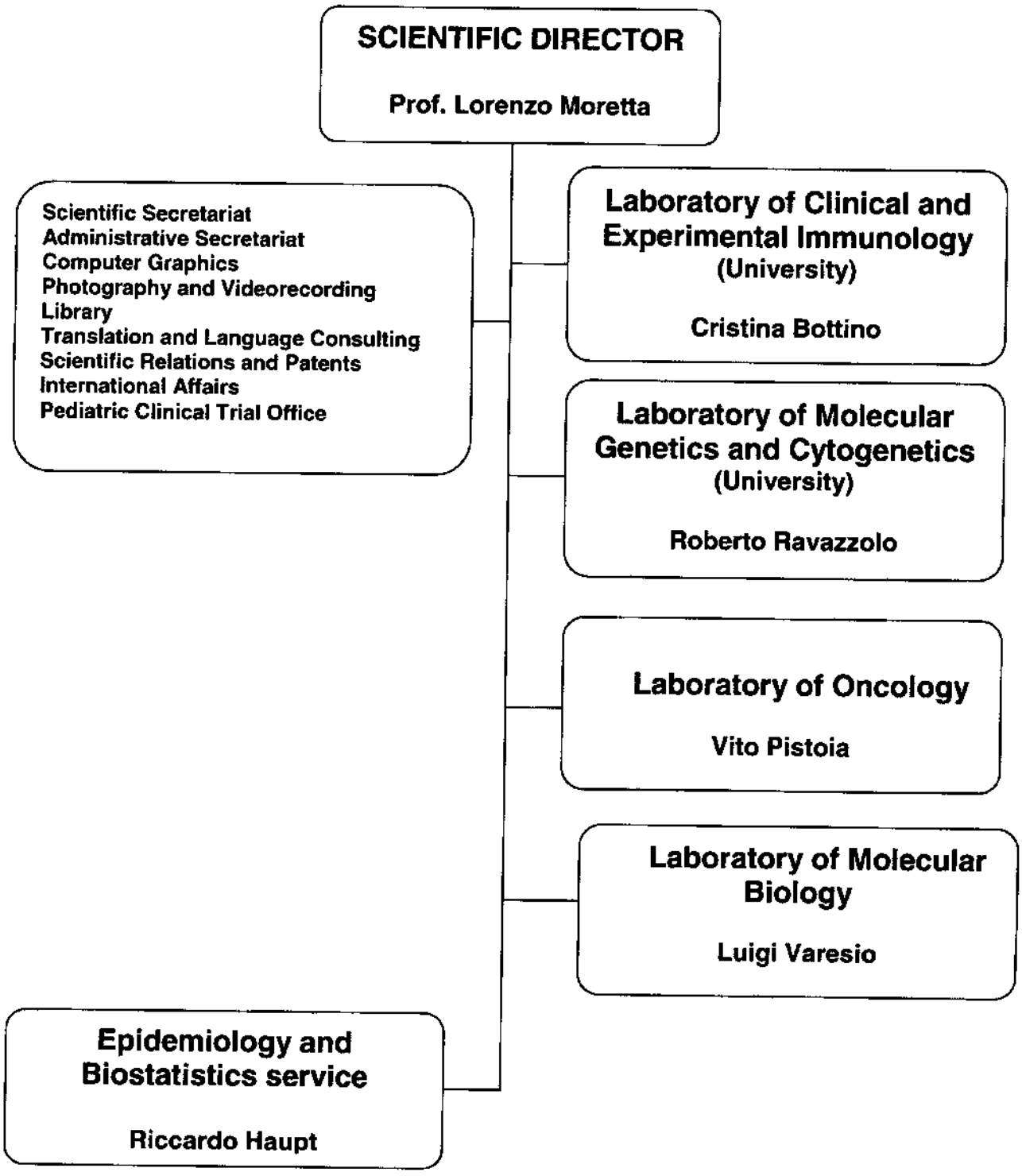
Susy Cappiello

ADMINISTRATIVE DIRECTION



SCIENTIFIC DIRECTION



INTERNATIONAL SCIENTIFIC COMMITTEE

Anthony S. **Fauci** (Chairman)
Director, National Institute of Allergy and Infectious Diseases National Institutes of Health, Bethesda, Maryland, USA

Max D. **Cooper**
Georgia Research Alliance Eminent Scholar , Professor of Pathology and Laboratory Medicine - Emory University School of Medicine, Atlanta

Alain **Fischer**
Groupe Hospitalier Necker- Enfants Malades, Parigi, Francia

Sergio **Romagnani**
Istituto di Clinica Medica III, Servizio di Immuno - Allergologia, Università di Firenze

ETHICS COMMITTEE FOR SCIENTIFIC AND BIOMEDICAL RESEARCH AND FOR CLINICAL EXPERIMENTATION

President	Francesco **De Stefano**
Members	Giambattista **Bonanno** Paolo **Bruzzi** Elio **Castagnola** Adele **Comelli** Mario **Fiscella** Giulio **Gavotti** Paolo **Moscatelli** Marina **Picconi** Roberto **Ravazzolo** Michele **Schiavoni**
Members by right	Lorenzo **Moretta** Silvio **Del Buono** Paola **Barabino**
Scientific Secretariat	Rossella **Rossi,** Giuseppina **Fabbri**

Lorenzo Moretta, M.D.
Curriculum Vitae

Lorenzo Moretta
Born on September 26, 1948 in Genoa.
Married, two children

Education	1966	Maturità Classica, Genoa
	1972	Degree in Medicine and Surgery (MD) with honors, University of Genoa
Board certifications	1974	Medical Microbiology
	1982	Clinical Immunology and Allergology
Positions held	1972-80	Assistant, Institute of Microbiology, University of Genoa
	1975-77	Visiting Scientist, Dept. of Pediatrics and Microbiology, Cancer Center, University of Alabama, Birmingham, USA
	1980-84	Director of Clinical Immunology Laboratories, Ludwig Institute for Cancer Research, Lausanne, Switzerland
	1984-89	Associate Professor of Immunopathology, University of Genoa. Director of Immunopathology Laboratories, Cancer Research Institute, Genoa
	1990-91	Temporary Full Professor of General Pathology, University of L'Aquila
	1991-94	Temporary Full Professor of Immunology, University of Turin, Novara
	1994-to date	Full Professor of General Pathology, University of Genoa
	1994-2000	Director of Immunopathology Laboratories, National Cancer Research Institute, Genova
	Nov.1, 2000 - to date	Scientific Director, Istituto Giannina Gaslini, Genoa
	2009	President Elect, European Federation of Immunological Societies (EFIS)
Awards	1989	Lyon's Prize for the best Italian contribution to Immunology/Oncology (co-winner Robin Foà) (Giardini Naxos, Italy)
	1998	Cancer Research Institute W.B. Coley Award for Distinguished Research in Basic and Tumor Immunology (co-winners K. Kärre and R. Steinman) (New York)
	1998	Biotec Award for outstanding contribution to Biotechnology-oriented research in Italy (co-winners A. Mantovani, E. Pinna) (Siena)
	1999	The 2nd PISO International Prize for Research (co-winner A.S. Fauci) (Cagliari)
	2000	Invernizzi Prize for major advances in Medicine (Milan)
	2000	San Salvatore Prize 2000 for excellence in Biomedical research in Immunology and Oncology (Lugano)
	2001	Yvette Mayent Prize, Institut Curie (co-winners K. Kärre, A. Moretta) for their work on the natural killer cells of the immune system (Paris)
	2001	Novartis Award for Basic Immunology (co-winners K. Kärre, Wayne Yokoyama) (Stockholm)
	2001	Liguria Region Prize for fundamental contribution to scientific research (Genova, Italy)
	2002	Galeno Prize for outstanding University Career (Milan)
	2003	Cristoforo Colombo Medal for scientific merits (Genova)
	2004	Highly Cited Scientists Award, University of Genova, Genova, Italy
	2006	"Guido Venosta" Prize for excellence in Cancer Research (FIRC/AIRC Foundation) (Rome)
	2011	"Delfini D'Argento" Award (Cascina, Pisa)
Memberships (by invitation):	2000	Academia Europaea
	2003	European Molecular Biology Organization (EMBO)
	2003	Gruppo 2003 (highly cited scientists)
	2009	Accademia dei Lincei
Honours	2006	"Commendatore" of the Italian Republic for excellence in science (Rome)

International Publications *in extenso*	**over 550**
Total Impact Factor	**over 3200**
Total number of citations	**Over 35,000 among the "highly cited scientists" of ISI**
H-index	**109** (Via Academy); **106** (ISI)

Professor Lorenzo Moretta is Full Professor of General Pathology and Pathophysiology at the Medical School, University of Genoa and Scientific Director of the G. Gaslini Institute.
Professor Moretta carried out research studies that are considered fundamental in Immunology. He first identified T lymphocyte subpopulations in humans and these studies laid the foundations for understanding the diseases affecting the immune system such as immunodeficiencies and autoimmune diseases. The publication of this research was identified as "citation classic" in the Current Contents Life Science (vol. 28, n. 50, December 16, 1985), it has now been cited over 1500 times. Professor Moretta is author of over **550** publications *in extenso* in prestigious international journals and books and has been the most cited Italian researcher in the scientific literature in a 10-year period (as reported in "The Scientist", Current Contents, February 19, 1990).
The total number of citations is now over 35 thousands. Professor Moretta is in the ISI list of "Highly Cited Scientists", that includes only a limited number of Italian researchers. His h-index is **109**. Taken together, these data represent an important indicator of the considerable impact of the research studies carried out by Professor Moretta and his collaborators on international biomedical research.
Professor Moretta is (or was) in the Editorial board of the following international journals: Trends in Immunology, European Journal of Immunology, International Immunology, Immunology Letters, J. Clinical Immunology, Human Immunology, The Hematology Journal, European Journal of Inflammation.

Prof. Moretta has been Member of **Academia Europaea** since 2000 and Member of **Accademia dei Lincei** since 2009. He has been an **EMBO** Ordinary Member since 2003.

Professor Moretta is usually invited to participate in the major international and national meetings of Immunology as speaker and/or chairman of symposia and plenary sessions. He has often been invited individually to propose nominations for the Nobel prize for Medicine and Physiology and for other prestigious international prizes.
The research laboratory directed by Professor Moretta carries out basic and applied research in basic and tumor immunology. Research studies are mainly focused on human T lymphocytes and NK cells.
A fundamental contribution of the Laboratory directed by Professor Moretta, in close collaboration with the Laboratory directed by Alessandro Moretta, Professor of Histology at the University of Genoa, is the definition of the mechanisms regulating NK cell function (tumor cell killing) thanks to the discovery of inhibiting receptors specific for HLA class I molecules (named KIR) and of receptors responsible for NK cell activation and for induction of tumor cell killing processes. The genes coding for these receptors were cloned in the Laboratory of Professor Moretta. Overall, 15 new receptor molecules were identified and cloned by his research group.
Following the discovery of NK receptors by the Moretta's group, preclinical and clinical studies revealed the major role of NK cells (and of KIR-HLA-class I mismtaches) in the eradication of acute myeloid leukemias in the haploidentical bone marrow transplantation setting. Prof. Moretta and coworkers have provided evidence that this approach is particularly efficient also in high risk (otherwise fatal) ALL in pediatric patients, thanks to definition of a suitable approach allowing the selection of the most appropriate (haploidentical) donors.
Overall, the discoveries of Professor Moretta and his collaborators had a considerable impact on biomedical research, also for their well established applications to immunotherapy of leukemias and, possibly, of solid tumors and to immunodeficiencies, and won Professor Moretta prestigious international prizes (see list in table).

STAFF

Scientific Director secretariat
Cinzia Miriello (University)

Scientific Director secretariat and editorial activities
Stefano Canu
Administrative activities related to the research projects carried out by the Scientific Director and to his activity as editor and/or referee for various international journals.

Scientific Direction secretariat
Roberta Fossati
Secretarial activity (reservation of meeting rooms, supplies and maintenance work orders, correspondence)

Scientific Secretariat
Laura Diamanti
Collection of publications, updating of the authors' database, and reporting on scientific production (IF monitoring).

Seminars Secretariat
Orietta Poggi
Administrative management of scientific seminars

Administrative Secretariat
Maria Gabriella Marinari
Alessandra Della Rovere
Giuseppina Fabbri
Giorgio Sangalli
Anna Cesarini
Vincenza Nalbone
Eva Canepa
Administrative management of research project funding by public and private institutions

Computer Graphics Service
Anna Cesarini
Computer processing of images and texts for scientific presentations to national and international congresses. Preparation of images and tables for scientific publications in national and international journals. Graphic and typographic preparation and revision of Gaslini's Annual Report. Graphic preparation (including accounting) of intermediate and final reports on research programs necessary for obtaining appropriate funding. Management of the mailing lists of the Scientific Direction.

Photography and Videorecording unit
Franco Prefumo, Raffaella Camusso, Luca Tedeschi
Patient image documentation and production of videos. Digitalization of all radiographs, reproduction of images, pictures, US images, production of images and videos for scientific divulgation. Graphic updating of forms used in hospital. Design and production of brochures and posters. Technical assistance and preparation of seminars and meetings at Gaslini. Production of staff badges.

Library
Angela Carbonaro, Orietta Poggi
Bibliosan service, document delivery for Gaslini's staff and for external users. Training and information to users for optimal use of available resources.

Translation and Language Consulting
Anna Capurro
Translation, writing and revision (in English and French) of scientific papers, research projects, Gaslini's Annual Report, presentations at congresses, contracts and agreements, guidelines and clinical protocols, various clinical documentation and informative material. Translation of documentation related to the Institute's accreditation by Joint Commission International (JCI).

Scientific Relations and Patents
Rosa Bellomo
Maintenance of relations between the Scientific Direction and the Ministry of Health, the Regione Liguria and other national public and private bodies or institutions giving financial support to research. Support to the Scientific Director and Gaslini's researchers in planning, managing and reporting on Ministry-of-Health-funded research programs. Coordination of the preparation of Gaslini's annual report requested by the Ministry of Health. Rosa Bellomo is reference person for Quality Management System for the Scientific Direction.

International Affairs
Thomas John Wiley
Support and liaison services for the identification, design and planning, and management of research activity and collaborative actions financed by international funding agencies (the European Commission, the European Science Foundation, the NATO Science Program). Consultation and assistance on the selection of international fellowship programs and mobility schemes.

Pediatric Clinical Trial Office (PCTO)
Ornella Della Casa Alberighi
Highly qualified support to the preparation and management of clinical research proposals and clinical development plans of drugs and pharmacovigilance in pediatrics. Design and conduction of collaborative clinical trials in pediatrics (from phase I to phase IV studies – pharmacovigilance) in collaboration with specialized networks of pediatric institutes of excellence, with national institutions (Istituto Superiore di Sanità) and international organizations (European Community, Orphanet), with regulatory agencies (EMEA and FDA, AIFA), and with national and international pharmaceutical companies. Continuing education of health care professionals in performing clinical trials in pediatrics.

EPIDEMIOLOGY AND BIOSTATISTICS

Associated with the Scientific Direction

PERSON IN CHARGE: Riccardo Haupt

STAFF

Francesca Bagnasco
Luisella Bertoluzzo
Maria Grazia Calevo
Silvia Caruso
Giovanni Erminio
Annarita Gigliotti
Angela Pistorio

MAIN RESEARCH ACTIVITIES YEAR 2011

The unit collaborates on two EU-funded projects. Within the ENCCA (European Network for Cancer Research in Children and Adolescents) project, it coordinates the development of the "Survivorship Passport" to be given to all cancer patients at the end of treatment. Within PanCareSurFup, the unit contributes with more than 15,000 cases to the European cohort of childhood cancer survivors. Within the cohort, a study on late mortality and two case-control studies on carcinomas and sarcomas as second malignant tumors and on cardiac events are being conducted. It has coordinated the development of guidelines for the diagnosis and treatment of Langerhans cell histiocytosis.
The unit also collaborates on the design and analysis of clinical trials or observational studies mainly in the rheumatologic and oncologic fields.
We have also developed and validated questionnaires and instruments for clinical and radiologic evaluation of patients with juvenile idiopathic arthritis, and other rheumatologic disorders. Studies have also been conducted on disease classification in rheumatology.

RESEARCH PROGRAM YEAR 2012

Continuation of activities linked to the ENNCA e PanCareSurFup European projects with major focus on the development of the Survivorship Passport and on the long term analysis of the European cohort of childhood cancer survivors.
Collaboration with the "PRINTO" (Pediatric Rheumatology International Trials Organization") network for the set up of a pharmacovigilance project with long term follow-up for moderate and severe side effects in children with juvenile idiopathic arthritis treated with methotrexate or biological drugs.
Continuation of the validation process of different clinical instruments and radiologic tools to evaluate disease activity and joint damage in children with arthritis.
Continuation of the collaboration on classification projects and analysis of clinical trials.

MAIN COLLABORATIONS

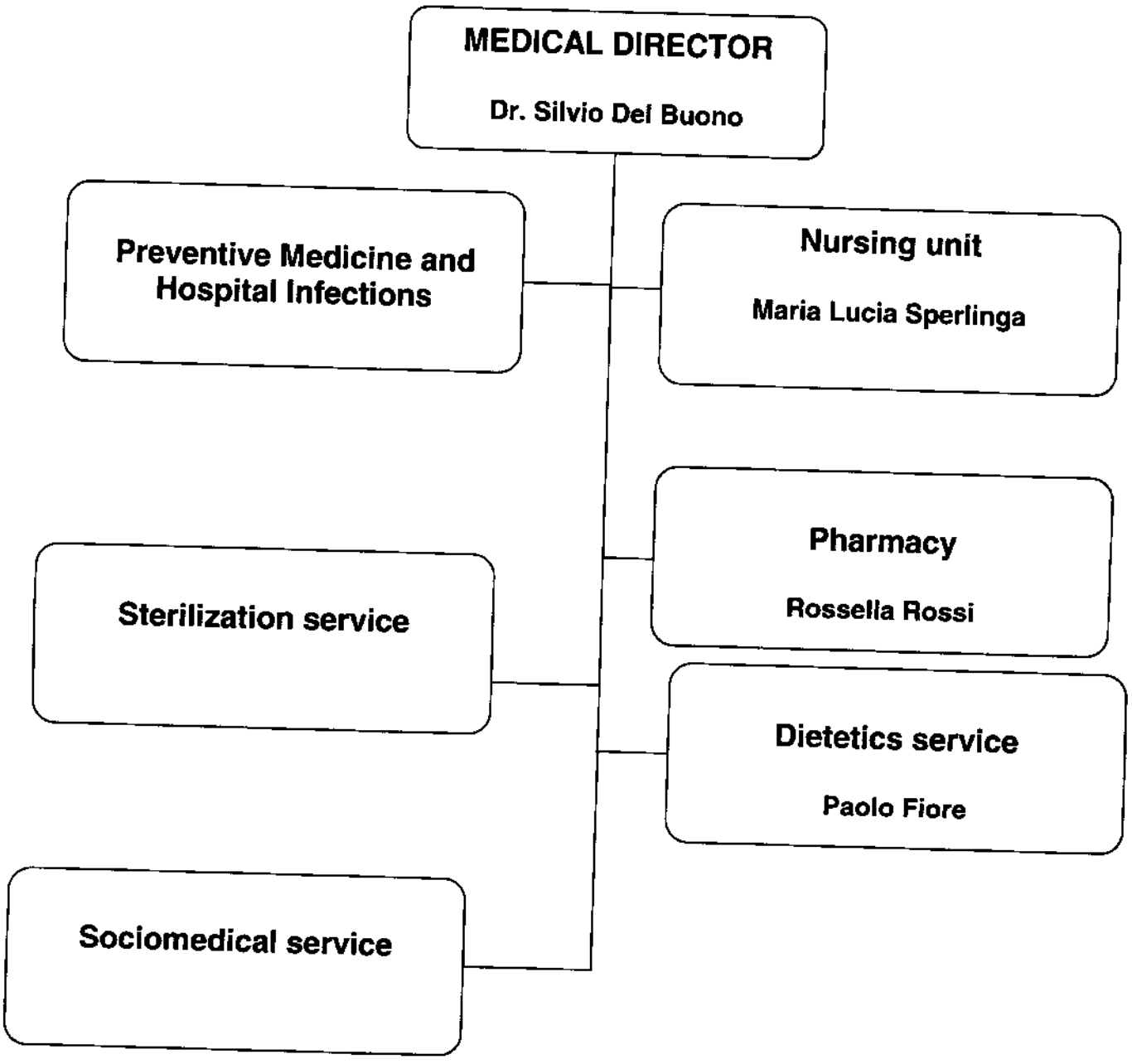
- **Clinica Pediatrica dell'Università di Milano-Bicocca:** National registry of off therapy patients (ROT);
- **CINECA:** Web-based data base for follow-up of survivors of childhood cancers;
- **Neonatology and Ear-Nose-throat departments of the Liguria Region:** Regional screening for neonatal deafness (STERN). Regional Registry of congenital deafness
- **"PRINTO" (Pediatric Rheumatology International Trials Organization"):** Analysis of clinical trials and of longitudinal data from the pharmacovigilance registry of children treated with methotrexate or other biologic drugs

MAIN PUBLICATIONS YEARS 2009-2011

1. Apaz MT, Saad-Magalhães C, Pistorio A, Ravelli A, de Oliveira Sato J, Marcantoni MB, Meiorin S, Filocamo G, Pilkington C, Maillard S, Al-Mayouf S, Prahalad S, Fasth A, Joos R,

Schikler K, Mozolova D, Landgraf JM, Martini A, Ruperto N; Paediatric Rheumatology International Trials Organisation. Health-related quality of life of patients with juvenile dermatomyositis: results from the Pediatric Rheumatology International Trials Organisation multinational quality of life cohort study. Arthritis Rheum 2009;61(4):509-517. (IF_{JCR-08}: 6.787; IF_{Minist}: 6).

2. Garrè ML, Cama A, Bagnasco F, Morana G, Giangaspero F, Brisigotti M, Gambini C, Forni M, Rossi A, Haupt R, Nozza P, Barra S, Piatelli G, Viglizzo G, Capra V, Bruno W, Pastorino L, Massimino M, Tumolo M, Fidani P, Dallorso S, Schumacher RF, Milanaccio C, Pietsch T. Medulloblastoma variants: age-dependent occurrence and relation to Gorlin syndrome--a new clinical perspective. Clin Cancer Res 2009;15(7):2463-2471. (IF_{JCR-08}: 6.488; IF_{Minist}: 6).
3. Parodi A, Davi S, Pringe AB, Pistorio A, Ruperto N, Magni-Manzoni S, Miettunen P, Bader-Meunier B, Espada G, Sterba G, Ozen S, Wright D, Magalhães CS, Khubchandani R, Michels H, Woo P, Iglesias A, Guseinova D, Bracaglia C, Hayward K, Wouters C, Grom A, Vivarelli M, Fischer A, Breda L, Martini A, Ravelli A; Lupus Working Group of the Paediatric Rheumatology European Society. Macrophage activation syndrome in juvenile systemic lupus erythematosus: a multinational multicenter study of thirty-eight patients. Arthritis Rheum 2009;60(11):3388-99. Review. (IF_{JCR-08}: 6.787; IF_{Minist}: 6).
4. Foell D, Wulffraat N, Wedderburn LR, Wittkowski H, Frosch M, Gerss J, Stanevicha V, Mihaylova D, Ferriani V, Tsakalidou FK, Foeldvari I, Cuttica R, Gonzalez B, Ravelli A, Khubchandani R, Oliveira S, Armbrust W, Garay S, Vojinovic J, Norambuena X, Gamir ML, García-Consuegra J, Lepore L, Susic G, Corona F, Dolezalova P, Pistorio A, Martini A, Ruperto N, Roth J; Paediatric Rheumatology International Trials Organization (PRINTO). Methotrexate withdrawal at 6 vs 12 months in juvenile idiopathic arthritis in remission: a randomized clinical trial. JAMA 2010;303(13):1266-73. (IF_{JCR-09}: 28.899; IF_{Minist}: 15).
5. Haupt R, Garaventa A, Gambini C, Parodi S, Cangemi G, Casale F, Viscardi E, Bianchi M, Prete A, Jenkner A, Luksch R, Di Cataldo A, Favre C, D'Angelo P, Zanazzo GA, Arcamone G, Izzi GC, Gigliotti AR, Pastore G, De Bernardi B. Improved survival of children with neuroblastoma between 1979 and 2005: a report of the Italian Neuroblastoma Registry. J Clin Oncol 2010;28(14):2331-2338. (IF_{JCR-09}: 17.793; IF_{Minist}: 15).
6. Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, Buoncompagni A, Lazar C, Bilge I, Uziel Y, Rigante D, Cantarini L, Hilario MO, Silva CA, Alegria M, Norambuena X, Belot A, Berkun Y, Estrella AI, Olivieri AN, Alpigiani MG, Rumba I, Sztajnbok F, Tambic-Bukovac L, Breda L, Al-Mayouf S, Mihaylova D, Chasnyk V, Sengler C, Klein-Gitelman M, Djeddi D, Nuno L, Pruunsild C, Brunner J, Kondi A, Pagava K, Pederzoli S, Martini A, Ruperto N; Paediatric Rheumatology International Trials Organisation (PRINTO). EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis 2010;69(5):798-806. (IF_{JCR-09}: 8.111; IF_{Minist}: 8).
7. Malattia C, Damasio MB, Pistorio A, Ioseliani M, Vilca I, Valle M, Ruperto N, Viola S, Buoncompagni A, Magnano GM, Ravelli A, Tomà P, Martini A. Development and preliminary validation of a paediatric-targeted MRI scoring system for the assessment of disease activity and damage in juvenile idiopathic arthritis. Ann Rheum Dis 2011;70(3):440-446. (IF_{JCR-10}: 9.082; IF_{Minist}: 8).
8. Pezzolo A, Parodi F, Marimpietri D, Raffaghello L, Cocco C, Pistorio A, Mosconi M, Gambini C, Cilli M, Deaglio S, Malavasi F, Pistoia V. Oct-4+/Tenascin C+ neuroblastoma cells serve as progenitors of tumor-derived endothelial cells. Cell Res 2011;21(10):1470-1486. (IF_{JCR-10}: 9.417; IF_{Minist}: 8).
9. Pimentel A, Haupt R, Sihelnik SA, Kimmel WB, Swierczynski SL. Focal Langerhans cell histiocytosis (LCH) coexisting with renal cell carcinoma. J Clin Oncol 2011;29(5):e107-e109. (IF_{JCR-10}: 18.97; IF_{Minist}: 15).
10. Ravelli A, Varnier GC, Oliveira S, Castell E, Arguedas O, Magnani A, Pistorio A, Ruperto N, Magni-Manzoni S, Galasso R, Lattanzi B, Dalprà S, Battagliese A, Verazza S, Allegra M, Martini A. Antinuclear antibody-positive patients should be grouped as a separate category in the classification of juvenile idiopathic arthritis. Arthritis Rheum 2011;63(1):267-275. (IF_{JCR-10}: 8.435; IF_{Minist}: 8).


MEDICAL DIRECTOR
Dr. Silvio Del Buono
Preventive Medicine and Hospital Infections
Nursing unit
Maria Lucia Sperlinga
Pharmacy
Rossella Rossi
Sterilization service
Dietetics service
Paolo Fiore
Sociomedical service

PHARMACY

DIRECTOR: Rossella Rossi

STAFF
Paola Barabino
Tullia Emanueli
Chiara Intra
Ines Lorenzi
Eleonora Panetta

MAIN RESEARCH ACTIVITIES YEAR 2011

Pharmacovigilance

RESEARCH PROGRAM YEAR 2012

Pharmacovigilance: continuation of the research project on drug adverse reactions requiring admission to the Emergency Department

MAJOR COLLABORATIONS

- Istituto Superiore di Sanità: multiregional research project of which Regione Liguria with the Istituto Giannina Gaslini is national coordinator.
- AIFA: participation in the Pediatric Working Group and working group on pharmacovigilance and vaccine vigilance
- University of Genoa: Dr. Rossi is regional reference person for the University residency program in Hospital Pharmacy
- Regione Liguria and Regional Health Agency for CRIFF (Regional Centre of Pharmacovigilance and Drug Independent Information), of which Dr. Rossi is coordinator
- Regional Purchase Centre, of which Dr. Emanueli is expert consultant
- SIFO (Italian Society of Hospital Pharmacy): collaboration of Dr. Panetta on the creation of the Galenic Code for magistral pharmaceutical formulations

MAIN PUBLICATIONS YEARS 2009-2011

1. Italian Multicenter Study Group for Drug and Vaccine Safety in Children: Francesca Menniti-Ippolito, Roberto Da Cas, Luciano Sagliocca, Giuseppe Traversa (National Centre for Epidemiology, National Institute of Health, Rome); Fernanda Ferrazin, Carmela Santuccio, Loriana Tartaglia, Francesco Trotta (Italian Medicines Agency, Rome); Pasquale Di Pietro, Salvatore Renna, Rossella Rossi, Bianca Domenichini,Stefania Gamba, Francesco Trovato (Giannina Gaslini Paediatric Hospital, Genoa); et al.
   Effectiveness and safety of the A-H1N1 vaccine in children: a hospital-based case control study
   BMJ Open 2011;2:e000167. doi:10.1136/bmjopen-2011-000167.
2. Ravani P, Magnasco Alberto, Edefonti A, Murer L, Rossi R, Ghio L, et Al.
   Short-term effects of Rituximab in children with steroid- and calcineurim-dependent nephrotic syndrome: a randomized controlled trial.
   CLIN J AM SOC NEPHRO 2011;6:1308-15.

EXPERIMENTAL AND LABORATORY MEDICINE

Dr. Giovanni Melioli

LAB. OF CLINICAL CHEMICAL ANALYSIS AND MICROBIOLOGY

Giovanni Melioli

LABORATORY OF MOLECULAR BIOLOGY

Luigi Varesio

MOLECULAR GENETICS
(University)

Roberto Ravazzolo

LABORATORY OF CLINICAL AND EXPERIMENTAL IMMUNOLOGY
(University)

Cristina Bottino

LABORATORY OF ONCOLOGY

Vito Pistoia

CORE FACILITIES

Lorenzo Moretta
Giovanni Melioli (Coordinator)

CLINICAL AND EXPERIMENTAL IMMUNOLOGY

DIRECTOR: Cristina Bottino
(University)

STAFF
Claudia Cantoni
Michela Falco
Antonio Puccetti
Grazia Maria Spaggiari
Laura Chiossone

Francesco Frassoni (Laboratory of postnatal stem cells and cell therapies)
Marina Podestà

MAIN RESEARCH ACTIVITIES YEAR 2011

- Haplo-HSC transplantation in pediatric leukemic patients: genotypic/phenotypic analysis of 61 potential donors and selection of the donor characterized by the best NK-alloreactivity against the recipient.
- Characterization of the role of KIR2DS1 in KIR/KIR-ligand mismatched alloreactivity.
- Identification of alternatively spliced NKp30 isoforms and of their different involvement in the prognosis of gastrointestinal stromal tumors.
- Analysis of the crosstalk between human NK cells and autologous macrophages and identification of a membrane-bound form of IL-18.
- Identification of CD34+ cells in the decidua and of their ability to differentiate into decidual NK cells.
- Identification of new pathogenetically relevant autoantigen targets in type I diabetes and dermatomyositis that can be used to set up diagnostic assays.

RESEARCH PROGRAM YEAR 2012

- Analysis of the KIR repertoire in HSC donors: collection of new cases to reach a cohort of donor/recipient pairs large enough to perform statistical correlation with post-transplant clinical data (including survival, relapses)
- Analysis of the role of HCMV infection in NK cell function/development after HSC umbilical cord blood transplantation (UCBT)
- Analysis of the crosstalk between NK cells and tumor-associated macrophages (TAM) from cancer patients.
- Analysis of the ability of tumor-derived factors to modulate NK cell function and phenotype
- Development of novel proteomic approaches for the identification of cellular ligands specific for Natural Cytotoxicity Receptors (NCRs)
- Identification of new serological markers of autoimmune diseases such as dermatitis herpetiformis and seronegative Rheumatoid arthritis by using peptide libraries and gene array technology.

MAJOR COLLABORATIONS

- Prof. A. Moretta, Dr. S. Sivori, Dr. R. Castriconi, Dr. F. Bellora. Di. Me.S, University of Genova Prof. M.C. Mingari, Di.Me.S, University of Genova and S.Martino-IST hospital
- Dr. D. Pende, Dr. M. Vitale, Dr. P. Vacca, Dr. F. Frassoni, Dr. A. Pessino, S. Martino-IST hospital, Genova
- Prof. A. De Maria, DISSAL, University of Genova

- Prof. E. Fulcheri, DISC, University of Genova
- Prof. F. Locatelli, Pediatric Onco-Hematology Department, Bambino Gesù Hospital, Rome
- Prof. C. Lunardi, Dept. Medicine, University of Verona
- Prof. L. Frulloni, Gastroenterology unit, University of Verona
- Prof. L. Zitvogel, Institut Gustave Roussy and Université Paris Sud-XI, Villejuif, France
- Prof. Miguel Lopéz-Botet, Universitat Pompeu Fabra, Barcelona, Spain

MAIN PUBLICATIONS YEARS 2009-2011

1. Balsamo, M., Scordamaglia, F., Pietra, G., Manzini, C., Cantoni, C., Boitano, M., Queirolo, P., Vermi, W., Facchetti, F., Moretta, A., Moretta, L., Mingari, M. C. and Vitale, M., Melanoma-associated fibroblasts modulate NK cell phenotype and antitumor cytotoxicity. Proc Natl Acad Sci U S A 2009. 106: 20847-20852.
2. Castriconi, R., Daga, A., Dondero, A., Zona, G., Poliani, P. L., Melotti, A., Griffero, F., Marubbi, D., Spaziante, R., Bellora, F., Moretta, L., Moretta, A., Corte, G. and Bottino, C., NK cells recognize and kill human glioblastoma cells with stem cell-like properties. J Immunol 2009. 182: 3530-3539.
3. Frulloni, L., Lunardi, C., Simone, R., Dolcino, M., Scattolini, C., Falconi, M., Benini, L., Vantini, I., Corrocher, R. and Puccetti, A., Identification of a novel antibody associated with autoimmune pancreatitis. N Engl J Med 2009. 361: 2135-2142.
4. Pende, D., Marcenaro, S., Falco, M., Martini, S., Bernardo, M. E., Montagna, D., Romeo, E., Cognet, C., Martinetti, M., Maccario, R., Mingari, M. C., Vivier, E., Moretta, L., Locatelli, F. and Moretta, A., Anti-leukemia activity of alloreactive NK cells in KIR ligand-mismatched haploidentical HSCT for pediatric patients: evaluation of the functional role of activating KIR and redefinition of inhibitory KIR specificity. Blood 2009. 113: 3119-3129.
5. Bellora, F., Castriconi, R., Dondero, A., Reggiardo, G., Moretta, L., Mantovani, A., Moretta, A. and Bottino, C., The interaction of human natural killer cells with either unpolarized or polarized macrophages results in different functional outcomes. Proc Natl Acad Sci U S A 2010. 107: 21659-21664.
6. Falco, M., Romeo, E., Marcenaro, S., Martini, S., Vitale, M., Bottino, C., Mingari, M. C., Moretta, L., Moretta, A. and Pende, D., Combined genotypic and phenotypic killer cell Ig-like receptor analyses reveal KIR2DL3 alleles displaying unexpected monoclonal antibody reactivity: identification of the amino acid residues critical for staining. J Immunol 2010. 185: 433-441.
7. De Maria, A., Bozzano, F., Cantoni, C. and Moretta, L., Revisiting human natural killer cell subset function revealed cytolytic CD56(dim)CD16+ NK cells as rapid producers of abundant IFN-gamma on activation. Proc Natl Acad Sci U S A 2011. 108: 728-732.
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LABORATORY OF ONCOLOGY

DIRECTOR: Vito Pistoia

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MAIN RESEARCH ACTIVITIES YEAR 2011

In the last year, research activity has been focused on the following, i) studies on the mechanisms involved in cell-to cell interactions in the tumor microenvironment. It has been demonstrated that soluble HLA-G, often released by neoplastic cells, downregulates the expression of some chemokine receptors and of the cytotoxicity activating heterodimer CD94-NKG2A on the surface of CD56bright and CD56dim NK cells. In addition, it has been shown that the chemokine CX_3CL1 and its receptor CX_3CR1 participate in the complex interactions between stroma and tumor cells in proliferation centers from B chronic lymphocytic leukemia patients; ii) development of novel therapeutic approaches for neuroblastoma. Liposomal nanoparticles carrying anti-GD2 antibody on the outer surface and small interfering RNA (siRNA) anti-ALK inside have been generated. ALK is an important oncogene in neuroblastoma and these nanoparticles have shown potent anti-tumor activity in vitro and in vivo. Such results provide the foundation for a new highly selective therapeutic strategy; iii) studies on vascular mimicry in human neuroblastoma. It has been shown that a small subset of tumor cells expressing tenascin C on the cell surface is enriched for progenitors capable of trans-differentiating into endothelial cells.

RESEARCH PROGRAMME YEAR 2012

The research lines discussed above will continue in 2012. As far as studies on tumor microenvironment are concerned, the role of fasting in reinstating as efficient anti-tumor immune response will be investigated. These experiments, that will be carried out using in vitro and in vivo models, will make it possible to expand knowledge of the mechanisms whereby fasting performed shortly before and after chemotherapy administration sensitizes malignant cells and protects normal cells, thus increasing the therapeutic index of anti-cancer drugs. The role of the cytokines IL-25 and IL-31 in the control of the growth of B cell lymphomas originating from the germinal center will be investigated. The studies on liposomal nanoparticles carrying the ALK gene will be further developed by combining siRNA mediated ALK silencing with replenishment of microRNA which act physiologically as tumor suppressors and whose expression is downregulated in human neuroblastoma. Finally, studies on vascular mimicry will be directed to understand whether depletion of endothelial cells of tumor origin by monoclonal antibody treatment results in decreased growth of human neuroblastoma in immunodeficient mice.

MAJOR COLLABORATIONS

- Prof. Fabio Malavasi, University of Turin
- Prof. Roberto Chiarle, University of Turin
- Dr. Angelo Corti, S. Raffaele Institute, Milan
- Prof. Antonio Uccelli, University of Genova
- Prof. Paolo Bianco, University of Rome
- Prof. Maria Cristina Mingari, University of Genova
- Prof. Francesco Di Virgilio, University of Ferrara
- Prof. Soldano Ferrone, Pittsburgh Cancer Center, USA
- Prof. Arturo Sala, Brunel University, London, UK
- Prof. Vincenzo Bronte, University of Verona
- Prof. Gianpietro Semenzato, University of Padova
- Prof. Holger Lode, University of Greisswald, Germany
- Prof. Claudio Tripodo, University of Palermo
- Prof. Nicola Giuliani, University of Parma
- Prof. Emma Di Carlo, University of Chieti

BEST SCIENTIFIC PUBLICATIONS (2006-2011)

1. Morandi F, Ferretti E, Castriconi R, Dondero A, Petretto A, Bottino C, Pistoia V. Soluble HLA-G dampens CD94/NKG2A expression and function and differentially modulates chemotaxis and cytokine and chemokine secretion in CD56bright and CD56dim NK cells.Blood. 2011 Nov 24;118(22):5840-50.
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5. Pistoia V, Cocco C, Airoldi I. Interleukin-12 receptor beta2: from cytokine receptor to gatekeeper gene in human B-cell malignancies. J Clin Oncol. 2009 Oct 1;27(28):4809-16. Epub 2009 Aug 31.
6. Uccelli A, Moretta L, Pistoia V. Mesenchymal stem cells in health and disease. Nat Rev Immunol. 2008 Sep;8(9):726-36.
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8. Pezzolo A, Parodi F, Corrias MV, Cinti R, Gambini C, Pistoia V.Tumor origin of endothelial cells in human neuroblastoma. J Clin Oncol. 2007 Feb 1;25(4):376-83.
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MOLECULAR GENETICS

DIRECTOR: Roberto Ravazzolo
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MAIN RESEARCH ACTIVITIES YEAR 2011

The Molecular Genetics and Cytogenetics Unit has mainly carried out research on rare genetic diseases through the following strategies:

- identification of genes responsible for monogenic inherited disorders;
- setting up of diagnostic methods for monogenic inherited disorders;
- setting up of innovative diagnostic tools by Next Generation Sequencing Technology;
- studies on pathogenic mechanisms of monogenic inherited disorders;
- studies on functional genomics approaches to identify inter-relationships among disease genes;
- studies on innovative therapeutic approaches for rare genetic diseases;
- studies on cytogenetic anomalies responsible for rare genetic diseases;
- studies of genomic imbalances by Comparative Genomic Hybridization.

Results have been recently obtained in the following fields: Cystic Fibrosis, Congenital Central Hypoventilation Syndrome; Hirschsprung Disease; Alexander Disease; Fibrodysplasia Ossificans Progressiva; Intestinal innervation defects; congenital anomalies of the kidney and urinary tract (CAKUT); Recurrent Fevers with genetic cause; Limb Congenital anomalies; Poland Syndrome; Animal model of Cerebellar Ataxia; Nail Patella Syndrome

RESEARCH PROGRAM YEAR 2012

The Molecular Genetics and Cytogenetics Unit will continue its studies on rare genetic diseases and will focus in particular on the following issues:

A. Application of new technologies. The new available Next Generation Sequencing technologies will be utilized to search for molecular variants associated with rare genetic diseases in panels of genes for those disorders characterized by genetic heterogeneity. In addition, exome sequencing will be utilized to find genes responsible for rare conditions for which no causative gene has been identified yet. Resequencing of entire genomic regions will be performed to identify variants that, being located in regulatory regions, might be responsible for variable gene expression.

B. Innovative therapeutic approaches for genetic diseases. We will continue and extend the application of High Throughput Screening (HTS) of small chemical compounds in cell-based assays. For Cystic Fibrosis, for which significant results have already been obtained, a screening of siRNAs will be carried out to verify whether downregulation of specific genes can improve the processing and transport of the mutated CFTR to cell membrane. For Fibrodysplasia Ossificans Progressiva and Alexander Disease, for which the aim is to reduce expression of the respective mutated proteins (ALK2 and GFAP), HTS will be performed by targeting the gene promoters.

MAJOR COLLABORATIONS

- Fred Kaplan and Eileen Shore, The University of Pennsylvania, School of Medicine: Pathogenic mechanisms of Fibrodysplasia Ossificans Progressiva.
- Petra Seemann, Max Planck Institute for molecular genetics and Charite, CVK, Berlin: Mechanisms of BMP signaling in embryonic development and disease.
- Maria Pia Rastaldi, IRCCS Ospedale Maggiore Policlinico, Fondazione D'Amico per la Ricerca sulle Malattie Renali, Milano: Studies on the role of the mGlu1 receptor in the renal function.
- Giambattista Bonanno, Department of Experimental Medicine, University of Genova: Role of mGlu1 and mGlu5 receptors in neurodegeneration and mechanisms of excitotoxicity.
- International Consortium on Hirschsprung Disease: since 2004, among groups in Baltimore, Paris, Groningen, Hong Kong, Seville and Genova (our lab)
- 2nd Pediatric Division and Lab Immunology & Rheumatic Diseases, IGG: Genetic aspects and molecular diagnosis of autoinflammatory diseases
- Pascale Fanen, INSERM 955 (equipe 11) - Université Paris-Est: Study of mechanisms of action of mutations causing Cystic Fibrosis.
- Carlos Flores, Centro de Estudios Cientificos (CECS), Valdivia, Chile: Expression and function of the TMEM16A protein.

MAIN PUBLICATIONS YEARS 2009-2011

1. Bachetti T, Parodi S, Di Duca M, Santamaria G, Ravazzolo R, Ceccherini I: Low amounts of PHOX2B expanded alleles in asymptomatic parents suggest unsuspected recurrence risk in congenital central hypoventilation syndrome. J Mol Med 2011 May;89(5):505-13.
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4. Puliti A, Rossi PI, Caridi G, Corbelli A, Ikehata M, Armelloni S, Li M, Zennaro C, Conti V, Vaccari CM, Cassanello M, Calevo MG, Emionite L, Ravazzolo R, Rastaldi MP: Albuminuria and glomerular damage in mice lacking the metabotropic glutamate receptor 1. Am J Pathol 2011 Mar;178(3):1257-69.
5. Jacquemont S, Reymond A, Zufferey F, et al. Gimelli G, et al. Ravazzolo R, et al. Stefansson K, Blakemore AI, Beckmann JS, Froguel P.: Mirror extreme BMI phenotypes associated with gene dosage at the chromosome 16p11.2 locus. Nature. 2011 Aug 31;478(7367):97-102.
6. Cuoco C, Ronchetto P, Gimelli S, Béna F, Divizia MT, Lerone M, Mirabelli-Badenier M, Mascaretti M, Gimelli G.: Microarray based analysis of an inherited terminal 3p26.3 deletion, containing only the CHL1 gene, from a normal father to his two affected children. Orphanet J Rare Dis. 2011 Apr 1;6:12.
7. Weese-Mayer DE, Berry-Kravis EM, Ceccherini I, Keens TG, Loghmanee DA, Trang H; ATS Congenital Central Hypoventilation Syndrome Subcommittee: An official ATS clinical policy statement: Congenital central hypoventilation syndrome: genetic basis, diagnosis, and management. Am J Respir Crit Care Med. 2010 Mar 15;181(6):626-44.
8. Emison ES, Garcia-Barcelo M, Grice EA, Lantieri F, Amiel J, Burzynski G, Fernandez RM, Hao L, Kashuk C, West K, Miao X, Tam PK, Griseri P, Ceccherini I, Pelet A, Jannot AS, de Pontual L, Henrion-Caude A, Lyonnet S, Verheij JB, Hofstra RM, Antiñolo G, Borrego S, McCallion AS, Chakravarti A.: Differential contributions of rare and common, coding and noncoding ret mutations to multifactorial Hirschsprung disease liability. Am J Hum Genet
9. Ferrera L, Caputo A, Ubby I, Bussani E, Zegarra-Moran O, Ravazzolo R, Pagani F, Galietta LJ.: Regulation of TMEM16A chloride channel properties by alternative splicing. J Biol Chem. 2009 Nov 27;284(48):33360-8. I.F. 5.520Verkman AS, Galietta LJ. Chloride channels as drug targets. Nat Rev Drug Discov. 2009 F

LABORATORY OF CYTOGENETICS

Associated with the Laboratory of Genetics

PERSON IN CHARGE: Giorgio Gimelli

MAIN RESEARCH ACTIVITIES YEAR 2011

The Cytogenetics laboratory has recently introduced, among its diagnostic activities, the technique of analysis by array-CGH. This method not only proved to be more successful in the diagnosis of genetic diseases compared to traditional cytogenetic techniques, but also allowed us to study many rare anomalies and therefore diseases and pathogenic mechanisms unknown so far.

RESEARCH PROGRAM YEAR 2012

The research activity will focus on the study of other genetic diseases and of the possible genes involved. Research on the NPPC gene responsible for bone growth that causes a Marfan-like phenotype when overexpressed and short stature when mutated or deleted is ongoing. We are investigating other interesting cases of anomalies caused by microdeletions or microduplications.

MAIN PUBLICATIONS YEARS 2009-2011

1. Griseri P, Vos Y, Giorda R, Gimelli S, Beri S, Santamaria G, Mognato G, Hofstra RM, Gimelli G, Ceccherini I. Complex pathogenesis of Hirschsprung's disease in a patient with hydrocephalus, vesico-ureteral reflux and a balanced translocation t(3;17)(p12;q11). EUR J HUM GENET. 2009 Apr;17(4):483-90.
2. Coppola A, Striano P, Gimelli S, Ciampa C, Santulli L, Caranci F, Zuffardi O, Gimelli G, Striano S, Zara F A de novo 11p12-p15.4 duplication in a patient with pharmacoresistant epilepsy, mental retardation, and dysmorphisms. BRAIN DEV. 2010 Mar;32(3):248-52.
3. Gimelli S, Beri S, Drabkin HA, Gambini C, Gregorio A, Fiorio P, Zuffardi O, Gemmill RM, Giorda R, Gimelli G. The tumor suppressor gene TRC8/RNF139 is disrupted by a constitutional balanced translocation t(8;22)(q24.13;q11.21) in a young girl with dysgerminoma. MOL CANCER. 2009 Jul 30;8:52.
4. Puliti A, Rizzato C, Conti V, Bedini A, Gimelli G, Barale R, Sbrana I. Low copy repeats on chromosome 22q11.2 show replication timing switches, DNA flexibility peaks and stress inducible asynchrony, sharing instability features with fragile sites. MUTAT RES. 2010 Apr 1;686(1-2):74-83.
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7. Gimelli S, Caridi G, Beri S, McCracken K, Bocciardi R, Zordan P, Dagnino M, Fiorio P, Murer L, Benetti E, Zuffardi O, Giorda R, Wells JM, Gimelli G, Ghiggeri GM. Mutations in SOX17 are associated with congenital anomalies of the kidney and the urinary tract. HUM MUTAT. 31:1352–1359, 2010
8. Cuoco C, Ronchetto P, Gimelli S, Béna F, Divizia MT, Lerone M, Mirabelli-Badenier M, Mascaretti M, Gimelli G. Microarray based analysis of an inherited terminal 3p26.3 deletion, containing only the CHL1 gene, from a normal father to his two affected children. ORPHANET J RARE DIS. 2011 Apr 1;6:12.
9. De Greef JC, Wang J, Balog J, den Dunnen JT, Frants RR, Straasheijm KR, Aytekin C, van der Burg M, Duprez L, Ferster A, Gennery AR, Gimelli G, Reisli I, Schuetz C, Schulz A, Smeets DF, Sznajer Y, Wijmenga C, van Eggermond MC, van Ostaijen-Ten Dam MM,

Lankester AC, van Tol MJ, van den Elsen PJ, Weemaes CM, van der Maarel SM. Mutations in ZBTB24 Are Associated with Immunodeficiency, Centromeric Instability, and Facial Anomalies Syndrome Type 2. AM J HUM GENET. 88,(6), 10 June 2011, 796-804

10. Jacquemont S, Reymond A, Zufferey F, Harewood L, Walters RG, Kutalik Z, Martinet D, Shen Y, Valsesia A, Beckmann ND, Thorleifsson G, Belfiore M, Bouquillon S, Campion D, de Leeuw N, de Vries BB, Esko T, Fernandez BA, Fernández-Aranda F, Fernández-Real JM, Gratacòs M, Guilmatre A, Hoyer J, Jarvelin MR, Kooy RF, Kurg A, Le Caignec C, Männik K, Platt OS, Sanlaville D, Van Haelst MM, Villatoro Gomez S, Walha F, Wu BL, Yu Y, Aboura A, Addor MC, Alembik Y, Antonarakis SE, Arveiler B, Barth M, Bednarek N, Béna F, Bergmann S, Beri M, Bernardini L, Blaumeiser B, Bonneau D, Bottani A, Boute O, Brunner HG, Cailley D, Callier P, Chiesa J, Chrast J, Coin L, Coutton C, Cuisset JM, Cuvellier JC, David A, de Freminville B, Delobel B, Delrue MA, Demeer B, Descamps D, Didelot G, Dieterich K, Disciglio V, Doco-Fenzy M, Drunat S, Duban-Bedu B, Dubourg C, El-Sayed Moustafa JS, Elliott P, Faas BH, Faivre L, Faudet A, Fellmann F, Ferrarini A, Fisher R, Flori E, Forer L, Gaillard D, Gerard M, Gieger C, Gimelli S, Gimelli G, Grabe HJ, Guichet A, Guillin O, Hartikainen AL, Heron D, Hippolyte L, Holder M, Homuth G, Isidor B, Jaillard S, Jaros Z, Jiménez-Murcia S, Helas GJ, Jonveaux P, Kaksonen S, Keren B, Kloss-Brandstätter A, Knoers NV, Koolen DA, Kroisel PM, Kronenberg F, Labalme A, Landais E, Lapi E, Layet V, Legallic S, Leheup B, Leube B, Lewis S, Lucas J, MacDermot KD, Magnusson P, Marshall C, Mathieu-Dramard M, McCarthy MI, Meitinger T, Mencarelli MA, Merla G, Moerman A, Mooser V, Morice-Picard F, Mucciolo M, Nauck M, Ndiaye NC, Nordgren A, Pasquier L, Petit F, Pfundt R, Plessis G, Rajcan-Separovic E, Ramelli GP, Rauch A, Ravazzolo R, Reis A, Renieri A, Richart C, Ried JS, Rieubland C, Roberts W, Roetzer KM, Rooryck C, Rossi M, Saemundsen E, Satre V, Schurmann C, Sigurdsson E, Stavropoulos DJ, Stefansson H, Tengström C, Thorsteinsdóttir U, Tinahones FJ, Touraine R, Vallée L, van Binsbergen E, Van der Aa N, Vincent-Delorme C, Visvikis-Siest S, Vollenweider P, Völzke H, Vulto-van Silfhout AT, Waeber G, Wallgren-Pettersson C, Witwicki RM, Zwolinksi S, Andrieux J, Estivill X, Gusella JF, Gustafsson O, Metspalu A, Scherer SW, Stefansson K, Blakemore AI, Beckmann JS, Froguel P. Mirror extreme BMI phenotypes associated with gene dosage at the chromosome 16p11.2 locus. NATURE. 2011 Aug 31;478(7367):97-102.

LABORATORY OF CLINICAL CHEMICAL ANALYSIS AND MICROBIOLOGY

DIRECTOR: Giovanni Melioli

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MAIN RESEARCH ACTIVITIES YEAR 2011

- Molecular Allergy
- Hospital infections and bacterial resi stance
- Cell therapy and Clean Room
- Immunotherapy of patients with respiratory tract infections

RESEARCH PROGRAM YEAR 2012

- Use of Next Generation Sequencing in typing of bacteria responsible of hospital infection
- Molecular allergy and its impact on diagnosis and therapy
- Cell manipulation for the generation of virus-specific effectors in immunocompromised patients.

MAJOR COLLABORATIONS

- Università di Genova, prof. Canonica
- Università di Genova, prof. Debbia

BEST SCIENTIFIC PUBLICATIONS (2006-2011)

1. Ratto GB, Costa R, Maineri P, Alloisio A, Piras MT, D'Agostino A, Tripodi G, Rivabella L, Dozin B, Bruzzi P, Melioli G. Neo-adjuvant chemo/immunotherapy in the treatment of stage III (N2) non-small cell lung cancer: a phase I/II pilot study. Int J Immunopathol Pharmacol. 2011 Oct-Dec;24(4):1005-16.
2. Melioli G, Marcomini L, Agazzi A, Bazurro G, Tosca M, Rossi GA, Minale P, Rossi R, Reggiardo G, Canonica GW, Passalacqua G. The IgE repertoire in children and adolescents resolved at component level: A cross-sectional study. Pediatr Allergy Immunol. 2011 Nov 22.
3. Cangemi G, Barco S, Barbagallo L, Di Rocco M, Paci S, Giovannini M, Biasucci G, Lia R, Melioli G. Erythrocyte Galactose-1-phosphate measurement by GC-MS in the monitoring of classical galactosemia. Scand J Clin Lab Invest. 2012 Feb;72(1):29-33.

4. Melioli G, Bonifazi F, Bonini S, Maggi E, Mussap M, Passalacqua G, Rossi ER, Vacca A, Canonica GW; Italian Board for ISAC (IBI). The ImmunoCAP ISAC molecular allergology approach in adult multi-sensitized Italian patients with respiratory symptoms. Clin Biochem. 2011 Aug;44(12):1005-11. Epub 2011 May 19.
5. Melioli G, Risso FM, Sannia A, Serra G, Bologna R, Mussap M, Mangraviti S, Fortini P, Facco F, Reggiardo G, Buonocore G, Corsello G, Fanos V, Del Vecchio A, Fabris C, Gazzolo D. Reference values of blood cell counts in the first days of life. Front Biosci (Elite Ed). 2011 Jun 1;3:871-8.
6. Morandi B, Agazzi A, D'Agostino A, Antonini F, Costa G, Sabatini F, Ferlazzo G, Melioli G. A mixture of bacterial mechanical lysates is more efficient than single strain lysate and of bacterial-derived soluble products for the induction of an activating phenotype in human dendritic cells. Immunol Lett. 2011 Jul;138(1):86-91.
7. Ugolotti E, Bandettini R, Marchese A, Gualco L, Vanni I, Borzi L, Di Marco E, Castagnola E, Melioli G, Biassoni R. Molecular characterization of hospital-acquired methicillin-resistant Staphylococcus aureus strains in pediatric outbreaks using variable tandem repeat analysis with spa and ClfB typing. Diagn Microbiol Infect Dis. 2011 Feb;69(2):213-7.
8. Castagnola E, Furfaro E, Caviglia I, Licciardello M, Faraci M, Fioredda F, Tomà P, Bandettini R, Machetti M, Viscoli C. Performance of the galactomannan antigen detection test in the diagnosis of invasive aspergillosis in children with cancer or undergoing haemopoietic stem cell transplantation. Clin Microbiol Infect. 2010 Aug;16(8):1197-203.
9. Haupt R, Garaventa A, Gambini C, Parodi S, Cangemi G, Casale F, Viscardi E, Bianchi M, Prete A, Jenkner A, Luksch R, Di Cataldo A, Favre C, D'Angelo P, Zanazzo GA, Arcamone G, Izzi GC, Gigliotti AR, Pastore G, De Bernardi B. Improved survival of children with neuroblastoma between 1979 and 2005: a report of the Italian Neuroblastoma Registry.J Clin Oncol. 2010 May 10;28(14):2331-8.

LABORATORY OF MOLECULAR BIOLOGY

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Daniela Segalerba
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MAIN RESEARCH ACTIVITIES YEAR 2011

- Gene therapy of glycogen storage disease 1a using hematopoietic stem cells
- Discovery of Trem-1 as marker of hypoxic dendritic cells
- Identification of hypoxic dendritic cells in the inflammatory synovial fluid of patients with juvenile idiopathic arthritis
- Set up of a classifier able to predict the survival of patients with neuroblastoma based on the extent of tumor hypoxia

RESEARCH PROGRAM YEAR 2012

- Analysis of different sources of stem cells, including spermatogons, to repopulate liver and kydney of glycogen storage disease 1a patients
- Analysis of the effects of hypoxia in the differentiation of skin dendritic cells (Langerhans) and identification of surface biomarkers characteristic of the hypoxic subpopulation
- Identification of algorithms for the study of gene espression in primary neuroblastoma tumors and able to identify rules immediately applicable to patient therapy

MAJOR COLLABORATIONS

- Prof. Giovanni Melillo (NCI, Frederick, USA)
- Prof. Alessandro Verri (DISI, University of Genova)
- Dr. Rogier Veersteg (AMC, University of Amsterdam)
- Dr. Janice Chou (NIH, NICHD HDB, Bethesda, USA)
- Prof. Bruce Zwilling (Dept. of Microbiology, Ohio State University, Columbus, USA)
- Prof. G. Forni (Dept. Chemical and Biological Sciences, University of Torino)
- Dr. Yi Zheng (Dept. of Biochemistry, University of Tennessee, Memphis, USA)
- Dr.ssa Fiorella Altruda (Dept. Genetics, Biology and Medical Chemistry, Torino)
- Prof.ssa Maria Cristina Mingari (Dept. Oncology, Biology, and Genetics, University of Genova)
- Dr. Maurizio Luisetti (Inst. Tisiology and Respiratory Diseases, S.Matteo Hospital, University of Pavia)
- Dr. Giuseppe Lungarella (University of Siena)
- Dr. Bruno Bembi (Metabolic Disease Unit, Burlo Garofolo Institute, Trieste
- Dr. David Munroe (SAIC A Division of Science Applications International Corporation, Frederick, USA)

MAIN PUBLICATIONS YEARS 2009-2011

1. Fardin, P., Barla, A., Mosci, S., Rosasco, L., Verri, A., and Varesio, L. (2009). The l1-l2 regularization framework unmasks the hypoxia signature hidden in the transcriptome of a set of heterogeneous neuroblastoma cell lines. BMC Genomics 10, 474.
2. Cavarra, E., Fardin, P., Fineschi, S., Ricciardi, A., De Cunto, G., Sallustio, F., Zorzetto, M., Luisetti, M., Pfeffer, U., Lungarella, G., and Varesio, L. (2009). Early response of gene clusters is associated with mouse lung resistance or sensitivity to cigarette smoke. Am J Physiol Lung Cell Mol Physiol 296, L418-L429.
3. Varesio, L., Battaglia, F., Raggi, F., Ledda, B., and Bosco, M. C. (2010). Macrophage-inflammatory protein-3alpha/CCL-20 is transcriptionally induced by the iron chelator desferrioxamine in human mononuclear phagocytes through nuclear factor (NF)-kappaB. Mol Immunol 47 , 685-693.
4. Fardin, P., Barla, A., Mosci, S., Rosasco, L., Verri, A., Versteeg, R., Caron, H. N., Molenaar, J. J., Ora, I., Eva, A., Puppo, M., and Varesio, L. (2010). A biology-driven approach identifies the hypoxia gene signature as a predictor of the outcome of neuroblastoma patients. Mol Cancer 9, 185.
5. Fardin, P., Cornero, A., Barla, A., Mosci, S., Acquaviva, M., Rosasco, L., Gambini, C., Verri, A., and Varesio, L. (2010). Identification of multiple hypoxia signatures in neuroblastoma cell lines by l1-l2 regularization and data reduction. J Biomed.Biotechnol. 2010, 878709.
6. Bosco, M. C., Pierobon, D., Blengio, F., Raggi, F., Vanni, C., Gattorno, M., Eva, A., Novelli, F., Cappello, P., Giovarelli, M., and Varesio, L. (2011). Hypoxia modulates the gene expression profile of immunoregulatory receptors in human mature dendritic cells: identification of TREM-1 as a novel hypoxic marker in vitro and in vivo. Blood 117, 2625-2639.
7. Sica, A., Melillo, G., and Varesio, L. (2011). Hypoxia: a double-edged sword of immunity. J Mol Med 89, 657-665.
8. Ognibene, M., Barbieri, O., Vanni, C., Mastracci, L., Astigiano, S., Emionite, L., Salani, B., Fedele, M., Resaz, R., Tenca, C., Fais, F., Sabatini, F., De Santanna, A., Altruda, F., Varesio, L., Hirsch, E., and Eva, A. (2011). High frequency of development of B cell lymphoproliferation and diffuse large B cell lymphoma in Dbl knock-in mice. J Mol Med 89, 493-504.
9. Resaz, R., Emionite, L., Vanni, C., Astigiano, S., Puppo, M., Lavieri, R., Segalerba, D., Pezzolo, A., Bosco, M. C., Oberto, A., Eva, C., Chou, J. Y., Varesio, L., Barbieri, O., and Eva, A. (2011). Treatment of newborn G6pc(-/-) mice with bone marrow-derived myelomonocytes induces liver repair. J Hepatol. 55, 1263-1271.
10. Ognibene, M., Vanni, C., Segalerba, D., Mancini, P., Merello, E., Torrisi, M. R., Bosco, M. C., Varesio, L., and Eva, A. (2011). The tumor suppressor hamartin enhances Dbl transforming activity through interaction with ezrin. J Biol Chem. 89, 493-504.

START UP AIRC (ASSOCIAZIONE ITALIANA PER LA RICERCA SUL CANCRO) IMMUNOLOGY AND TUMORS

COORDINATOR: Irma Airoldi

STAFF
Irma Airoldi
Claudia Cocco

MAIN RESEARCH ACTIVITIES YEAR 2011

The research activity was focused on the investigation of the role of cytokines as anti-tumor agents against acute pediatric leukemias of myeloid and lymphoid origin. We have developed pre-clinical models using immuno-deficient animals in which human leukemia cells isolated from patients efficiently engrafted and spread, thus recapitulating the clinical course of patient disease. Such models made it possible to demonstrate that IL-23 and IL-27 strongly inhibited leukemia cell growth *in vivo* through different and complementary mechanisms, including their direct activity on neoplastic blasts, on leukemia initiating cells, and on tumor microenvironment. We documented that IL-27 reduced the angiogenic potential of leukemia cells, thus compromising the formation of efficient vascular network that supports leukemia cell growth and spreading. IL-27 also acted on osteoblast and osteoclast compartments that play a crucial role in bone homeostasis. In this context, we highlighted the ability of this cytokine to induce osteoblast proliferation and to inhibit osteoclast activity, thus reducing bone resorption and tumor metastasis. Taken together, our studies supported the concept that especially IL-27 may represent a novel drug for treatment of leukemic patients unresponsive to current therapeutic standards and encouraged the development of future clinical trials to evaluate the toxicity and efficacy of IL-27 in childhood leukemia patients.

RESEARCH PROGRAM YEAR 2012

Taken together, the results obtained in the last years provide a strong background supporting the concept that IL-27 may represent a good candidate to be tested in future clinical trials and to be translated in the post-transplant management of pediatric leukemic patients. Before that, the *in vivo* role of IL-27 in the human immune system reconstituted by hematopoietic stem cells (HSC) obtained from donors needs to be addressed. Thus, we plan to develop a novel pre-clinical model to investigate the *in vivo* role of IL-27 in terms of i) HSC differentiation and proliferation, ii) anti-leukemic activity in the presence of immune cells, and iii) modulation of leukemic microenvironment. The final aim of this proposal is to provide the proof of concept that IL-27 represents an efficacious agent to eradicate leukemia growth or recurrence in transplanted patients. Furthermore, we plan to design a phase I/II clinical trial aimed at testing the safety and efficacy of IL-27 in humans.

MAJOR COLLABORATIONS

- Prof. Franco Locatelli, Director Department of Pediatric Hematology/Oncology, IRCCS Bambino Gesù Children Hospital, Rome, Italy
- Prof. Giorgio Trinchieri, Director, Cancer and Inflammation Program, Chief Laboratory of Experimental Immunology, Center for Cancer Research, NCI, NIH
- Prof. Domenico Ribatti, University of Bari , Italy
- Prof. Emma Di Carlo, Department of Oncology and Experimental Medicine, University of Chieti, Italy
- Prof. Christian Munz, Viral Immunobiology, Institute of Experimental Immunology, University of Zürich, Switzerland
- Prof. Nicola Giuliani, Hematology and Blood and Marrow Transplantation (BMT) Center, University of Parma, Italy

- Prof. Giuseppe Basso, Department of Pediatrics, Laboratory of Hematology-Oncology. Università di Padova
- Dr.ssa Emanuela Ognio, Animal Facility, San Martino – IST hospital, Genova

MAIN PUBLICATIONS YEARS 2009-2011

1. C. Cocco, E. Di Carlo, S. Zupo, S. Canale, A. Zorzoli, D. Ribatti, F. Morandi, E. Ognio e I. Airoldi. Complementary IL-23 and IL-27 anti-tumor activities cause strong inhibition of human follicular and diffuse large B cell lymphoma growth in vivo. Leukemia 2011 Dec 23. doi: 10.1038/leu.2011.363
2. N. Giuliani and I. Airoldi. Novel insights into the role of IL-27 and IL-23 in human malignant and normal plasma cells. Clinical Cancer Res 2011, doi:10.1158/1078-0432
3. E. Ferretti, D. Montagna, E. Di Carlo, C. Cocco, D. Ribatti, E. Ognio, C. Sorrentino, D. Lisini, A. Bertaina, F. Locatelli, V.Pistoia and I. Airoldi. Absence of IL-12Rβ2 in $CD33^{+}CD38^{+}$ pediatric acute myeloid leukemia cells favours progression in NOD/SCID/IL2RγC-deficient mice. Leukemia 2011, doi:10.1038/leu.2011.213
4. C. Cocco and Irma Airoldi. Cytokines and microRNA in pediatric B-acute lymphoblastic leukemia. Cytokine and growth factor reviews 2011, 22:149-156.
5. S. Canale, C. Cocco, C. Frasson, E. Ognio, E. Seganfreddo, D. Ribatti, A. Zorzoli, G. Basso, C. Dufour and I. Airoldi. Interleukin-27 inhibits pediatric B-acute lymphoblastic leukemia cell spreading in a pre-clinical model. Leukemia 2011 Jun 24. doi: 10.1038/leu.2011.158.
6. C. Cocco, F. Morandi and I. Airoldi. IL-27 and IL-23 modulate human plasmacell functions. Journal of Leukocyte Biology 2011, 89:729-734.
7. C. Cocco, S. Canale, C. Frasson, E. Di Carlo, E. Ognio, D. Ribatti, I. Prigione, G. Basso and I. Airoldi. Interleukin (IL)-23 acts as anti-tumor agent on childhood B-acute lymphoblastic leukemia cells. Blood 2010,116: 3887-3898.
8. C. Cocco, N. Giuliani, E. Di Carlo, E. Ognio, P. Storti, M. Abeltino, C. Sorrentino, M. Ponzoni, D. Ribatti and I. Airoldi. IL-27 acts as multifunctional anti-tumor agent in multiple myeloma. Clinical Cancer Research 2010; 16: 4188-4197.
9. I. Airoldi, E. Di Carlo and V. Pistoia. The enigmatic role of IL-12 in the pathogenesis of Sjögren's syndrome. Arthritis & Reumathism 2010; 62: 2180.
10. V. Pistoia, C. Cocco and I. Airoldi. IL-12RB2: from cytokine receptor to gatekeeper gene in human B cell malignancies. Journal of Clinical Oncology 2009; 27: 4808-4816.

PEDIATRICS
Prof. Renata Lorini (pro-tempore)

- **PEDIATRIC CLINIC (University)** — Renata Lorini
- **DERMATOLOGY** — Corrado Occella
- **NEPHROLOGY, DIALYSIS AND TRANSPLANTATION** — Gianmarco Ghiggeri
- **PEDIATRIC RHEUMATOLOGY (University)** — Alberto Martini
- **PEDIATRIC GASTROENTEROLOGY** — Arrigo Barabino
- **PNEUMOLOGY** — Giovanni A. Rossi

PEDIATRIC RHEUMATOLOGY

DIRECTOR: Alberto Martini
(University)

STAFF
Antonella Buoncompagni
Maja Di Rocco
Marco Gattorno
Clara Malattia
Paolo Picco
Angelo Ravelli
Nicolino Ruperto
Stefania Viola

MAIN RESEARCH ACTIVITIES YEAR 2011

The Rheumatology unit has been designated by EULAR (European League Against Rheumatisms), the European society of rheumatology, as Centre of Excellence in Rheumatology (years 2008-2013). The unit is the only EULAR centre of excellence in rheumatology in Italy and the unique Centre of Excellence in paediatric rheumatology in Europe. Moreover, the unit hosts PRINTO (Pediatic Rheumatology International Trial Organization), the widest network for the identification of new therapies in childhood rheumatic diseases. A full scientific research agenda is the mainstay of the Unit, encompassing several rheumatic disorders (Juvenile Idiopathic Arthritis, Systemic Lupus Erythematosus, Juvenile Dermatomyositis, Scleroderma, vasculitides etc.), as well as auto-inflammatory diseases (familial Mediterranean fever, Hyper-IgD syndrome, TRAPS, CINCA, etc.). The unit is also a referral center for metabolic diseases, mainly lysosomal disorders and carbohydrate metabolic deficiencies (glycogenosis, metabolic disorders of fructose and galactose) as well as other rare genetic disorders (genetic mental retardation, neuro-degenerative diseases, skeletal dysplasia).

RESEARCH PROGRAM YEAR 2012

- Controlled clinical trials with new drugs for rheumatic diseases
- Safety registries for biological agents in pediatric rheumatic diseases
- Assessment of disease activity, clinical damage, functional ability and health-related quality of life of children with rheumatic diseases
- Imaging (Ultrasound and MRI) studies in juvenile idiopathic arthritis
- Laboratory investigations in rheumatic and auto-inflammatory conditions
- Optimization and improvement of new therapeutic options in metabolic disorders

MAJOR COLLABORATIONS

- Children's Hospital, Cincinnati, Ohio, USA
- Children's Hospital, Utrecht, Netherlands
- Institute for Research in Biomedicine, Bellinzona, Switzerland
- National Institute of Arthritis and Muscoloskeletal and Skin Disease (NIH-Bethesda USA)
- Sanford-Burnham Medical Research Institute, La Jolla, California, USA
- More than 200 Centers in 50 different countries belonging to PRINTO

MAIN PUBLICATIONS YEARS 2009-2011

1. Vilca I, Garcia Munitis P, Pistorio A, Ravelli A, Buoncompagni A, Bica B, Campos L, Häfner R, Hofer M, Ozen S, Huemer C, Cheol Bae S, Sztajnbok F, Arguedas O, Foeldvari I, Huppertz HI, Gamir ML, Magnusson B, Dressler F, Uziel Y,. van Rossum MAJ, Hollingworth P, Cawkwell G, Martini A, Ruperto N. Predictors of poor response to methotrexate in polyarticular-course juvenile idiopathic arthritis. analysis of the printo methotrexate trial. Ann Rheum Dis 2010;69:1479-83.
2. Schena F, Gambini C, Gregorio A, Mosconi M, Reverberi D, Gattorno M, Casazza S, Uccelli A, Moretta L, Martini A, Traggiai E. IFN-gamma dependent inhibition of B cell activation by bone marrow derived mesenchymal stem cells in a murine model of systemic lupus erythematosus. Arthritis Rheum 2010;62:2776-86.
3. Ravelli A, Varnier GC, Oliveira S, Castell E, Arguedas O, Magnani A, Pistorio A, Ruperto N, Magni-Manzoni S, Galasso R, Lattanzi B, Dalprà S, Battagliese A, Verazza S, Allegra M, Martini A. Antinuclear antibody positive patients should be grouped as a separate category in the classification of juvenile idiopathic arthritis. Arthritis Rheum. 2011;63:267-75.
4. Malattia C, Damasio MB, Pistorio A, Ioseliani M, Vilca I, Valle M, Ruperto N, Viola S, Buoncompagni A, Magnano GM, Ravelli A, Tomà P, Martini A. Development and preliminary validation of a pediatric-targeted MRI scoring system for the assessment of disease activity and damage in juvenile idiopathic arthritis. Ann Rheum Dis 2011;70:440-6.
5. Pelagatti MA, Meini A, Caorsi R, Cattalini M, Federici S, Zulian F, Calcagno G, Tommasini A, Bossi G, Sormani MP, 7 Caroli F, Plebani A, Ceccherini I, Martini A, Gattorno M. Long-term follow up of children with the low penetrance R92Q mutation of TNFRSF1A gene. Arthritis Rheum 2011;63:1141-50.
6. Prakken B, Albani S, Martini A. Juvenile idiopathic arthritis.Lancet 2011;377:2138-49.
7. Hasija R, Pistorio A, Ravelli A, Demirkaya E,Khubchandani R, Guseinova D, Malattia C, Canhao H, Harel L, Foell D, Wouters C, De Cunto C, Huemer C, Kimura Y, Mangge H, Minetti C, Nordal EB, Philippet P, Garozzo R, Martini A, Ruperto N. Therapeutic approaches in the treatment of juvenile dermatomyositis in patients with recent-onset disease and in those experiencing disease flare: an international multicenter PRINTO study. Arthritis Rheum 2011;63:3142-52.
8. Ardissone V, Radaelli E, Zaratin P, Ardizzone M, Ladel C, Gattorno M, Martini A, Grassi F, Traggiai E. Pharmacological purinergic P2X antagonism in the treatment of experimental collagen-induced arthritis. Arthritis Rheum 2011;63:3323-32.

NEPHROLOGY, DIALYSIS AND TRANSPLANTATION

DIRECTOR: Gian Marco Ghiggeri

STAFF

Giancarlo Barbano
Roberta Bertelli
Cinzia Boaretto
Giovanni Candiano
Alberto Canepa
Gianluca Caridi
Alba Maria Carrea
Maria Ludovica Degl'Innocenti
Armando Di Donato
Marco Di Duca
Fabrizio Ginevri
Carla Lanteri
Alberto Magnasco
Giorgio Piaggio
Orietta Scarlini
Antonella Trivelli
Enrico Verrina

MAIN RESEARCH ACTIVITIES YEAR 2011

- Humoral mechanisms of proteinuric glomerulonephritis.
- Cellular mechanisms of renal damage of the podocyte.
- Mapping and identifications of new gene(s) responsible for hereditary nephropathies such as Focal Segmental Glomerulosclerosis (FSGS) , IgA Nephropathies (IgAN) and Congenital Anomalies Kidney Urinary Tract (CAKUT).
- Genetic of hyperuricemic cystic kidney diseases. Functional genomic studies on responsible genes and implications in other nephropathies.
- New methodologies for analysis of protein-protein interactions by proteomic approaches.
- Proteomics of seric and urinary components of renal diseases during dialysis.

RESEARCH PROGRAM YEAR 2012

- Humoral mechanisms of proteinuric glomerulonephritis. Research and characterization of circulating factor(s) with permeability activity during Focal Segmental Glomerulosclerosis.
- Cellular mechanisms of renal damage of the podocyte. Research and identification of new targets and activation of intracellular signalling.
- Autoimmunity mechanisms of Membranous Glomerulonephritis.
- Identification of new genes responsible of hereditary nephropathies taking advantage of Next Generation Sequencing Technologies (Exome Sequencing).

MAJOR COLLABORATIONS

Mapping of new loci and identification of new genes responsible of FSGS, IgAN and CAKUT:

- Lab. Genetics of Renal Disease, Columbia University, New York, USA
- Cattedra di Nefrologia, University of Brescia, Italy

Consortium on Genetic and Pathogenesis of Medullary Cystic Diseases .

- Dulbecco Telethon Institute, HSR Milano
- Human Molecular Genetics Unit, DIBIT- San Raffaele, Milano
- Cattedra di Nefrologia, University of Brescia, Italy

MAIN PUBLICATIONS YEARS 2009-2011

1. Caridi G, Gigante M, Ravani P, Trivelli A, Barbano G, Scolari F, Dagnino M, Murer L, Murtas C, Edefonti A, Allegri L, Amore A, Coppo R, Emma F, De Palo T, Penza R, Gesualdo L, Ghiggeri GM. Clinical Features Of Nephrotic Syndrome And Long Term Outcome Associated With Heterozygous NPHS1 And NPHS2 Mutations. Clin J Am Soc Nephrol 4(6):1065-1072, 2009
2. Prunotto M, Carnevali ML, Candiano G, Murtas C, Bruschi M, Corradini E, Trivelli A, Magnasco A, Petretto A, Santucci L, Mattei R, Gattiç R, Scolari F, Kador P, Allegri L, and Ghiggeri GM. Autoimmunity in Membranous Nephropathy Targets Aldose Reductase and SOD2. J Am Soc Nephrol 21(3): 507-519, 2010
3. Louie CM, Caridi G, Lopes VS, Brancati F, Kispert A, Lancaster MA, Schlossman AM, Otto EA, Leitges M, Gröne HJ, Lopez I, Gudiseva HV, O'Toole JF, Vallespin E, Ayyagari R, Ayuso C, Cremers FP, den Hollander AI, Koenekoop RK, Dallapiccola B, Ghiggeri GM, Hildebrandt F, Valente EM, Williams DS, Gleeson JG. AHI1 is required for photoreceptor outer segment development and is a modifier for retinal degeneration in nephronophthisis. Nat Genet 42(2):175-180, 2010
4. Prunotto M, Compagnone A, Bruschi M, Candiano G, Colombatto S, Bandino B, Petretto A, Moll S, Bochaton-Piallat ML, Gabbiani G, Dimuccio V, Parola M, Citti L, and Ghiggeri GM. Endocellular polyamine availability modulates epithelial to mesenchymal transition and unfolded protein response in MDCK cells. Lab Invest 90(6):929-939, 2010
5. Bertelli R, Trivelli A, Magnasco A, Cioni M, Bodria M, Carrea A, Montobbio G, Barbano G, Ghiggeri GM. Failure of regulation results in an amplified oxidation burst by neutrophils in children with primary nephrotic syndrome. Clin Exp Immunol 161(1):151-8, 2010
6. Gimelli S, Caridi G, Beri S, McCracken K, Bocciardi R, Zordan P, Dagnino M, Fiorio P, Murer L, Benetti E, Zuffardi O, Giorda R, Wells JM, Gimelli G, Ghiggeri GM. Mutations in SOX17 are associated with congenital anomalies of the kidney and the urinary tract. Hum Mutat 31(12):1352-1359, 2010
7. Ravani P, Magnasco A, Edefonti A, Murer L, Rossi R, Ghio L, Benetti E, Scozzola F, Pasini A, Dallera N, Sica F, Belingheri M, Scolari F, Ghiggeri GM. Short-Term Effects of Rituximab in Children with Steroid- and Calcineurin-Dependent Nephrotic Syndrome: A Randomized Controlled Trial. Clin J Am Soc Nephrol 6(6):1308-1815, 2010
8. Prunotto M, Ghiggeri GM, Candiano G, Lescuyer P, Hochstrasser D, Moll S. Urinary Proteomics and Drug Discovery in Chronic Kidney Disease: A New Perspective. J Proteom Res 10:126-132, 2010
9. Sanna-Cherchi S, Burgess KE, Nees SN, Caridi G, Weng PL, Dagnino M, Bodria M, Carrea A, Allegretta MA, Kim HR, Perry BJ, Gigante M, Clark LN, Kisselev S, Cusi D, Gesualdo L, Allegri L, Scolari F, D'Agati V, Shapiro LS, Pecoraro C, Palomero T, Ghiggeri GM, Gharavi AG. Exome sequencing identified MYO1E and NEIL1 as candidate genes for human autosomal recessive steroid-resistant nephrotic syndrome. Kidney Int 80(4):389-96, 2010
10. Gharavi AG, Kiryluk K, Choi M, Li Y, Hou P, Xie J, Sanna-Cherchi S, Men CJ, Julian BA, Wyatt RJ, Novak J, He JC, Wang H, Lv J, Zhu L, Wang W, Wang Z, Yasuno K, Gunel M, Mane S, Umlauf S, Tikhonova I, Beerman I, Savoldi S, Magistroni R, Ghiggeri GM, Bodria M, Lugani F, Ravani P, Ponticelli C, Allegri L, Boscutti G, Frasca G, Amore A, Peruzzi L, Coppo R, Izzi C, Viola BF, Prati E, Salvadori M, Mignani R, Gesualdo L, Bertinetto F, Mesiano P, Amoroso A, Scolari F, Chen N, Zhang H, Lifton RP. Genome-wide association study identifies susceptibility loci for IgA nephropathy. Nat Genet 13;43(4):321-327, 2011.

PNEUMOLOGY

DIRECTOR: Giovanni A. Rossi

STAFF
Donata Girosi
Roberta Olcese
Serena Panigada
Oliviero Sacco
Michela Silvestri
Mariangela Tosca

MAIN RESEARCH ACTIVITIES YEAR 2011

- Evaluation of the bronchopulmonary defense mechanisms and characterization of the immune response in patients with: a) chronic or recurrent respiratory infections and b) allergic sensitization and clinical manifestations in different organs.
- "In vitro" studies on the morphologic and functional characteristics of the structural cells of the respiratory system with replication in the test tube of the immunological mechanisms involved in allergic sensitization and inflammation.
- Evaluation at cellular and molecular level of the activity of drugs to be used in patients with acute or chronic respiratory disorders.
- Analysis of risk factors predisposing to or inducing allergic sensitization and respiratory disorders.
- Epidemiologic studies on viral and bacterial infections of the airways and on their short and long-term evolution with analysis of risk factors.
- Pharmacologic studies to evaluate the efficacy and safety of drugs to be used in pediatric patients with acute or chronic respiratory disorders.

RESEARCH PROGRAM YEAR 2012

"In vitro" Research

- Evaluation of the changes induced by harmful chemical (cigarette smoke), biochemical (cytokine) or mechanical (scraping) agents on fibroblast and ciliated bronchial epithelial cell structure and function. In detail, the aim will be to study the possible modifications of cell viability, "tight junctions" expression and organization, epithelial barrier integrity, and tissue repair processes, evaluating the intracellular mechanisms involved and the activity of molecules to be used in the treatment of respiratory disorders.

Clinical Research

- Epidemiological studies with analysis of individual and environmental risk factors predisposing to the development of respiratory disorders induced by allergic sensitization and/or infections.
- Evaluation of the efficacy of pharmacological and/or environmental prophylaxis interventions in reducing the development and/or the severity of wheezing disorders in preschool-aged children and of asthma exacerbations in school-aged children and adolescents.
- Guidelines for the diagnosis, treatment and follow-up of children with chronic respiratory disorders, acquired (asthma, chronic bronchitis, bronchiectasis) or genetically determined (primary ciliary dyskinesia, surfactant protein abnormalities).
- Clinical studies to evaluate the efficacy and safety of drugs to be used in the prevention of the clinical manifestations of allergic sensitization.

MAJOR COLLABORATIONS

- **Fabio LM. Ricciardolo.** Dpt of Clinical and Biological Sciences, University of Torino, San Luigi Hospital, Torino, Italy. Mechanisms of bradykinin-induced contraction in human fetal lung fibroblasts.
- **Andrew Bush.** Dpt of Paediatric Respirology, Royal Brompton Hospital, London, UK. Inflammation and asthma in children.
- **Andrew A. Colin.** Division of Pediatric Pulmonology, Miller School of Medicine, University of Miami, Miami, FL, USA. Mediated inflammation in obstructive airway diseases in children.
- **Giorgio Ciprandi.** Dpt of Internal Medicine, Azienda Ospedaliera Universitaria San Martino, University of Genova, Genova, Italy. Respiratory manifestations and comorbidities in allergic children.
- **Marcello Lanari.** Pediatrics and Neonatology Unit, Imola Hospital, Imola, Italy. Respiratory syncytial virus risk factors in children.
- **Franca Rusconi**. Unit of Epidemiology Anna Meyer Children's University Hospital, Firenze, Italy. Passive smoking exposure and respiratory disease in children.
- **Angelo Barbato**. Pediatric Dpt, General Hospital, University of Padova, Italy. Diagnosis, clinical phenotypes and prevalence of Primary Ciliary Dyskinesia (PCD) in Italian pediatric population.
- **Anna Marchese.** Associate Professor of Microbiology, Microbiology Unit, University of Genova, Italy. Prevalence of antibiotic resistance in Mycoplasma pnemoniae.

MAIN PUBLICATIONS YEARS 2009-2011

1. Petecchia L, Sabatini F, Varesio L, Camoirano A, Usai C, Pezzolo A, Rossi GA. Bronchial airway epithelial cell damage following exposure to cigarette smoke includes disassembly of tight junction components mediated by the extracellular signal-regulated kinase 1/2 pathway. Chest. 2009 ;135(6):1502-1512.
2. Tosca MA, Villa E, Silvestri M, D'Annunzio G, Pistorio A., Minicucci L., Lorini R., Rossi GA. Discrepancy between sensitization to inhaled allergens and respiratory symptoms in paediatric patients with type 1 diabetes mellitus. Pediatric Allergy Immunology 2009: 64:1463-1471.
3. Papi A, Nicolini G, Baraldi E, Boner A, Cutrera R, Rossi GA, Fabbri LM; on behalf of the best for children study group. Regular vs prn nebulized BEclomethasone and Salbutamol combination in preschool children.with persistent wheezing. Allergy. 2009 Oct;64(10):1463-71.
4. Ullmann N, Sacco O, Gandullia P, Silvestri M, Pistorio A, Barabino A, Disma N. M., Rossi GA.Usefulness and safety of double endoscopy in children with gastroesophageal reflux and respiratory symptoms. Respiratory Medicine. 2010 Apr;104(4):593-9.
5. Tosca MA, Silvestri M., Morandi F., Prigione I,., Ciprandi G, Pistorio A, Rossi GA. Impairment of lung function might be related to IL-10 and IFN-gamma defective production in allergic Children. IMMUNOL LETT 2011;140:104-6.
6. Prigione I, Morandi F, Tosca M. A., Silvestri M, Pistoia V, Ciprandi G & G. A Rossi. Interferon-gamma and IL-10 may protect from allergic polysentization in children: preliminary evidence. Allergy. 2010;65:740-742.
7. Sabatini F, Petecchia L, Boero S, Silvestri M, Klar J, Tenor H, Beume R, Hatzelmann A, Rossi GA A phosphodiesterase 4 inhibitor, roflumilast N-oxide, inhibits human lung fibroblast functions *in vitro*. Pulmonary Pharmacology Therapeutics. 2010 Aug;23(4):283-91.
8. Petecchia L, Sabatini F, Usai C, Carnevali S, Ognibene M, Vanni C, Eva A, Fabbri LM, Rossi GA, Ricciardolo FL. Mechanisms of bradykinin-induced contraction in human fetal lung fibroblasts. European Respiratory Journal. March 31, 2010.
9. Silvestri M, Pistorio A, Battistini E, Rossi GA. IgE in childhood asthma: relevance of demographic characteristics and polysensitisation. Archives Disease in Childhood. July 23, 2010.
10. Ghezzi M, Silvestri M, Guida E, Pistorio A, Sacco O, Mattioli G, Jasonni V,Rossi GA. Acid and weakly acid gastroesophageal refluxes and type of respiratory symptoms in different agw group children. Respir Med. 2011;105:972-8.

PEDIATRIC CLINIC

DIRECTOR: Renata Lorini
(University)

STAFF
Maria Giannina Alpigiani
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Giuseppe d'Annunzio
Alessandra De Alessandri
Teresa de Toni
Eliana Di Battista
Natascia Di Iorgi
Roberto Gastaldi
Mohamad Maghnie
Laura Minicucci
Nicola Minuto
Flavia Napoli
Anna Maria Paolillo
Vita Patrizia Salusciev
Maria Cristina Schiaffino
Marina Vignolo
Maria Luisa Zunino

LABORATORY FOR THE STUDY OF INBORN ERRORS OF METABOLISM (LABSIEM)

Ubaldo Caruso*
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MAIN RESEARCH ACTIVITIES YEAR 2011

- **DIABETES MELLITUS:** Clinical, genetic and molecular diagnosis and follow-up of patients with Type 1 Diabetes and of patients with non autoimmune forms of diabetes mellitus, in particular: Monogenic forms of diabetes mellitus (Maturity-Onset Diabetes of the Young – MODY, Wolfram Syndrome, neonatal diabetes)
- **ENDOCRINE DISEASES:** Long-term follow up of newborns with congenital hypothyroidism; bone mineral density in preterms and in children with chronic diseases; metabolic syndrome in oncological patients; hypogonadotropic hypogonadism; septo-optic dysplasia; diagnosis of growth hormone deficiency in the transition period
- **CYSTIC FIBROSIS:** CF Italian Registry in collaboration with Istituto Superiore di Sanità; Study of calpain/calpastatin system in CF patients in collaboration with Dept of Experimental Medicine, University of Genoa; Study of genotype/phenotype correlation in CF patients in collaboration with Genetic Service, Burlo Garofolo Institute, Trieste
- **METABOLIC DISEASES**: Development and improvement of newborn screening extended to newborns with metabolic diseases; Assessment of long term safety in subjects with different types of phenylketonuria treated with sapropterin dihydrochloride (International Kamper study). Biochemical, clinical and genetic aspects of disorders of synthesis and transport of creatine.

RESEARCH PROGRAM YEAR 2012

DIABETES MELLITUS: Prosecution of molecular diagnosis of monogenic forms of DM. T1DM: 1) Epidemiological data collection in Liguria Region; 2) Coordination of national multicenter AIFA study to establish the efficacy and safety of premixed insulin in T1DM pts with suboptimal glycemic control; 3) Participation in multicenter trial to establish the efficacy and safety of a new insulin analogue (Deglutec); 4)

Risk assessment for T1DM in I and II-degree relatives of T1DM pts. **ENDOCRINE DISEASES:** Epigenetic study in short stature: analysis of the methylation status of regulatory CpG islands in the whole genome; bone mineral density and body composition in neonates with different growth patterns; bone mineral density in chronic diseases in childhood and adolescence (brain tumor pts, DMD pts, SMA pts); hypogonadotropic hypogonadism; septo-optic dysplasia; diagnosis of GH deficiency in the transition period. **CYSTIC FIBROSIS:** Eradication strategies of Methicillin resistant S. aureus in collaboration with European CF Clinical trial Network; Review of lung transplantation criteria for waiting list registration with Italian Society of CF; Intestinal bacteria overgrowth in CF pts with exocrine pancreatic insufficiency. **METABOLIC DISEASES**: Assessment of long term safety in pts with different types of PKU treated with sapropterin dihydrochloride (International Kamper study); Psychometric validation of questionnaires assessing the impact of PKU on the quality of life of pts and their parents; Development of 2nd control test to increase positive predictive value (PPV) in newborn screening extended to metabolic diseases.

MAJOR COLLABORATIONS

Vita e Salute University, San Raffaele Hospital, Milano (TrialNet and Neo DXA), Campus Biomedico, University of Roma (Double Diabetes), Piemonte Orientale University of Novara (Type 1 Diabetes Genes), University of Pittsburgh (Genetics of Diabetic Nephropathy), Bambino Gesù Hospital, Rome, Hospital of Padova, Padova, Meyer Hospital, Florence ,University of Catania, Catania, Microcytemic Hospital, Cagliari, Auxological Institute, Milano, Galliera Hospital, Genoa, Regional Hospital, Bolzano, Federico II University, Naples, San Giovanni Battista-Molinette Hospital, University of Turin, Istituto Superiore di Sanità, Department of Experimental Medicine, University of Genoa, Genetic Service, Burlo Garofolo Institute, Trieste, European Cystic Fibrosis Clinical Trial Network, Cystic Fibrosis Italian Society, Biochemical Genetic Laboratory, Mayo Clinic, USA, Division of Clinical Chemistry and Biochemistry, Kinderspital, Zurich, Pediatrics Dept, University Childrens' Hospital, Zurich, Experimental Medicine Department, Genetic-Metabolic Diseases, La Sapienza University, Rome, Laboratory of Genetic Metabolic Diseases, University Hospital Amsterdam, Pediatrics Department, Regina Margherita Hospital,Turin

MAIN PUBLICATIONS YEARS 2009-2011

1. Reassessment of the growth hormone status in young adults with childhood-onset growth hormone deficiency: reappraisal of insulin tolerance testing. Secco A, di Iorgi N, Napoli F, Calandra E, Calcagno A, Ghezzi M, Frassinetti C, Fratangeli N, Parodi S, Benassai M, Leitner Y, Gastaldi R, Lorini R, Maghnie M, Radetti G. J Clin Endocrinol Metab. 2009 Nov;94(11):4195-204.
2. The accuracy of the glucagon test compared to the insulin tolerance test in the diagnosis of adrenal insufficiency in young children with growth hormone deficiency. di Iorgi N, Napoli F, Allegri A, Secco A, Calandra E, Calcagno A, Frassinetti C, Ghezzi M, Ambrosini L, Parodi S, Gastaldi R, Loche S, Maghnie M. J Clin Endocrinol Metab. 2010 May;95(5):2132-9.
3. Bone acquisition in healthy young females is reciprocally related to marrow adiposity. Natascia Di Iorgi, Aschely O Mo, Kate Grimm, Tysha A. L. Wren, Vicente Gilsanz J Clin Endocrinol Metab. 2010 Jun;95(6):2977-82.
4. Evidence for alteration of calpain/calpastatin system in PBMC of cystic fibrosis patients. Averna M, Stifanese R, De Tullio R, Minicucci L, Cresta F, Palena S, Salamino F, Pontremoli S, Melloni E. Biochim Biophys Acta. 2011 Dec;1812(12):1649-57.
5. Impact of the A (H1N1) pandemic influenza (season 2009-2010) on patients with cystic fibrosis.Viviani L, Assael BM, Kerem E; ECFS (A) L.Minicucci for Genova CF Center in H1N1 study group.J Cyst Fibros. 2011 Sep;10(5):370-6.
6. Phenotypic variability, neurological outcome and genetics background of 6-pyruvoyl-tetrahydropterin synthase deficiency Leuzzi V, Carducci C, Carducci C, Pozzessere S, Burlina A, Cerone R, Concolino D, Donati MA, Fiori L, Meli C, Ponzone A, Porta F, Strisciuglio P, Antonozzi I, Blau N. Clin Genet. 2010 77(3):249-57.
7. Clinical validation of cutoff target ranges in newborn screening of metabolic disorders by tandem mass spectrometry: A worldwide collaborative project David M. S. McHugh, Cynthia A. Cameron, U Caruso, M Cassanello et al. Genetics In Medicine 2011, Volume 13, Number 3: 230 – 254.
8. Study Group. Maturity-onset diabetes of the young in children with incidental hyperglycemia: a multicenter Italian study of 172 families Lorini R, Klersy C, d'Annunzio G, Massa O, Minuto N, Iafusco D, Bellannè-Chantelot C, Frongia AP, Toni S, Meschi F, Cerutti F, Barbetti F; Italian Society of Pediatric Endocrinology and Diabetology (ISPED). Diabetes Care. 2009;32:1864-66 .
9. Genetic investigation in an Italian child with an unusual association of atrial septal defect, attributable to a new familial GATA4 gene mutation, and neonatal diabetes due to pancreatic agenesis. D'Amato E, Giacopelli F, Giannattasio A, D'Annunzio G, Bocciardi R, Musso M, Lorini R, Ravazzolo R. Diabet Med. 2010;27:1195-200.
10. Neonatal Diabetes Caused by Pancreatic Agenesia: Which other genes should be used for diagnosis? Salina A, Pasquali L, Aloi C, Lugani F, d'Annunzio G, Lorini R. Diabetes Care 2010;33:e112.

PEDIATRIC GASTROENTEROLOGY

DIRECTOR: Arrigo Barabino

STAFF
Serena Arrigo
Angela Calvi
Emanuela Castellano
Paolo Gandullia
Lia Giovannini
Silvia Vignola

MAIN RESEARCH ACTIVITIES YEAR 2011

- Retrospective single centre survey on clinical outcome of children with steroid-resistant severe attack of ulcerative colitis treated with cyclosporine
- National multicenter survey on clinical outcome of benign esophageal stenosis in children after endoscopic dilatation
- Thiopurine therapy in children with IBD: correlation of drug efficacy-safety with their blood metabolites and enzymatic genotype
- On-line National Registry of pediatric IBD diagnosed in our Centre from 2009 to 2011
- Study on the follow-up of children with IBD treated with thalidomide
- Very long term observational study of children with Crohn's disease treated or not with biologics.

RESEARCH PROGRAM YEAR 2012

- Continuation of the above reported research activities
- Survey on the clinical outcome of children with Crohn's disease referred to adult gastroenterologists after 18 years of age
- Study on the safety of budesonide in inducing remission of children with Crohn's disease
- Study on the safety of budesonide in maintaining remission of children with Crohn's disease

MAJOR COLLABORATIONS

- Bambino Gesù Pediatric Hospital, Roma
- Transplantation Centre, Hospital of Bergamo
- Pediatric Surgery, Hospital of Brescia
- Digestive Pediatric Surgery, Manchester UK
- Pediatric Gastroenterology, La Sapienza University, Rome
- Gastroenterology Department, Galliera Hospital, Genoa

MAIN PUBLICATIONS YEARS 2009-2011

1. Gandullia P, Lugani F, Costabello L, Arrigo S, Calvi A, Castellano E, Vignola S, Pistorio A, Barabino A. Long-term home parenteral nuitrition in children with chronic intestinal failure: a 15-year experience at a single centre. Dig Liver Dis 2011;43:28-33.
2. De Iudicibus S., Stocco G., Martelossi S, Londero M., Ebner E., Pontillo A., Lionetti P., Barabino A. et al. Genetic predictors of glucocorticoid response in pediatric patients with inflammatory bowel disease. J Clin Gastroenterol 2011;45:1-7.

3. Barabino A., Gandullia P., Arrigo S., Vignola S., Mattioli G., Grattarola C. Succesfull endoscopic treatment of a double duodenal web in a infant. Gastrointest Endosc 2011;73:401-3.
4. Mattioli G, Pini-Prato A, Barabino A, Gandullia P, Avanzini S, Guida E, Rossi V, Pio L, Disma N, Mameli L, Mirta DR, Montobbio G, Jasonni V. Laparoscopic approach for children with inflammatory bowel diseases . Pediatr Surg Int. 2011; 27:839-46.
5. Barabino A, Gandullia P, Calvi A, Vignola S, Arrigo S, De Marco R. Sudden Blindness in a child with Crohn's disease. World J Gastroenterol 2011.
6. Pini Prato A, Rossi V, Fiore M, Avanzini S, Mattioli G, Sanfilippo F, Michelazzi A, Borghini S, Disma N, Montobbio G, Barabino A, Nozza P, Ceccherini I, Gimelli S, Jasonni V. Megacystis, megacolon, and malrotation: A new syndromic association? Am J Med Genet A. 2011;155:1798-802.
7. Ulmann N, Sacco O, Gandullia P, Silvestri M, Pistorio A, Barabino A et al. Usefulness and safety of double endoscopy in children with gastroesophageal reflux and respiratory symptoms. Respiratory Medicine 2010;104:593-9.
8. Di Nardo G, Oliva S, Passariello M, Pallotta N, Civitelli F, Frediani S, Gualdi G, Gandullia P, Mallardo S, Cucchiara S Intralesional steroid injection after endoscopic balloon dilation in pediatric Crohn's disease with stricture: a prospective, randomized, double-blind, controlled trial. Gastrointest Endosc. 2010;72:1201-8.
9. Wang K, Zhang H, Kugathasan S, Annese V, Bradfield JP, Russell RK, Sleiman PM, Imielinski M,Glessner J, Hou C, Wilson DC, Walters T, Kim C, Frackelton EC, Lionetti P, Barabino A, Van Limbergen J, Guthery S, Denson L, Piccoli D, Li M, Dubinsky M, Silverberg M, Griffiths A, Grant SF, Satsangi J, Baldassano R, Hakonarson H. Diverse genome-wide association studies associate the IL12/IL23 pathway with Crohn Disease. Am J Hum Genet. 2009;84:399-405.
10. D'Annunzio G, Giannattasio A, Poggi E, Castellano E, Calvi A, Pistorio A, Barabino A, Lorini R. Beta-cell autoimmunity in pediatric celiac disease: the case for routine screening? Diabetes Care. 2009;32:254-256.

DERMATOLOGY

DIRECTOR: Corrado Occella

STAFF
Odette Nemelka
Dario Bleidl
Gianmaria Viglizzo

MAIN RESEARCH ACTIVITIES YEAR 2011

Clinical-dermatological longitudinal study on the evolution of congenital naevus during childhood

Aim of the study is to evaluate the possibility for congenital naevi to change their dermoscopic pattern over time

All patients admitted to the Dermoscopic Service for evaluation of congenital naevi are enrolled in a follow up program.

Dermoscopic images taken during the first visit and the follow up visit are compared in order to detect any structural change.

To date, 130 lesions diagnosed as congenital naevi have been obseved in the Dermoscopic service and all of them have been enrolled in the follow up program.

A congenital naevus observed in a 3-yr-old female showed, after 3 years' follow-up, a modification of the dermoscopic pattern from globular (most commun dermoscopic pattern in infancy) to reticular.

MAIN PUBLICATIONS YEARS 2009-2011

1. Alpigiani MG, Salvati P, Schiaffino MC, Occella C, Castiglia D, Covaciu C, Lorini R.A New SPINK5 Mutation in a Patient with Netherton Syndrome: A Case Report.Pediatr Dermatol. 2011 Jun 22.
2. Garrè ML, Cama A, Bagnasco F, Morana G, Giangaspero F, Brisigotti M, Gambini C, Forni M, Rossi A, Haupt R, Nozza P, Barra S, Piatelli G, Viglizzo G, Capra V, Bruno W, Pastorino L, Massimino M, Tumolo M, Fidani P, Dallorso S, Schumacher RF, Milanaccio C, Pietsch T.Medulloblastoma variants: age-dependent occurrence and relation to Gorlin syndrome--a new clinical perspective.Clin Cancer Res. 2009 Apr 1;15(7):2463-71.

NEUROSCIENCES

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MUSCULAR AND NEURODEGENERATIVE DISEASES
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Carlo Minetti

PHYSICAL THERAPY

Paolo Moretti

CHILD NEUROPSYCHIATRY
(University)

Edvige Veneselli

LAB. PRE-POSTNATAL DIAGNOSIS METABOLIC DISEASES

Mirella Filocamo

PSYCHOLOGY
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NEUROMUSCULAR DISEASES

DIRECTOR: Carlo Minetti
(University)

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MAIN RESEARCH ACTIVITIES YEAR 2011

Neuromuscular disorders and neurodegenerative diseases: muscular dystrophies, spinal muscular atrophies, congenital myopathies, metabolic myopathies, mitochondrial encephalopathies, inflammatory myopathies, genetic metabolic leucodystrophies, neurofibromatosis, idiopathic epilepsies of genetic origin.

RESEARCH PROGRAM YEAR 2012

- Pathogenetic mechanisms of myopathies
- Genetic and metabolic characterization of encephalomyopathies
- Molecular analysis and genotype-phenotype correlation in congenital myopathies
- Genetic of Idiopathic Epilepsies
- Clinical and molecular characterization of leucodystrophies
- Clinical and genetic study of neurofibromatosis

MAJOR COLLABORATIONS

- Dept. of Neurology, Columbia University, New York, USA (Prof. S. Di Mauro)
- T. Jefferson University, Philadelphia, USA, (Prof. M.P. Lisanti)
- Molecular Medicine unit, Stella Maris Foundation, Calambrone, Pisa, (Prof. G. Cioni, Dott. F.M. Santarelli)
- Laboratory of Human Genetics, Galliera Hospital, Genova
- Molecular Medicine, Bambin Gesù hospital, Roma (Dott. E. Bertini)
- Dept. Pediatric Neurology, Catholic University, Roma (Prof. E. Mercuri)
- Tigem, Napoli (Prof. V. Nigro)
- Dept. of Pediatrics, University of Catania
- Italian League against Epilepsy (LICE)
- Neurologic Clinic, University of Genova

MAIN PUBLICATIONS YEARS 2009-2011

1. Striano P, Weber YG, Toliat MR, Schubert J, Leu C, Chaimana R, Baulac S, Guerrero R, Leguern E, Lehesjoki AE, Polvi A, Robbiano A, Serratosa JM, Guerrini R, Nürnberg P, Sander T, Zara F, Lerche H, Marini C; On behalf of the EPICURE Consortium. GLUT1 mutations are a rare cause of familial idiopathic generalized epilepsy. Neurology. 2012 Feb 21;78(8):557-562.
2. Striano P, Coppola A, Paravidino R, Malacarne M, Gimelli S, Robbiano A, Traverso M, Pezzella M, Belcastro V, Bianchi A, Elia M, Falace A, Gazzerro E, Ferlazzo E, Freri E, Galasso R, Gobbi G, Molinatto C, Cavani S, Zuffardi O, Striano S, Ferrero GB, Silengo M,

Cavaliere ML, Benelli M, Magi A, Piccione M, Dagna Bricarelli F, Coviello DA, Fichera M, Minetti C, Zara F. Clinical significance of rare copy number variations in epilepsy: a case-control survey using microarray-based comparative genomic hybridization. Arch Neurol. 2012 Mar;69(3):322-30.

3. Striano P, Paravidino R, Sicca F, Chiurazzi P, Gimelli S, Coppola A, Robbiano A, Traverso M, Pintaudi M, Giovannini S, Operto F, Vigliano P, Granata T, Coppola G, Romeo A, Specchio N, Giordano L, Osborne LR, Gimelli G, Minetti C, Zara F. West syndrome associated with 14q12 duplications harboring FOXG1. Neurology. 2011 May 3;76(18):1600-2.
4. Striano P, Busolin G, Santulli L, Leonardi E, Coppola A, Vitiello L, Rigon L, Michelucci R, Tosatto SC, Striano S, Nobile C. Familial temporal lobe epilepsy with psychic auras associated with a novel LGI1 mutation. Neurology. 2011 Mar 29;76(13):1173-6.
5. Falace A, Filipello F, La Padula V, Vanni N, Madia F, De Pietri Tonelli D, de Falco FA, Striano P, Dagna Bricarelli F, Minetti C, Benfenati F, Fassio A, Zara F. TBC1D24, an ARF6-interacting protein, is mutated in familial infantile myoclonic epilepsy. Am J Hum Genet. 2010 Sep 10;87(3):365-70.
6. Striano P, Minetti C. Epilepsy: old drugs do the trick in childhood absence epilepsy. Nat Rev Neurol. 2010 Aug;6(8):420-1.
7. Gazzerro E, Assereto S, Bonetto A, Sotgia F, Scarfi S, Pistorio A, Bonuccelli G, Cilli M, Bruno C, Zara F, Lisanti MP, Minetti C. Therapeutic potential of proteasome inhibition in Duchenne and Becker muscular dystrophies. Am J Pathol. 2010 Apr;176(4):1863-77.
8. Messina S, Bruno C, Moroni I, Pegoraro E, D'Amico A, Biancheri R, Berardinelli A, Boffi P, Cassandrini D, Farina L, Minetti C, Moggio M, Mongini T, Mottarelli E, Pane M, Pantaleoni C, Pichiecchio A, Pini A, Ricci E, Saredi S, Sframeli M, Tortorella G, Toscano A, Trevisan CP, Uggetti C, Vasco G, Comi GP, Santorelli FM, Bertini E, Mercuri E. Congenital muscular dystrophies with cognitive impairment. A population study. Neurology. 2010 Sep 7;75(10):898-903.
9. Striano P, Zara F, Minetti C, Striano S. Chitosan may decrease serum valproate and increase the risk of seizure reappearance. BMJ. 2009 Sep 24;339:b3751.
10. Mercuri E, Messina S, Bruno C, Mora M, Pegoraro E, Comi GP, D'Amico A, Aiello C, Biancheri R, Berardinelli A, Boffi P, Cassandrini D, Laverda A, Moggio M, Morandi L, Moroni I, Pane M, Pezzani R, Pichiecchio A, Pini A, Minetti C, Mongini T, Mottarelli E, Ricci E, Ruggieri A, Saredi S, Scuderi C, Tessa A, Toscano A, Tortorella G, Trevisan CP, Uggetti C, Vasco G, Santorelli FM, Bertini E. Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. Neurology. 2009 May 26;72(21):1802-9.

LABORATORY OF PRE- AND POSTNATAL DIAGNOSIS OF METABOLIC DISEASES

DIRECTOR: Mirella Filocamo

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Marina Stroppiano
Barbara Tappino

MAIN RESEARCH ACTIVITIES YEAR 2011

- Enzymatic and molecular testing for lysosomal disorders, Glycogenosis 1a, and Pelizaeus-Merzbacher
- Methylation test for Prader Willi and Angelman
- Genetic Biobank management
- Coordination of the Italian Network of Genetic Biobanks
- Molecular/functional characterization of mutant alleles and genotype/phenotype correlation studies in lysosomal diseases and hypomyelinating disorders.
- Characterization of key pathogenetic pathways leading to bone abnormalities in Type 1 Gaucher patients through a biosensor fish model.
- Analysis of the pathogenetic mechanisms underlying lysosomal disorders using zebrafish biosensors

RESEARCH PROGRAM YEAR 2012

Continuation of all ongoing activities/projects and starting up of new projects as follows:

- Elucidation of in vivo correction mechanisms, at RNA level, of heritable genomic mutations identified in Hunter disease. Specific aims: (i) set up of 'in vitro' system, based on transfection of plasmids carrying mutated and normal full-length IDS cDNAs into controls' and patients' fibroblasts as well as in Hek293 cell lines, in order to confirm the occurrence of the phenomenon; and (ii) characterization of minimum sequences required for RNA editing to be used for the identification of the potential involved factors.
- Identification of new genes in hypomyelinating leukoencephalopathies using high-density array CGH and next-generation sequencing (exome sequencing) technologies
- Molecular and functional characterization in Pelizaeus-Merzbacher, a myelin disorder, due to PLP1 mutations ranging from gene duplications of variable size to intragenic lesions. Specific aims: (i) in vitro correction of specific splicing mutations using antisense oligonucleotide technologies; (ii) assessment of potential intracellular signaling modifications resulting from the overexpression of PLP1 gene using PCR-arrays.

MAJOR COLLABORATIONS

- Regional Coordinating Centre for Rare Diseases, "Santa Maria della Misericordia" Hospital, Udine
- Institute of Medical Genetics, School of Medicine, Cardiff University, Cardiff, UK
- Faculté de Médecine, Clermont Ferrand, Cedex, France

- Institut National de la Sante et de la Recherche Medicale INSERM, Paris, France
- Bambino Gesù Hospital, Roma
- Dept. of Sciences for the health of woman and child, University of Firenze
- Biopolymers and Proteomics, San Martino-IST Hospital, Genova
- Dept. of Chemistry, Biochemistry and Biotechnologies for Medicine, University of Milano
- Dept. of Biomedical Sciences, University of Padova
- Research and Development Unit, Department of Genetics, CGMJM, INSA, Portugal
- The Center for RNA Biology, Department of Biochemistry and Biophysics, University of Rochester, Rochester NY USA

MAIN PUBLICATIONS YEARS 2009-2011

1. Fancello T, Dardis A, Rosano C, Tarugi P, Tappino B, Zampieri S, Pinotti E,Corsolini F, Fecarotta S, D'Amico A, Di Rocco M, Uziel G, Calandra S, Bembi B,Filocamo M. Molecular analysis of NPC1 and NPC2 gene in 34 Niemann-Pick C Italian patients: identification and structural modeling of novel mutations. Neurogenetics. 2009;10:229-39.
2. Regis S, Grossi S, Corsolini F, Biancheri R, Filocamo M. PLP1 gene duplication causes overexpression and alteration of the PLP/DM20 splicing balance in fibroblasts from Pelizaeus-Merzbacher disease patients. Biochim Biophys Acta. 2009; 1792:548-54.
3. Tappino B, Chuzhanova NA, Regis S, Dardis A, Corsolini F, Stroppiano M, Tonoli E, Beccari T, Rosano C, Mucha J, Blanco M, Szlago M, Di Rocco M, Cooper DN, Filocamo M. Molecular characterization of 22 novel UDP-N-acetylglucosamine-1-phosphate transferase alpha- and beta-subunit (GNPTAB) gene mutations causing mucolipidosis types IIalpha/beta and IIIalpha/beta in 46 patients. Hum Mutat. 2009, 30:E956-73.
4. Lualdi S, Tappino B, Di Duca M, Dardis A, Anderson CJ, Biassoni R, Thompson PW, Corsolini F, Di Rocco M, Bembi B, Regis S, Cooper DN, Filocamo M, Enigmatic in vivo iduronate-2-sulfatase (IDS) mutant transcript correction to wild-type in Hunter syndrome. Hum Mutat, 2010; 31(4):E1261-85.
5. Tappino B, Biancheri R, Mort M, Regis S, Corsolini F, Rossi A, Stroppiano M, Lualdi S, Fiumara A, Bembi B, Di Rocco M, Cooper DN, Filocamo M. Identification and characterization of 15 novel GALC gene mutations causing Krabbe disease. Hum Mutat. 2010, 31:E1894-914.
6. Chiefari E, Tanyolaç S, Paonessa F, Pullinger CR, Capula C, Iiritano S, Mazza T, Forlin M, Fusco A, Durlach V, Durlach A, Malloy MJ, Kane JP, Heiner SW, Filocamo M, Foti DP, Goldfine ID, Brunetti A. Functional variants of the HMGA1 gene and type 2 diabetes mellitus. JAMA. 2011 Mar 2;305(9):903-12.
7. Bertola F, Filocamo M, Casati G, Mort M, Rosano C, Tylki-Szymanska A, n Tüysüz B, Gabrielli O, Grossi S, Scarpa M, Parenti G, Antuzzi D, Dalmau J, Di Rocco M, Dionisi Vici C, Okur I, Rosell J, Rovelli A, Furlan F, Rigoldi M, Biondi A, d N Cooper D, Parini R. IDUA Mutational Profiling of a Cohort of 102 European Patients with Mucopolysaccharidosis type I: Identification and Characterization of 35 Novel □-L-iduronidase (IDUA) Alleles. Hum Mutat, 2011 32(6):E2189-210. doi: 10.1002/humu.21479.
8. Biancheri R, Rossi A, Zara F, Filocamo M. AIMP1/p43 Mutation and PMLD. Am J Hum Genet. 2011 Mar 11;88(3):391.
9. the BRIF workshop group, Cambon-Thomsen A, Thorisson GA; Named collaborators, Andrieu S, Bertier G, Boeckhout M, Cambon-Thomsen A, Carpenter J, Dagher G, Dalgleish R, Deschênes M, di Donato JH, Filocamo M, Goldberg M, Hewitt R, Hofman P, Kauffmann F, Leitsalu L, Lomba I, Mabile L, Melegh B, Metspalu A, Miranda L, Napolitani F, Oestergaard MZ, Parodi B, Pasterk M, Reiche A, Rial-Sebbag E, Rivalle G, Rochaix P, Susbielle G, Tarasova L, Thomsen M, Thorisson GA, Zawati MH, Zins M, Mabile L. The role of a bioresource research impact factor as an incentive to share human bioresources. Nat Genet. 2011 Jun;43(6):503-504.
10. Grossi S, Regis S, Biancheri R, Mort M, Lualdi S, Bertini E, Uziel G,Boespflug-Tanguy O, Simonati A, Corsolini F, Demir E, Marchiani V, Percesepe A,Stanzial F, Rossi A, Vaurs-Barriere C, Cooper DN, Filocamo M. Molecular Genetic Analysis of the PLP1 Gene in 38 Families with PLP1-related disorders: Identification and Functional Characterization of 11 Novel PLP1 Mutations. Orphanet J Rare Dis. 2011 Jun 16;6(1):40.

CHILD NEUROPSYCHIATRY

DIRECTOR: Edvige Veneselli
(University)

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Deborah Bertorello
Roberta Biancheri
Luca Boeri
Francesca Bollati (absent ; substitute Danila Trevisiol)
Fabia Brera
Maria Elena Celle
Maria Teresa Dapelo
Elisa De Grandis
Laura Doria-Lamba
Roberta Follo
Paolo Grosso
Maria Margherita Mancardi
Simona Martelli
Marco Martinoli
Monica Mascaretti
Simona Mendolia
Marisol Mirabelli-Badenier
Francesca Passano (contract until June 2011)
Maria Pintaudi
Tiziana Prastaro
Margherita Savoini
Lucia Sciarretta
Gloria Sodini
Michela Stagnaro
Elisabetta Zanotto

MAIN RESEARCH ACTIVITIES YEAR 2011

In our Unit, there are several research groups that are specifically dedicated to the study of patients affected by different disorders. The Centre for Pediatric Epilepsy and the Research Section on Developmental Neurosciences are specifically dedicated to the pre- and post-surgical evaluation of drug-resistant epilepsies and the study of epileptic encephalopathies. A specific protocol for neurological and neurophysiological assessment of these patients has been created. A retrospective correlation study has been carried out by the Rett syndrome study group that has identified the best drug options for early-onset and late-onset epilepsy, namely valproic acid and lamotrigine, respectively. The genotype-phenotype (clinical and neurophysiological phenotype) correlation has been studied by the peripheral neuropathies study group. The incidence of the creatine deficiency in 200 autistic patients has been evaluated by the autism and related disorders study group. The cognitive and neuropsychological profile of two patients with anti-MNDAR encephalitis has been described by the Neuroimmunology group that has also described a patient with anti-GAD limbic encephalitis without associated epilepsy. A database containing the clinical, neurophysiological, neuroradiologocal and treatment information on about 400 patients has been created by the Cerebral Palsy study group. The Preterm study group has collaborated on the Trouffle and GAS International Study. International therapeutic trials for drug-resistant epilepsy, Fragile-X syndrome and Tuberous Sclerosis complex are ongoing.

RESEARCH PROGRAM YEAR 2012

In addition to the above reported research studies, the following studies will be carried out: role of oxidative stress in the Rett syndrome, functional impairment related to the CSWS in patients with cerebral palsy, incidence of vertigo in patients presenting with headache in the Emergency Unit, management of complex neurological disabilities through a multidisciplinary approach, contribution of the EEG to the diagnosis of preterm newborn diseases, retrospective study on ADEM, retrospective study on CIDP, quality of life in families of patients affected by Alternating Hemiplegia, medium term follow-up of ADHD subjects.

MAJOR COLLABORATIONS

Epilepsy: C.Dravet, Member of ILAE Commission, Marseille – Laboratory of Genetics, Galliera hospital, Genova - E.Beghi, Laboratory of Neurologic Diseases, "Mario Negri" Institute, Milano. *Infantile cerebral palsy and movement disorders*: J.Campistol, Hospital Sant Joan de Déu, Universitat de Barcelona - G.Abruzzese, DiNOG, Genova - S.Soria, President of A.I.D.A.. *Leucoencephalopathies*: O.Boepsflug-Tanguy, Clermont-Ferrand - Marjo S.Van der Knaap, VU University, Amsterdam. *Ceroidolipofuscinosis:* A.Simonati, University of Verona. *Hereditoary spastic paraparesis*: F.M.Santorelli, Stella Maris hospital of Pisa. *Peripheral neuropathies:* A.Schenone, P.Mandich, DiNOG, Genova. *Stroke*: C.Zavarone, Groupe Hospitalier Pitié-Salpêtrière, Paris. *Opsoclonus-Myoclonus s.*: B.Hero, University of Cologne. *Neuroimmunology*: A.Vincent, John Radcliffe Hospital, Oxford, UK - F.Montecucco, Geneva University Hospital - A.Uccelli, DiNOG, Genova. *Alternating hemiplegia*: B.Neville, UCL Institute of Child Health, London. *Tourette syndrome and Tics:* M.M.Robertson, University of London - D.Martino, University of Bari. *Infantile autism:* R.Faggioli, Centre for autism, San Paolo hospital of Milano - M.Zappella, University of Siena - E.Micheli, Robotics School, Genova. *Rett syndrome*: M.Pineda, Hospital Sant Joan de Deu, Barcelona - A.Clarke, University Hospital of Wales, - B.Ben Zeev, Safra Ped. Hospital, Ramat-Gan - G.Nguyen, Rett Syndrome Europe - S.Russo, It. Auxologic Inst., Milano - A.Renieri, Siena hospital - A.Voci and L.Vergani, Dept. Physiology and Biophysics, University of Genova. *Psychopahtology of infancy and adolescence:* D.Cohen, Groupe Hospitalier Pitié-Salpêtrière, Paris - F.Gabrielli and M.Maura, S. Martino hospital, Genova - E.Franzoni, University of Bologna - F.Neri, University of Milano-Bicocca – Ist. of Psychology and Cognitive-Behavioural Therapy - Genoese Centre of Family Therapy – The Therapeutic Role, Genova – PsiBA, Milano. *Fragile X syndrome:* M.G.Torrioli, Catholic University, Roma. *Neuropsychomotricity:* Regional Network of CL Therapy of Neuro- and Psychomotricity of Developmental Age - P.A.Veggiotti, C. Mondino Neurologic Institute, University of Pavia.

MAIN PUBLICATIONS YEARS 2009-2011

1. Hypomyelination and congenital cataract: broadening the clinical phenotype. Biancheri R, Zara F, Rossi A, Mathot M, Nassogne MC, Yalcinkaya C, Erturk O, Tuysuz B, Di Rocco M, Gazzerro E, Bugiani M, van Spaendonk R, Sistermans EA, Minetti C, van der Knaap MS, Wolf NI. Arch Neurol. 2011 Sep;68(9):1191-4.
2. Cerebral folate deficiency syndromes in childhood: clinical, analytical, and etiologic aspects. Pérez-Dueñas B, Ormazábal A, Toma C, Torrico B, Cormand B, Serrano M, Sierra C, De Grandis E, Marfa MP, García-Cazorla A, Campistol J, Pascual JM, Artuch R. Arch Neurol 2011;68(5):615-21.
3. Pontocerebellar hypoplasia: clinical, pathologic, and genetic studies. Cassandrini D, Biancheri R, Tessa A, Di Rocco M, Di Capua M, Bruno C, Denora PS, Sartori S, Rossi A, Nozza P, Emma F, Mezzano P, Politi MR, Laverda AM, Zara F, Pavone L, Simonati A, Leuzzi V, Santorelli FM, Bertini E. Neurology. 2010 Oct 19;75(16):1459-64.
4. Identification and characterization of 15 novel GALC gene mutations causing Krabbe disease. Tappino B, Biancheri R, Mort M, Regis S, Corsolini F, Rossi A, Stroppiano M, Lualdi S, Fiumara A, Bembi B, Di Rocco M, Cooper DN, Filocamo M. Hum Mutat. 2010 Dec;31(12):E1894-914.
5. Microarry based analysis of an inherited terminal 3p26.3 deletion, containing only the CHL1 gene, from a normal father to his two affected children. Cuoco C, Ronchetto P, Gimelli S, Béna F, Divizia MT, Lerone M, Mirabelli-Badenier M, Mascaretti M, Gimelli G. Orphanet J Rare Dis 2011;6:12.
6. Molecular genetic analysis of the PLP1 gene in 38 families with PLP1-related disorders: identification ond functional characterization of 11 novel PLP1 mutations. Grossi S, Regis S, Biancheri R, Mort M, Lualdi S, Bertini E, Uziel G, Boespflug-Tanguy O, Simonati A, Corsolini F, Demir E, Marchiani V, Percesepe A, Stanzial F, Rossi A, Vaurs-Barrière C, Cooper DN, Filocamo M. Orphanet J Rare Dis 2011;6:40.
7. Anti-N-methyl-D-aspartate-receptor encephalitis in a four-year-old girl. Biancheri R, Pessagno A, Baglietto MG, Irani SR, Rossi A, Giribaldi G, Mirabelli Badenier MM, Vincent A, Veneselli E. J Pediatr. 2010 Feb;156(2):332-4.
8. Type 1 diabetes and epilepsy: more than a casual association? Mancardi MM, Striano P, Giannattasio A, Baglietto MG, Errichiello L, Zara F, Prato G, Minuto N, Veneselli E, Lorini R, D'Annunzio G. Epilepsia. 2010 Feb;51(2):320-1.
9. Cavitating leukoencephalopathy in a child carrying the mitochondrial A8344G mutation. Biancheri R, Rossi D, Cassandrini D, Rossi A, Bruno C, Santorelli FM. AJNR Am J Neuroradiol. 2010 Oct;31(9):E78-9.
10. Epilepsy in Rett syndrome: Clinical and genetic features. Pintaudi M, Calevo MG, Vignoli A, Parodi E, Aiello F, Baglietto MG, Hayek Y, Buoni S, Renieri A, Russo S, Cogliati F, Giordano L, Canevini M, Veneselli E. Epilepsy Behav. 2010 Nov, 19(3):296-300.

PHYSICAL MEDICINE AND REHABILITATION

DIRECTOR: Paolo Moretti

STAFF
Luca Doglio
Maria Carla Guenza
Ilaria Pernigotti

MAIN RESEARCH ACTIVITIES YEAR 2011

Multicentric research on functional evaluation tools in children with neuromuscular disease

RESEARCH PROGRAM YEAR 2012

- Robotic rehabilitation of upper limb in children
- Diagnostic and therapeutic pathways in children with complex or chronic health conditions and special health care needs
- Exoskeletal brace in children with secondary scoliosis
- Multisensory stimulations in children with severe disability

MAJOR COLLABORATIONS

- Italian Institute of Technology-Genoa
- University of Bologna
- Don Gnocchi Institute, Milan
- Angeli di padre Pio Institute, Foggia

MAIN PUBLICATIONS YEARS 2009-2011

1. Mazzone E, Doglio L. e al. "Reliability of the North Star Ambulatory Assessment in a multicentric setting".Neuromuscul Disord.. 2009 Jul; 19(7):458-61.
2. Mazzone E, Doglio L "North Star Ambulatory Assessment, 6-minute walk test and timed items in ambulant boys with Duchenne muscular dystrophy" Neuromuscul Disord 2010 Nov; 20(11):712-6.
3. Mazzone E, Doglio L e al. "Functional changes in Duchenne muscular distrophy: a 12 month longitudinal cohort study" Neurology, 2011 Jul 19; 77(3): 250-6.
4. Doglio L., Pernigotti I e al. "Early signs of gait deviation in Duchenne Muscular distrophy. " Eur J Phys Rehabil Med 2011 Dec; 47(4): 587-94.

PSYCHOLOGY

DIRECTOR: Ezio F. Casari
(University)

STAFF
Alga Gioia Fantino
Lucia Gatti
Vincenza Lertora

RESEARCH ACTIVITY YEAR 2011

- Evaluation of cognitive development and psychodiagnostics for specific problems or disadvantage areas in developmental age
- Maladjustment and adjustment in chronic disease: evaluation of cognitive styles, psychological counseling at first visits and follow-up according to operative protocols agreed upon with units in patients with spina bifida, neurooncologic patients and patients on hemodialysis and their families
- Psychologic support and counseling for units in case of psychological problems, both preexisting and disease-related, problems of adjustment and compliance with disease and/or hospitalization in patients and/or their families
- Somatoform diseases
- Gender identity disorders: psychotherapy of children and preadolescents
- Learning and school adaptation disorders: dyslexia, dysgraphia, dysorthography and dyscalculation; vocational counseling; integration of disabled children and coordination with school sociomedical services
- Eating behaviour disorders in developmental age
- Psychological counseling for pregnant women
- Informed consent in Pediatric Psychology: shared cognitive processes and negotiation
- Doctor-patient psychological relationship: educational and research/development aspects
- Functional disability in the ill child: psychometric assessment of psychologic adaptation
- Study of resilience psychologic construct through psycometric techniques in normal subjects and in chronic disease populations
- Study of gender identity disorder (GID) in developmental age for the identification of etiopathogenetic components and for treatment in children and adolescents
- Psychometric study of familiar strain in brain tumor operated children
- Psychometric study of learning disorders in developmental age

HEMATOLOGY/ONCOLOGY

Dr. Giorgio Dini

PEDIATRIC HEMATOLOGY/ ONCOLOGY

Giorgio Dini

IMMUNOHEMATOLOGY AND TRANSFUSION CENTRE

Gino Tripodi

INFECTIOUS DISEASES

Elio Castagnola (pro-tempore)

HEMATOLOGY AND ONCOLOGY

Director: Giorgio Dini

STAFF

Maura Acquila
Stefano Amato
Laura Banov
Maria Luisa Belli
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Enrico Cappelli
Daniela Caprino
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Sandro Dallorso
Daniela Di Martino
Carlo Dufour
Maura Faraci
Francesca Fioredda
Alberto Garaventa
M. Luisa Garré
Guia Hanau
Stefania Indaco
Marina Lanciotti
Edoardo Lanino
Tiziana Lanza
Luca Manfredini
Carla Manzitti
Maurizio Miano
Concetta Micalizzi
Claudia Milanaccio
A. Claudio Molinari
Giuseppe Morreale
Marilina Nantron
Paolo Perutelli
Francesca Scuderi
Johanna Svahn
Paola Terranova

MAIN RESEARCH ACTIVITY YEAR 2011

- **Day-Hospital and Home Care:** off therapy project: management of medium- and long-term sequelae induced by provided treatments, surveillance for second cancers, in collaboration with other sections
- **Hematology:** Bone-marrow failure: a study of the mechanisms by which the damage on the bone marrow occurs; leukemia: study of the genetic/metabolic factors that favor the development of the disease, and the adverse prognostic markers
- **Hemostasis and Thrombosis:** Characterization of the anti-phospholipid antibodies in children; Identification and prevention of venous thrombotic risk; Non-invasive prenatal diagnosis; Epidemiological study of genetic and acquired risk factors related to thromboembolic diseases
- **Neuro-Oncology:** study of malignant tumors in patients under 3 years of age; intracranial germ cell tumors and rhabdoid brain tumors
- **Oncology:** Neuroblastoma: prognostic factors and innovative therapeutic modalities, Phase I and II studies on new anticancer drugs in pediatrics
- **HSCT:** Prospective study on the incidence and evolution of hepatic veno-occlusive disease after HSCT: role of prophylaxis with defibrotide; Prospective phase II study on treatment of steroid-refractory graft-versus-host disease (GVHD)

RESEARCH PROGRAM YEAR 2012

- **Day-Hospital and Home Care:** off therapy project: management of medium- and long-term sequelae induced by provided treatments, surveillance for second cancers, in collaboration with other sections
- **Hematology:** Bone marrow failure: Damaging mechanisms in the bone marrow; Role of new protective molecules against damage. Experimental protocols on acute Leukemia rescue.
- **Hemostasis and Thrombosis:** Characterization of the anti-phospholipid antibodies in children; Identification and prevention of venous thrombotic risk; Non-invasive prenatal diagnosis; Epidemiological study of genetic and acquired risk factors related to thromboembolic diseases.
- **Neuro-Oncology:** study of malignant tumors in patients under 3 years old; intracranial germ cell tumors and rhabdoid brain tumors.
- **Oncology:** Neuroblastoma: prognostic factors and innovative therapeutic modalities, Phase I and II studies on new anticancer drugs in pediatrics.
- **HSCT:** Prospective study on the incidence and evolution of hepatic veno-occlusive disease after HSCT: role of prophylaxis with defibrotide; Prospective phase II study on treatment of steroid-refractory graft-versus-host disease (GVHD).

MAJOR COLLABORATIONS

- Italian Association of Pediatric Hematology and Oncology (Associazione Italiana di Ematologia ed Oncologia Pediatrica - A.I.E.O.P.)
- European Cooperative Group Neuroblastoma
- Biochemistry Department, University of Naples
- Hemophilia and Thrombosis Centre, Ospedale Maggiore of Milan and Castelfranco Veneto Hospital (Genetic Working Group A.I.C.E)

- Galliera Hospital: Tissue Laboratory and Italian Registry of Bone Marrow Donors (IBMDR); Urology; Nuclear Medicine; Thyroid Surgery
- San Martino-IST and National Cancer Research Institute: Department of Oncology, Biology and Genetics; Laboratory of Immunogenetics; DIMES; DOBIG,; Hematology-Oncology Department (DEMO); Laboratory of Cell Differentiation; Radiotherapeutic Oncology
- European Commission, Contract QLRT-2001-01768, SIOPEN-R-NET, "Optimization of leucoapheretic procedures in Europe in patients with high-risk neuroblastoma"
- Department of Haematology Hospital's Center of Science and Innovation. Aalborg, Denmark
- National Forum on Pediatric Palliative Care, Fondazione Vaticana Maruzza Lefebvre D'Ovidio
- Neuropathology Department University of Bonn (for neurologic diseases and genetic study of brain tumors)
- Kinderklinik University of Dusseldorf for the study of germ cell tumors
- Dept. Pediatrics, University of Padova for the genetic study of tumors in NF1
- Société Internationale d'Oncologie Pediatrique (S.I.O.P.): CNS Sub-Committee
- Thrombosis Centre, DIMI, University of Genova
- AOSP, Napoli
- Surgical Orthopedics unit, Ospedale Careggi, Firenze
- Cancer Center, Portland, Oregon (USA)
- Fundeni Hospital, Bucarest
- Prosthetic Orthopedic Surgery, S. Corona Hospital, Pietra Ligure

MAIN PUBLICATIONS YEARS 2009-2011

1. Puga I, Cols M, Barra CM, Calvillo M, Dufour C, et al B cell-helper neutrophils stimulate the diversification and production of immunoglobulin in the marginal zone of the spleen Nat Immunol. 2011 Dec 25;13(2):170-80. doi: 10.1038/ni.2194.
2. Nozza Paolo, Casciana ML, Rossi Andrea, Cama Armando, Milanaccio Claudia, Raso Alessandro, et Al. Post-chemotherapy maturation of a pineoblastoma. ACTA NEUROPATHOL 2010;119:651-653.
3. Massimo Luisa. Back home. Letter. J CLIN ONCOL 2010;28(22):E379.
4. Dufour C, Bacigalupo A, Oneto R, et al. Rabbit ATG for aplastic anaemia treatment: a backward step? The Lancet, Volume 378, Issue 9806, Pages 1831 - 1833, 26 November 2011.
5. Rubie H, De Bernardi Bruno, Gerrard M, Canete A, Ladenstein R, Couturier J, et Al Excellent outcome with reduced treatment in infants with nonmetastatic and unresectable neuroblastoma without MYCN amplification: results of the prospective INES 99.1 J CLIN ONCOL 2011;29(4):449-55.
6. Ladenstein R, Potschger, Siabalis D, Garaventa Alberto, Bergeron C, Lewis IJ, et AlDose finding study tor the use of subcutanous recombinant interleukin-2 to augment natural killer cell numbers in an outpatient setting for stage 4 neuroblastoma after megatherapt and autologous stem-cell reinfusion J CLIN ONCOL 2011;29(4):441-8.
7. Mussolin L, Pillon M, d'Amore ESG, Conter V, Piglione M, Lo Nigro L, et Al. Minimal disseminated disease in high-risk Burkitt's lymphoma identifies patients with different prognosis J CLIN ONCOL 2011;29(13):1779-84.
8. Taggart DR, London WB, Schmidt ML, Du Bois SG0, Monclair TF, Nakagawara A, et Al Prognostic value of the stage 4S metastatic pattern and tumor biology in patients with metastatic neuroblastoma diagnosed between birth and 18 months af age J CLIN ONCOL 2011;29(33):4358-64.
9. Faraci Maura, Lanino Edoardo, Morreale Giuseppe, Giardino S, Fossati M, Moroni Cristina, et Al Bacteremias and invasive fungal diseases in children receiving etanercept for steroid-resistant acute GVHD. Letter. BONE MARROW TRANSPL 2011;46:159-60.
10. G Dini, M Zecca, A Balducci, C Messina, F Locatelli et all No difference in outcome between children and adolescents transplanted for acute lymphoblastic leukemia in second remission Blood (2011)118:6683-6690.

INFECTIOUS DISEASES

DIRECTOR: Elio Castagnola

STAFF
Elisabetta Bondi
Ilaria Caviglia
Emilio Cristina
Francesca Ginocchio
Giuseppe Losurdo
Anna Loy
Cristina Moroni
Angela Tacchella

MAIN RESEARCH ACTIVITIES YEAR 2011

- Epidemiology and risk factors for bacteremias and invasive fungal diseases in children receiving antineoplastic chemotherapy or hemopoietic stem cell transplant
- Safety of new anti-infective drugs in children
- Epidemiology and clinical features of invasive fungal diseases in pediatrics

RESEARCH PROGRAM YEAR 2012

- Epidemiology and risk factors for bacteremias and invasive fungal diseases in children receiving antineoplastic chemotherapy or hemopoietic stem cell transplant
- Safety of new anti-infective drugs in children
- Epidemiology and clinical features of invasive fungal diseases in pediatrics
- Epidemiology of antibiotic resistance in infectious diseases occurring in different pediatric conditions (antineoplastic chemotherapy, renal diseases, surgery)

MAJOR COLLABORATIONS

- Pediatric Fungal Network (PFN), international group for the study of invasive fungal diseases in pediatrics
- European Society for Clinical Microbiology and Infectious Diseases (ESCMID), implementation of guidelines
- European Conference of Infections in Leukemia, (ECIL) implementation of guidelines
- International Pediatric Fever and Neutropenia Guideline Panel, implementation of guidelines
- PICNICC (Predicting Infectious Complications of Neutropenic sepsis in Children with Cancer) Collaboration, implementation of clinical prediction rules
- Associazione Italiana di Ematologia ed Oncologia Pediatrica (AIEOP), studies on infections in children with cancer and implementation of guidelines
- Gruppo Italiano Trapianto Midollo Osseo (GITMO), studies on infections in children undergoing hemopoietic stem cell transplant

MAIN PUBLICATIONS YEARS 2009-2011

1. Castagnola E, Garrè ML, Bertoluzzo L, Pignatelli S, Pavanello M, Caviglia I, Caruso S, Bagnasco F, Moroni C, Tacchella A, Haupt R. Epidemiology of febrile neutropenia in children with central nervous system tumor: results from a single center prospective study. J Pediatr Hematol Oncol. 2011 Oct;33(7):e310-5.
2. Garazzino S, Krzysztofiak A, Esposito S, Castagnola E, Plebani A, Galli L, Cellini M, Lipreri R, Scolfaro C, Bertaina C, Calitri C, Bozzola E, Lancella L, Quondamcarlo A, Bosis S, Pugni L,

Losurdo G, Soresina A, De Gaudio M, Mariotti I, Mancini L, Gabiano C, Tovo PA. Use of linezolid in infants and children: a retrospective multicentre study of the Italian Society for Paediatric Infectious Diseases. J Antimicrob Chemother. 2011 Oct;66(10):2393-7.

3. Castagnola E, Rossi MR, Cesaro S, Livadiotti S, Giacchino M, Zanazzo G, Fioredda F, Beretta C, Ciocchello F, Carli M, Putti MC, Pansini V, Berger M, Licciardello M, Farina S, Caviglia I, Haupt R. Incidence of bacteremias and invasive mycoses in children with acute non-lymphoblastic leukemia: results from a multi-center Italian study. Pediatr Blood Cancer. 2010 Dec 1;55(6):1103-7.
4. Caselli D, Carraro F, Castagnola E, Ziino O, Frenos S, Milano GM, Livadiotti S, Cesaro S, Marra N, Zanazzo G, Meazza C, Cellini M, Aricò M. Morbidity of pandemic H1N1 influenza in children with cancer. Pediatr Blood Cancer. 2010 Aug;55(2):226-8.
5. Castagnola E, Bandettini R, Lorenzi I, Caviglia I, Macrina G, Tacchella A. Catheter-related bacteremia caused by methicillin-resistant coagulase negative staphylococci with elevated minimal inhibitory concentration for vancomycin. Pediatr Infect Dis J. 2010 Nov;29(11):1047-8.
6. Faraci M, Lanino E, Morreale G, Giardino S, Fossati M, Moroni C, Caviglia I, Castagnola E. Bacteremias and invasive fungal diseases in children receiving etanercept for steroid-resistant acute GVHD. Bone Marrow Transplant. 2011 Jan;46(1):159-60.
7. Caselli D, Cesaro S, Ziino O, Zanazzo G, Manicone R, Livadiotti S, Cellini M, Frenos S, Milano GM, Cappelli B, Licciardello M, Beretta C, Aricò M, Castagnola E; Infection Study Group of the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP). Multidrug resistant Pseudomonas aeruginosa infection in children undergoing chemotherapy and hematopoietic stem cell transplantation. Haematologica. 2010 Sep;95(9):1612-5.
8. Castagnola E, Furfaro E, Caviglia I, Licciardello M, Faraci M, Fioredda F, Tomà P, Bandettini R, Machetti M, Viscoli C. Performance of the galactomannan antigen detection test in the diagnosis of invasive aspergillosis in children with cancer or undergoing haemopoietic stem cell transplantation. Clin Microbiol Infect. 2010 Aug;16(8):1197-203.
9. Viscoli C, Castagnola E. Geoclimatic factors and invasive aspergillosis after allogeneic hematopoietic stem cell transplantation: new perspectives for patient management? Clin Infect Dis. 2010 Jun 15;50(12):1598-600.
10. Prigione I, Castagnola E, Imberti L, Gambini C, Gradoni L, Dianzani U, Ramenghi U, Giacopelli F, Moretta A, Moretta L, Plebani A, Fischer A, Pistoia V. Multiple relapses of visceral leishmaniasis in an adolescent with idiopathic CD4+ lymphocytopenia associated with novel immunophenotypic and molecular features. Pediatr Infect Dis J. 2009 Feb;28(2):161-3.

IMMUNOHEMATOLOGY AND TRANSFUSION CENTRE

DIRECTOR: Gino Tripodi

STAFF
Francesca Cottalasso
Cinzia Lo Giudice
Marina Martinengo
Mariapina Montera
Marco Risso
Fulvia Sindaco

MAIN RESEARCH ACTIVITIES YEAR 2011

Selection of CD4 + and CD8 + T lymphocyte donors by apheresis for the prevention and treatment of intercurrent infections in patients transplanted with hematopoietic stem cells (HSCs); selection of Natural Killer lymphocyte donors by apheresis for the prevention and treatment of patients transplanted with HSCs; validation of protocols for the collection and selection of pathogen-specific CD4 + and CD8 + T lymphocytes (anti-CMV, EBV, adenovirus) in healthy donors; validation of protocols for the collection and selection of Natural Killer lymphocytes in healthy donors; assessment of immunomodulatory effects of apheretic procedures in healthy subjects and in patients with autoimmune diseases.

RESEARCH PROGRAM YEAR 2012

Development of GMP-approved protocols for the collection and selection of pathogen-specific CD4 + and CD8 + lymphocytes (anti-CMV, EBV, adenovirus) in healthy donors and definition of the production parameters of the cell product for clinical use; Development of GMP-approved protocols for the collection and selection of Natural Killer cells in healthy donors and definition of the production parameters of the cell product for clinical use,; evaluation of the immunomodulatory effects of apheretic procedures in healthy subjects and in patients with autoimmune diseases (continuation); study of the clinical effects of erythrocytes loaded with corticosteroids in the therapy of pediatric diseases (cystic fibrosis, nephrotic syndrome).Role of polymorphisms in the IL12 receptor in pediatric diseases.

MAJOR COLLABORATIONS

- Histology - Department of Experimental Medicine, University of Genoa
- IBMDR Italian Bone Marrow Donor Registry – Genoa
- Clinical Immunology - University of Genoa
- Regional Network of Transfusion Services

MAIN PUBLICATIONS YEARS 2009-2011

1. Corrias MV, Pistorio A, Cangemi G, Tripodi G, Carlini B, Scaruffi P, Fardin P, Garaventa A, Pistoia V, Haupt R. Detection of cell-free RNA in children with neuroblastoma and comparison with that of whole blood cell RNA. Pediatr Blood Cancer. 2010 Jul 1;54(7):897-903.
2. Motta M, Testa M, Tripodi G, Radicioni M. Changes in neonatal transfusion practice after dissemination of neonatal recommendations. Pediatrics. 2010 Apr;125(4):e810-7. Epub 2010 Mar 29.
3. Li Pira G, Ivaldi F, Moretti P, Risso M, Tripodi G, Manca F. Validation of a miniaturized assay based on IFNg secretion for assessment of specific T cell immunity. J Immunol Methods. 2010 Apr 15;355(1-2):68-75. Epub 2010 Mar 1.
4. Ghio M, Contini P, Setti M, Ubezio G, Mazzei C, Tripodi G. sHLA-I contamination, a novel mechanism to explain ex vivo/in vitro modulation of IL-10 synthesis and release in CD8(+) T

lymphocytes and neutrophils following intravenous immunoglobulin infusion. J Clin Immunol. 2010 May;30(3):384-92. Epub 2010 Feb 2.

5. Ratto GB, Costa R, Maineri P, Alloisio A, Piras MT, Agostino A, Tripodi G, Rivabella L, Dozin B, Bruzzi P, Melioli G. Neo-adjuvant chemo/immunotheraphy in the treatment of stage III (N2) non-small cell lung cancer: a phase I/II pilot study. Int J Immunopathol Pharmacol. 2011 Oct;24(4):1005-1016.
6. Corrias MV, Haupt R, Carlini B, Cappelli E, Giardino S, Tripodi G, Tonini GP, Garaventa A, Pistoia V, Pistorio A. Multiple target molecular monitoring of bone marrow and peripheral blood samples from patients with localized neuroblastoma and healthy donors. Pediatr Blood Cancer. 2012 Jan;58(1):43-9. doi: 10.1002/pbc.22960. Epub 2011 Jan 19.
7. Pierelli L, Perseghin P, Marchetti M, Accorsi P, Fanin R, Messina C, Olivieri A, Risso M, Salvaneschi L, Bosi A; for Società Italiana Di Emaferesi and Manipolazione Cellulare (SIDEM) and Gruppo Italiano Trapianto Midollo Osseo (GITMO). Best practice for peripheral blood progenitor cell mobilization and collection in adults and children: results of a Società Italiana Di Emaferesi e Manipolazione Cellulare (SIDEM) and Gruppo italiano Trapianto Midollo Osseo (GITMO) consensus process. Transfusion. 2011 Oct 7. doi: 10.1111/j.1537-2995.2011.03385.x.

SURGERY

Prof. Vincenzo Jasonni

SURGERY
(University)

Vincenzo Jasonni

INTENSIVE CARE

Pietro Tuo

NEUROSURGERY

Armando Cama

OPHTHALMOLOGY

Paolo Capris

DENTISTRY

Roberto Servetto
(pro-tempore)

ORTHOPEDICS

Silvio Boero
(pro-tempore)

OTOLARYNGOLOGY

Vincenzo Tarantino

NEUROSURGERY

DIRECTOR: Armando Cama

STAFF
Valeria Capra
Patrizia De Marco
Samantha Mascelli
Elisa Merello
Alessandro Raso

MAIN RESEARCH ACTIVITIES YEAR 2011

- Correlation between clinical-pathological features and gene expression profile in pediatric tumors of glial origin
- Stabilization of primary brain tumors cell lines
- Biological characterization of brain tumor initiating cells and their treatment-resistance features.
- Role of the Planar Cell Polarity (PCP) genes in the pathogenesis of the Neural Tube Defects (NTDs)
- Polymorphisms of genes involved in the folate metabolism and risk of NTDs
- Development of molecular diagnostics systems for neuro-oncology and for the primary prevention of NTDs.

RESEARCH PROGRAM YEAR 2012

- Identification of molecular markers in patients affected by low grade gliomas with rapid progression versus patients with spontaneous and durable stabilization.
- Biological characterization of brain tumor initiating cells and their treatment-resistance features.
- Massively parallel whole exome sequencing (WES) of familial cases of NTDs.
- Development of molecular diagnostics systems for neuro-oncology, for primary prevention of Neural Tube Defects and familial cases of multiple cerebral cavernomatosis

MAJOR COLLABORATIONS

- SIOP LGG Preclinical Working Group
- Prof.Alessandro Verri, DISI, University of Genoa
- Dott Guido Frosina, IST-S.Martino, Genoa
- Dott. Kibar Zoha, CHU Sainte Justine Research Center, Montreal, Canada
- Dott. Torban Elena, Department of Medicine, Mc Gill University, Montreal, Canada,
- Dott. Garcia-Barcelo Maria Mercedes., University of Hong Kong, China

MAIN PUBLICATIONS YEARS 2009-2011

1. Bosoi CM, et al. Hum Mut 2011 Dec; 32(12):1371-1375.
2. Seo JH, et al. Hum Mol Genet 2011 Nov 15;20(22):4324-4333.
3. De Marco P, et al. Biofactor 2011 Jul;37(4):261-268
4. Kibar Z, et al. Clin Genet. 2011 Jul;80(1):76-82.
5. Raso A, et al., J Clin Lab Anal. 2011 Nov;25(6):389-94.
6. Raso A, et al., Neuro Oncol. 2011 May;13(5):500-8.
7. De Marco P, et al.,Eur J Med Genet. 2011 Sep-Oct;54(5).
8. Raso A, et al., Diagn Mol Pathol. 2010 Jun;19(2):78-82.
9. Kibar Z, et al. Hum Mutat. 2009 Jul;30(7):E706-15.

PEDIATRIC SURGERY

DIRECTOR: Vincenzo Jasonni
(University)

STAFF
Stefano Avanzini
Giovanni Maria Bisio
Piero Buffa
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Silvio Ferretti
Giuseppe Fratino
Edoardo Guida
Girolamo Mattioli
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Alberto Michelazzi
Manuela Mosconi
Ludovico Muller
Alessio Pini Prato
Luca Pio
Emilio Podestà
Valentina Rossi
Fabio Sanfilippo
Pierluigi Scarsi
Michele Torre

MAIN RESEARCH ACTIVITIES YEAR 2011

Research has been mainly focused on Intestinal Dysganglionoses and, in particular, on Hirschsprung's disease. Our Unit represents an Italian and international referral centre for this disease. Since the early 60s, we have been performing advanced basic and clinical research. In December 2010, we started a multicentric multidisciplinary research project funded by the Italian Ministry of Health (GR-2008-1135082) entitled "*Hirschsprung's disease as a model of neuro-immune dysfunctions in the gut: role of RET proto-oncogene in the correct development and maintenance of microbial homeostasis*". The aim of our Unit is to identify the exact incidence of associated anomalies in Hirschsprung patients, which is suspected of being underestimated (Pini Prato et al, Medicine, 2009). During 2011, we enrolled over 100 patients. Sixty patients were completely screened for associated anomalies, that were identified in over 40% of cases. In the meanwhile, in collaboration with researchers from the Laboratory of Molecular Genetics of our Institution, the Laboratory of Experimental Immunology of the Humanitas Institute (Milan), the NIH of Bethesda (USA), and the University of Lisbon (Portugal), we are carrying out a complex multicentric research project involving molecular genetics, immunology, microbiology, and animal models to address the etiology of enterocolitis (the most serious complication of Hirschsprung's disease) and to improve its treatment and prevention.

RESEARCH PROGRAMME YEAR 2012

The GR-2008-1135082 research project will continue in 2012 until the complete phenotype definition of roughly 250-300 patients with Hirschsprung's disease. One of the most important aims of our project is to re-write the diagnostic algorithm of the disease and to identify the patients who deserve further diagnostic investigations. Basic research will be mainly focused on the etiological definition of enterocolitis. We will look for new mutations possibly presidposing to enterocolitis. Multicentric cooperation will allow the study of RET expression in tissue and circulating immune cells and the definition of RET role in immunity. Collaboration with NIH and the University of Lisbon will be useful for the metagenomic approach and animal model studies.

We will also implement further basic and clinical research projects focusing on other rare diseases such as Anorectal Malformation (ARM) and Poland Syndrome. We will address these diseases also in collaboration with other units. As we recently implemented the Gaslini Tracheal Team, laryngotracheal reconstruction and tissue engeneering will be addressed as well. Finally, oncology, minimally invasive surgery and new technologies will presumably represent a further field of research.

MAJOR COLLABORATIONS

- William J. Pavan, Senior Investigator, National Human Research Institute, NIH, Bethesda (USA)
- Gordon Alexander MacKinlay, Consultant Pediatric Surgeon, BAPS President, RHSC, Edinburgh, Scotland, UK
- Agostino Pierro, Professor of Pediatric Surgery, GOSH, London, UK
- Prem Puri, Newman Clinical Research Professor, Children's Research Centre, Our Lady's Children's Hospital, Dublin
- Keith Georgeson, Consultant Pediatric Surgeon, Birmingham Children Hospital (USA)
- Arnold Coran, Professor of Pediatric Surgery, Ann Arbor, Michigan (USA)

MAIN PUBLICATIONS YEARS 2009-2011

1. Pini Prato A, Rossi V, Fiore M, Avanzini S, Mattioli G, Sanfilippo F, Michelazzi A, Borghini S, Disma N, Montobbio G, Barabino A, Nozza P, Ceccherini I, Gimelli S, Jasonni V. Megacystis, megacolon, and malrotation: a new syndromic association? Am J Med Genet A. 2011 Aug;155A(8):1798-802.
2. Mattioli G, Pini-Prato A, Barabino A, Gandullia P, Avanzini S, Guida E, Rossi V, Pio L, Disma N, Mameli L, Mirta DR, Montobbio G, Jasonni V. Laparoscopic approach for children with inflammatory bowel diseases. Pediatr Surg Int. 2011 Aug;27(8):839-46.
3. Pini Prato A, Rossi V, Avanzini S, Mattioli G, Disma N, Jasonni V. Hirschsprung's disease: what about mortality? Pediatr Surg Int. 2011 May;27(5):473-8. Review.
4. Torre M, Guida E, Bisio G, Scarsi P, Piatelli G, Cama A, Buffa P. Risk factors for renal function impairment in a series of 502 patients born with spinal dysraphisms. J Pediatr Urol. 2011 Feb;7(1):39-43.
5. Avanzini S, Guida E, Conte M, Faranda F, Buffa P, Granata C, Castagnola E, Fratino G, Mameli L, Michelazzi A, Pini-Prato A, Mattioli G, Molinari AC, Lanino E, Jasonni V. Shifting from open surgical cut down to ultrasound-guided percutaneous central venous catheterization in children: learning curve and related complications. Pediatr Surg Int. 2010 Aug;26(8):819-24.
6. Pini-Prato A, Mattioli G, Giunta C, Avanzini S, Magillo P, Bisio GM, Jasonni V. Redo surgery in Hirschsprung disease: what did we learn? Unicentric experience on 70 patients. J Pediatr Surg. 2010 Apr;45(4):747-54.
7. Torre M, Baban A, Buluggiu A, Costanzo S, Bricco L, Lerone M, Bianca S, Gatti GL, Sénès FM, Valle M, Calevo MG. Dextrocardia in patients with Poland syndrome: phenotypic characterization provides insight into the pathogenesis. J Thorac Cardiovasc Surg. 2010 May;139(5):1177-82.
8. Mattioli G, Avanzini S, Pini-Prato A, Buffa P, Guida E, Rapuzzi G, Torre M, Rossi V, Montobbio G, Rosati U, Jasonni V. Risk management in pediatric surgery. Pediatr Surg Int. 2009 Aug;25(8):683-90.
9. Mattioli G, Palomba L, Avanzini S, Rapuzzi G, Guida E, Costanzo S, Rossi V, Basile A, Tamburini S, Callegari M, DellaRocca M, Disma N, Mameli L, Montobbio G, Jasonni V. Fast-track surgery of the colon in children. J Laparoendosc Adv Surg Tech A. 2009 Apr;19 Suppl 1:S7-9.
10. Pini Prato A, Musso M, Ceccherini I, Mattioli G, Giunta C, Ghiggeri GM, Jasonni V. Hirschsprung disease and congenital anomalies of the kidney and urinary tract (CAKUT): a novel syndromic association. Medicine (Baltimore). 2009 Mar;88(2):83-90.

INTENSIVE CARE

DIRECTOR: Pietro Tuo

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Alessia Franceschi
Sara Frontalini
Alberto Gandolfo
Paola Grasso
Claudia Grattarola
Sonia Inglese
Svetlana Kotzeva
Elisabetta Lampugnani
Mario Lattere
Leila Mameli
Giovanni Montobbio
Andrea Moscatelli
Federica Panello
Lara Petrucci
Franco Puncuh
Laura Ressia
Alessandro Simonini
Saverio Talia
Miriam Tumolo
Renato Vallarino
Maria Enrica Zamorani
Clelia Zanaboni

MAIN RESEARCH ACTIVITIES YEAR 2011

A multi-site RCT comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants (The GAS Study). This trial is aimed at determining whether regional and general anaesthesia, given to infants undergoing inguinal hernia repair, result in equivalent neurodevelopmental outcomes. Recruitment started in 2008 and is expected to be concluded before the end of 2012. 27 pediatric hospitals in 7 countries are actively recruiting 700 neonates. Neurodevelopmental assessment will occur at 2 and 5 years of age with standard neuropsychological tools. Apnoea events and related interventions will also be studied.

RESEARCH PROGRAM YEAR 2012

Recruitment of patients for the GAS Study will be concluded by the end of 2012 with early outcomes as postanesthesia apnoea and recovery data available for publication. In the meantime, patients will be assessed for the 2-year follow-up neurodevelopmental outcome, which

will be concluded by the end of 2014. This study will provide convincing evidence of the potential neurotoxicity of general anesthetics administered in the early stages of life.

MAJOR COLLABORATIONS

- Royal Children's Hospital, and Murdoch Childrens Research Institute, Melbourne, Australia
- Children's Hospital Boston, Boston, US
- Royal Hospital for Sick Children, Glasgow, UK
- Montreal Children's Hospital, Quebec, Canada

MAIN PUBLICATIONS YEARS 2009-2011

1. Disma N, Mameli L, Pini-Prato A, Montobbio G. One lung ventilation with Arndt pediatric bronchial blocker for thoracoscopic surgery in children: a unicentricexperience. Pa ediatr Anaesth. 2011 Apr;21(4):465-7.
2. Disma N, Frawley G, Mameli L, Pistorio A, Alberighi OD, Montobbio G, Tuo P. Effect of epidural clonidine on minimum local anesthetic concentration (ED50) of levobupivacaine for caudal block in children. Paediatr Anaesth. 2011 Feb;21(2):128-35.
3. Pini Prato A, Rossi V, Fiore M, Avanzini S, Mattioli G, Sanfilippo F, Michelazzi A, Borghini S, Disma N, Montobbio G, Barabino A, Nozza P, Ceccherini I, Gimelli S, Jasonni V. Megacystis, megacolon, and malrotation: a new syndromic association? Am J Med Genet A. 2011 Aug;155A(8):1798-802.
4. Røeggen II, Olischar M, Davidson A, Disma N. Sleep and the EEG in infants. Paediatr Anaesth. 2010 Apr;20(4):368-9.

OPHTHALMOLOGY

DIRECTOR: Paolo Capris

STAFF
Camicione Paola
De Marco Riccardo
Panarello Simona
Priolo Enrico
Sburlati Carlo
Spaletra Enrica

MAIN RESEARCH ACTIVITIES YEAR 2011

Morphological modifications and variability of the optic disc and nerve fibre layer thickness in patients affected by Sturge Weber syndrome with ocular involvement and glaucoma were studied. The morphological modifications seem not to be related with glaucoma even if a significant difference is present between the normal and the affected eye of the same patient. The functional damage, evaluated by perimetric fast threshold strategies, is studied.
The evaluation of threshold estimation by these strategies has to be confirmed in pediatric patients.
Clinical evaluation of the efficacy of the infrared retinography in detecting the early signs of retinal involvement in neurofibromatosis. Choroidal nodules represent an early involvement that may lead to a more precise diagnosis and prognostic assessment.

RESEARCH PROGRAM YEAR 2012

- An Italian multidisciplinary clinic for Wolfram Syndrome
- Morphological modifications and variability of the optic disc of nerve fibre layer thickness in patients affected by Sturge Weber syndrome
- Multidisciplinary project for visual rehabilitation in patients with multiple handicaps
- Clinical, neuroimaging and molecular studies by next generation Sequencing of midline brain abnormalities associated with pituitary hormone deficiencies: a multi-disciplinary network

MAJOR COLLABORATIONS

- Istituto David Chiossone , Genoa, Italy
- Department of Ofthalmology, University of Genoa
- Dept of Ophthalmology, University of Lausanne, Switzerland

MAIN PUBLICATIONS YEARS 2009-2011

1. Barabino Arrigo, Gandullia Paolo, Calvi A, Vignola Silvia, Arrigo Serena, De Marco Riccardo. Sudden blidness in a child with Crohn's disease WORLD J GASTROENTERO 2011;17(38):4344-6.
2. Iester M, Capris E, De Feo F, Polvicino M, Brusini P, Capris Paolo, et Al. Agreement to detect glaucomatous visual field progression by using three different methods: a multicentre study BRIT J OPHTHALMOL 2011;95:1276-83.
3. Barabino Arrigo, Gandullia Paolo, Calvi A, Vignola Silvia, Arrigo Serena, De Marco Riccardo Sudden blidness in a child with Crohn's disease. WORLD J GASTROENTERO 2011;17(38):4344-6.
4. Iester M, Capris E, De Feo F, Polvicino M, Brusini P, Capris Paolo, et Al. Agreement to detect glaucomatous visual field progression by using guided progression analysis and Hump BRIT J OPHTHALMOL 2011 6357.

5. Camicione P, Fodor E, Panarello S, Barbino S Retinal peripapillary nerve fiber layer thickness in a 13 year old boy with neuromyelitis optica EUR J OPHTHALMOL 2010.
6. Bernardini FP, Rose GE, Cruz AA, Priolo E Gross enophthalmos after cerebrospinal fluid shunting for childhood hydrocephalus: "the silent brain sindrome" OPTHAL PLAST RECONSTR SURG 2009 Nov-Dic 25(26).
7. Leoncini G, Signorello MG, Segantin A, Giacobbe E, Armani U, Piana A, Camicione P In retinal vein occlusion platelet response to thrombin is increased THROMB RES 2009 Aug 4.

ORTHOPEDICS AND TRAUMATOLOGY

DIRECTOR (PRO-TEMPORE): Silvio Boero

STAFF
Andaloro Antonio
Becchetti Flavio
Catena Nunzio
Di Stadio Mauro
Famà Paolo
Gregorio Sandro
Marrè Brunenghi Giorgio
Michelis Maria Beatrice
Senes Filippo Maria

MAIN RESEARCH ACTIVITIES YEAR 2011

- Study of the bone-metal interface in vertebral implants: the analysis of the stabilization devices for vertebral arthrodesis, subsequently removed in part or completely, and the study of the characteristics of bone directly in contact with the devices have permitted to verify the compatibility of commonly used systems.
- Selective delayed Neurotization in obstetrical and traumatic injuries of the brachial plexus during childhood: the study was conducted to verify the reliability of nerve surgery techniques (selective neurotization) in brachial plexus palsy, when performed a considerable period of time after the event.
- Retrospective study of axial correction and limb lengthening in patients affected by osteochondrodysplasia: the review of case series and the application of surgical methods in different groups of patients has made it possible to establish some parameters for growth definition during guided bone regeneration.

RESEARCH PROGRAM YEAR 2012

- Morphological changes of the fibrocartilage and ligaments in spine and foot: the analysis of the anatomical components will be correlated to the radiographic findings, to the clinical evaluation and to the skeletal development at medium and long-term follow-up.
- Application of selective delayed neurotization in early childhood: the previous research confirmed the reliability of nerve transfer techniques with satisfactory clinical results (publication in press). In 2012, the study will focus on the possibility of extending the procedure over a longer period of time using different nerve trunks.
- Skeletal growth prediction after axial correction and limb lengthening in the osteochondrodysplastic patients: the study will assess the extent of bone elongation and the time needed for consolidation in different age groups.

MAJOR COLLABORATIONS

- Dept. of Applied Mechanics (DI.MEC.) University of Genova
- Microsurgery unit, CTO, Torino
- Orthopedic Clinic, University of Turin, Turin

BEST SCIENTIFIC PUBLICATIONS (2006-2011)

1. Boero S, Michelis MB, Calevo MG, Stella M.: Multiple forearm diaphyseal fracture: reduction and plaster cast control at the end of growth.Int Orthop. 2007 Dec;31(6):807-10. Epub 2006 Nov 16.

2. Campus R, Di Rocco M, Sementa AR, Senes FM, Magillo P, Dodero P.: Gastric fibroid polyp in a 4-month-old girl with Costello sindrome; Pediatr Med Chir. 2007 Sep-Oct;29(5):267-9.
3. Senes FM, Campus R, Becchetti F, Catena N: Lower limb nerve injuries in children; Microsurgery;2007;27(1): 32-36.
4. Marrè-Brunenghi G, Camoriano R, Valle M, Boero S.: The psoas muscle as cause of low back pain in infantile cerebral palsy. J Orthop Traumatol. 2008 Mar;9(1):43-7. Epub 2008 Mar 13.
5. Boero S, Sénès FM, Catena N.: Pediatric cubital tunnel syndrome by anconeus epitrochlearis: a case report. -J Shoulder Elbow Surg. 2009 Mar-Apr;18(2):e21-3.
6. Catena N, Sénès FM.: Obstetrical chondro-epiphyseal separation of the distal humerus: a case report and review of literature. -J Perinat Med. 2009 Jul;37(4):418-419.
7. Senes FM, Campus R, Becchetti F, Catena N : Sciatic nerve injection palsy in the child: Early microsurgical treatment and long-term results. Microsurgery. 2009;29(6):443-8
8. Senes FM, Campus R, Becchetti F, Catena N.: Upper limb nerve injuries in developmental age. Microsurgery. 2009;29(7):529-35.
9. Torre M, Baban A, Buluggiu A, Costanzo S, Bricco L, Lerone M, Bianca S, Gatti GL, Sénès FM, Valle M, Calevo MG.: Dextrocardia in patients with Poland syndrome: phenotypic characterization provides insight into the pathogenesis.J Thorac Cardiovasc Surg. 2010 May;139(5):1177-82.
10. Baban A, Torre M, Costanzo S, Gimelli S, Bianca S, Divizia MT, Sénès FM, Garavelli L, Rivieri F, Lerone M, Valle M, Ravazzolo R, Calevo MG.: Familial Poland anomaly revisited.Am J Med Genet A. 2011 Nov 22. doi: 10.1002/ajmg.a.34370. [Epub ahead of print]

MAIN PUBLICATIONS YEARS 2009-2011

1. Boero S, Sénès FM, Catena N.: Pediatric cubital tunnel syndrome by anconeus epitrochlearis: a case report. -J Shoulder Elbow Surg. 2009 Mar-Apr;18(2):e21-3.
2. Catena N, Sénès FM.: Obstetrical chondro-epiphyseal separation of the distal humerus: a case report and review of literature. -J Perinat Med. 2009 Jul;37(4):418-419.
3. Senes FM, Campus R, Becchetti F, Catena N : Sciatic nerve injection palsy in the child: Early microsurgical treatment and long-term results. Microsurgery. 2009;29(6):443-8.
4. Senes FM, Campus R, Becchetti F, Catena N.: Upper limb nerve injuries in developmental age. Microsurgery. 2009;29(7):529-35.
5. Torre M, Baban A, Buluggiu A, Costanzo S, Bricco L, Lerone M, Bianca S, Gatti GL, Sénès FM, Valle M, Calevo MG.: Dextrocardia in patients with Poland syndrome: phenotypic characterization provides insight into the pathogenesis.J Thorac Cardiovasc Surg. 2010 May;139(5):1177-82.
6. Baban A, Torre M, Costanzo S, Gimelli S, Bianca S, Divizia MT, Sénès FM, Garavelli L, Rivieri F, Lerone M, Valle M, Ravazzolo R, Calevo MG.: Familial Poland anomaly revisited.Am J Med Genet A. 2011 Nov 22. doi: 10.1002/ajmg.a.34370. [Epub ahead of print].
7. Boero S, Michelis MB, Riganti S. Use of eight Plate for angular correction of knee deformities due to idiopathic and pathologic physis:initiating treatment according to etioogy J. Child Orthop (2011) 5:209-216.
8. Mantero E. Carbone M, Calevo Mg, Boero S.: Diagnosis and treatment of pediartric chronic osteomyelitis in developing countries: prospective study of 96 patients treated in Kenya Musculoskeletal Surg (2011) 95:-13-18.

DENTISTRY

DIRECTOR (PRO-TEMPORE): Roberto Servetto

STAFF
Laura Ailunno
Enrico Calcagno

MAIN RESEARCH ACTIVITIES YEAR 2011

Outpatient care:

- dental examination;
- orthodontic examination;
- dental prevention (sealants, fluorine applications, health care education, oral hygiene); conservative and endodontic treatment of caries in deciduous and permanent teeth;
- dental extraction;
- therapy of gingival and parodontal diseases;
- functional and fixed multibracket orthodontic treatment;
- orthodontic treatment in craniofacial malformations;
- removable and fixed functional appliances;
- pediatric oral surgery;
- osteointegrated implantology.

These outpatient care services are also offered to the disabled patient, under general anesthesia when the patient is not collaborating. Consultation activity and dental treatment are performed for other hospital units of the Gaslini Institute.
Surgery is performed in the operating room of the ENT unit and of the Hematology/Oncology unit-Ophthalmology unit. About 50 surgical operations under general anesthesia are performed every year, both scheduled and on an emergency basis.

MAJOR COLLABORATIONS

- Regional and national centres for disabled (CEPIM, ANFASS)
- SIOH (Italian Society of Orthodontics for Disabled)
- SIDO (Italian Society of Orthodontics)
- SILPS (Italian Society of Labiopalatoschisis and Craniofacial Syndromes)
- ANDI (National Association of Italian Dentists)
- SIP (Italian Society of Pediatrics)
- SIC (Italian Society of Celiac Disease)
- Odontostomatology unit, Galliera Hospital, Genoa
- Maxillofacial Surgery, Galliera Hospita, Genoa

OTORHINOLARYNGOLOGY

DIRECTOR: Vincenzo Tarantino

STAFF
Roberto D'Agostino
Andrea Melagrana
Adelina Porcu
Mauro Stura

MAIN RESEARCH ACTIVITIES YEAR 2011

- Diagnosis, etiology and therapy of congenital malformations of upper airways and digestive tract.
- Characterization of tonsil infiltration and gene expression profile of toll–like receptors in PFAPA

RESEARCH PROGRAM YEAR 2012

- Pediatric laryngomalacia:from diagnosis to therapy. Five-year case series and follow-up
- Publication of research on PFAPA in an international journal.

MAJOR COLLABORATIONS

- ENT Audiology and Phoniatric Unit (Prof. Stefano Berettini), University of Pisa
- ENT Department CHCV Lausanne (CH) (Prof. Philippe Monnier)

MAIN PUBLICATIONS YEARS 2009-2011

1. R. D'Agostino et al :" Post Tonsillectomy late haemorrhage: is it a preferably night-time event?" Int. J. of Ped ORL 73 (2009/713-16) R. D'Agostino, V.Tarantino, M.G. Calevo: post-tonsillectonmy late haemorrhage: it is a preferably night- time event? Int. J. Ped Otorhinolaringology: 73,713,2009.
2. A.Raso, S.Mascelli, P.Nozza, R.Biassone, F. Negri, A.Garaventa, V.Tarantino. Detection of transplacental melanoma metastasis using quantitative PCR. Diagn. Mol. Pathol. 19.78.2010

CARDIOVASCULAR DISEASES

Dr. Lucio Zannini

CARDIOVASCULAR SURGERY

Lucio Zannini

CARDIOLOGY

Maurizio Marasini

CARDIOLOGY

DIRECTOR: Maurizio Marasini

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Alessandro Rimini
Alessandra Siboldi
Gianluca Trocchio
Giulia Tuo

MAIN RESEARCH ACTIVITIES YEAR 2011

Prenatal diagnosis of congenital heart disease, with the aim of defining the intrauterine evolution of each cardiac disease and of improving the perinatal and neonatal therapeutic management.

Postanatal diagnosis and treatment of congenital heart disease including interventional procedures.

RESEARCH PROGRAM YEAR 2012

Continuation of the same research activities of last year, focusing in particular on the possible correlation between congenital heart disease and genetic substrate.

MAJOR COLLABORATIONS

- S.Martino Hospital, Genoa, Italy
- San Donato Children's Hospital
- Asti Hospital
- NEM Hospital, Paris, France

MAIN PUBLICATIONS YEARS 2009-2011

1. Selective pulmonary artery embolization in two patients with single ventricle and acquired pulmonary vein occlusion.
   Bondanza S, Derchi M, Marasini M.Catheter Cardiovasc Interv. 2011 Jul 29. doi: 10.1002/ccd.23272. [Epub ahead of print]PMID: 21805598 [PubMed - as supplied by publisher].
2. Impact of prenatal diagnosis on outcome of pulmonary atresia and intact ventricular septum.
   Tuo G, Volpe P, Bondanza S, Volpe N, Serafino M, De Robertis V, Zannini L, Pongiglione G, Calevo MG, Marasini M. J Matern Fetal Neonatal Med. 2011 Jun 24. [Epub ahead of print]PMID: 21699439 [PubMed - as supplied by publisher].
3. Fetal interrupted aortic arch: 2D-4D echocardiography, associations and outcome.
   Volpe P, Tuo G, De Robertis V, Campobasso G, Marasini M, Tempesta A, Gentile M, Rembouskos G. Ultrasound Obstet Gynecol. 2010 Mar;35(3):302-9.PMID: 20069674 [PubMed - indexed for MEDLINE].
4. Subclinical cardiac dysfunction and exercise performance in childhood cancer survivors.
   De Caro E, Smeraldi A, Trocchio G, Calevo M, Hanau G, Pongiglione G.Pediatr Blood Cancer. 2011 Jan;56(1):122-6.PMID: 21058389 [PubMed - indexed for MEDLINE].
5. Stenting of aortic coarctation and exercise-induced hypertension in the young.
   De Caro E, Spadoni I, Crepaz R, Saitta M, Trocchio G, Calevo MG, Pongiglione G.Catheter Cardiovasc Interv. 2010 Feb 1;75(2):256-61. Erratum in: Catheter Cardiovasc Interv. 2010 Jun 1;75(7):1143. Mg, Calevo [corrected to Calevo, Maria Grazia]. PMID: 20095012 [PubMed - indexed for MEDLINE].

6. Familial transposition of the great arteries caused by multiple mutations in laterality genes.
De Luca A, Sarkozy A, Consoli F, Ferese R, Guida V, Dentici ML, Mingarelli R, Bellacchio E, Tuo G, Limongelli G, Digilio MC, Marino B, Dallapiccola B.Heart. 2010 May;96(9):673-7. Epub 2009 Nov 20.PMID: 19933292 [PubMed - indexed for MEDLINE].

7. Pacemaker implantation in a patient with persistent left superior vena cava using a steerable catheter-delivered lead.
Porcellini S, Rimini A, Biasi S.J Cardiovasc Med (Hagerstown). 2010 Mar 19. [Epub ahead of print]PMID: 20308913 [PubMed - as supplied by publisher].

8. Prevalence of the congenital long-QT syndrome.
Schwartz PJ, Stramba-Badiale M, Crotti L, Pedrazzini M, Besana A, Bosi G, Gabbarini F, Goulene K, Insolia R, Mannarino S, Mosca F, Nespoli L, Rimini A, Rosati E, Salice P, Spazzolini C. Circulation. 2009 Nov 3;120(18):1761-7. Epub 2009 Oct 19.PMID: 19841298 PubMed - indexed for MEDLINE].

9. Long-term results of catheter-based treatment of pulmonary atresia and intact ventricular septum.
Marasini M, Gorrieri PF, Tuo G, Zannini L, Guido P, Pellegrini M, Bondanza S, Calevo MG, Pongiglione G.Heart. 2009 Sep;95(18):1520-4. Epub 2009 May 28.PMID: 19482848 [PubMed - indexed for MEDLINE].

10. Prenatal diagnosis and outcome of isolated vascular rings.
Tuo G, Volpe P, Bava GL, Bondanza S, De Robertis V, Pongiglione G, Marasini M.Am J Cardiol. 2009 Feb 1;103(3):416-9. Epub 2008 Nov 27.PMID: 19166700 [PubMed - indexed for MEDLINE].

CARDIOVASCULAR SURGERY

DIRECTOR: Lucio Zannini

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Giuseppe Panizzon
Elena Ribera
Francesco Santoro
Nadia Vercellino
Alfredo Virgone

RESEARCH ACTIVITY YEAR 2011

Efficacy of fenoldopam mesylate in the control of splanchnic ischemia during extracorporeal circulation in pediatric patients
Principal investigator: Franco Lerzo
During CPB, some circulatory districts of the organism, in particular splanchnic and renal ones, are exposed to a higher risk of hypoperfusion determining organ dysfunction up to pictures of postoperative acute renal failure (ARF).
Several studies demonstrated that the mechanism underlying renal damage is insufficient oxygen availability (DO2), which probably triggers a condition of masked cardiocirculatory shock in which organ metabolic requiriments are supported by an anaerobic mechanism, with consequent lactic acidosis.
Objective of the study is to evaluate whether treatment with fenoldopam mesylate (0.2 γ/kg/min) is able to improve splanchnic district perfusion and to limit the onset of lactic acidosis during CPB in pediatric patients. Treatment will be considered effective if the percentage of patients with hyperlactatemia at the end of CPB is reduced from about 40%, i.e. the expected value according to our retrospective analysis, to 20%.
Secondary objectives: to evaluate variations of hourly diuresis during CPB and during the first 6 hours postoperatively; to evaluate variations of plasma lactates during the first 6 hours postoperatively.

Gene expression profile in advanced cardiac decompensation: identification and validation of new biomarkers
Principal investigator: Giuseppe Cervo
Cardiac decompensation is a disease of great importance both in children and in adults. Treatment of cardiac decompensation is based essentially on clinical criteria and on few objective early indicators, which are insufficient for an accurate timing of therapy. The identification of new more sensitive and specific biomarkers is essential to improve treatment of this disease.
Objective of the project is to identify new biomarkers starting from the analysis of gene expression profile of the cardiac muscle in children affected by cardiac decompensation in congenital cardiopathies and undergoing surgery in the Cardiovascular Surgery unit of the Istituto Gaslini. The study will be concluded with the measurement of gene expression profiles of cardiac tissue samples and the definition of groups of genes characterizing cardiac decompensation ("signature"). After performing the analysis *in silico*, the genes of cardiac decompensation signature potentially present in blood or urine that can therefore be tested in a large population of patients, adults included, will be selected. The Laboratory of Molecular Biology of the Istituto Gaslini will be responsible for the definition of gene expression profiles through microarray and for the validation and interpretation of results.

RESEARCH PROJECTS YEAR 2012

- Efficacy of fenoldopam mesylate in the control of splanchnic ischemia during extracorporeal circulation in pediatric patients
  Principal investigator: Franco Lerzo

Conclusion of the ongoing project within the first semester of 2012 after reaching a statistically significant number of patients and publication of results.

- Gene expression profile in advanced cardiac decompensation: identification and validation of new biomarkers
  Principal investigator: Giuseppe Cervo
  Continuation of cardiac tissue sample collection during heart surgery and study of gene expression profiles through microarray.

MAJOR COLLABORATIONS

- Prof. Pascal Vouhé, Hôpital Necker, Paris, France: Surgery for congenitally corrected transposition of the great arteries (double switch); aortic surgery (Ross technique); surgery for pulmonary atresia with DIV and MAPCA in neonatal age.
- Prof. Patrick Diner, Hôpital Trousseau, Paris, France: Maxillofacial plastic reconstructive surgery for cervicofacial malformative vascular disease.
- Prof. Claude Laurian, Hôpital Saint Joseph, Paris, France: Surgery of complex musculoskeletal vascular malformations.
- Dr. Michel Wassef, Hôpital Lariboisiere, Paris, France: Pathologic anatomy and cytology of complex vascular malformations.
- Cooperation projects year 2012
- Training of medical and nursing staffs and execution of cardiac surgery
- Kossovo – Pediatric Cardiology, Pristina Hospital and Ministry of Health of Kossovo
- Kurdistan – Sulimania Teaching Hospital and Ministry of Health of Kurdistan (in collaboration with Le Scotte Hospital of Siena, Italy).

MAIN PUBLICATIONS YEARS 2009-2011

1. The Scimitar Syndrome: An Italian Multicenter Study. Vladimiro L. Vida, Simone Speggiorin, Massimo A. Padalino, Giancarlo Crupi, Carlo Marcelletti, Lucio Zannini, Alessandro Frigiola, Alessandro Varrica, Duccio Di Carlo, Roberto Di Donato, Bruno Murzi, Massimo Bernabei, Giovanna Boccuzzo, Giovanni Stellin Ann.Thorac.Surg. 2009 Aug;88(2):440-4.
2. Tracheal compression by aberrant innominate artery: clinical presentations in infants and children, indications for surgical correction by aortopexy and short- and long-term outcome. Chiara Gardella, Donata Girosi, Giovanni A. Rossi, Michela Silvestri, Paolo Tomà°, Gianlauro Bava* and Oliviero Sacco J Ped Surgery 2010; 45,564-573.
3. Impact of prenatal diagnosis on outcome of pulmonary atresia and intact ventricular septum. Tuo G, Volpe P, Bondanza S, Volpe N, Serafino M, De Robertis V, Zannini L, Pongiglione G, Calevo MG, Marasini M. J Matern Fetal Neonatal Med. 2011 un 24. [Epub ahead of print]
4. Dexamethasone prophylaxis in pediatric open heart surgery is associated with increased blood long pentraxin PTX3: potential clinical implications. Lerzo F, Peri G, Doni A, Bocca P, Morandi F, Pistorio A, Carleo AM, Mantovani A, Pistoia V, Prigione I. Clin Dev Immunol. 2011:730828 Epub 2011 Jul 9.

DIAGNOSTIC IMAGING

RADIOLOGY

Gian Michele Magnano (pro-tempore)

PATHOLOGIC ANATOMY

Claudio Gambini

NEURORADIOLOGY

Andrea Rossi

NEUROradiology

DIRECTOR: Andrea Rossi

STAFF
Carlo Gandolfo
Giovanni Morana
Mariasavina Severino

MAIN RESEARCH ACTIVITIES YEAR 2011

Functional advanced MR imaging (diffusion, tractography, perfusion, spectroscopy, cortical activation) in pediatric CNS diseases with a special focus on brain tumor imaging and congenital malformations
Fetal MR imaging of CNS abnormalities
Interventional neuroradiology (special focus on vein of Galen and arteriovenous malformations)

RESEARCH PROGRAM YEAR 2012

Continuation of ongoing research lines
Participation in the project funded by the Ministry of Health entitled: "creation of an MRI database of pediatric subjects, healthy and affected by rare neurological diseases" (Coordinator: prof. Fabio Triulzi – E. Medea Institute)

MAJOR COLLABORATIONS

- Dr L. Castellan (A.O San Martino Genova): endovascular interventional neuroradiology consultations
- Starting Grant project, financed by the European Research Council, "Understanding the basis of cerebellar and brainstem congenital defects: from clinical and molecular characterization to the development of a novel neuroembryonic in vitro model", coordinated by Prof. E.M. Valente (IRCCS Istituto Mendel di Roma), involving multiple National centers including Ospedale Bambin Gesu' in Rome, IRCCS Stella Maris in Pisa, Istituto Neurologico Mondino in Pavia, and the Besta Institute in Milano.
- Collaboration with the Neuroradiology Unit of the Children's Hospital of Philadelphia for superspecialistic training in a structure where four 3 Tesla MR unit are presently installed.

MAIN PUBLICATIONS YEARS 2009-2011

1. Rego I, Severino M, Micalizzi C, Faraci M, Pende D, Dufour C, Aricò M, Rossi A. Neuroradiologic findings and follow-up with magnetic resonance imaging of the genetic forms of haemophagocytic lymphohistiocytosis with CNS involvement. Pediatr Blood Cancer. 2011 Nov 21. [Epub ahead of print]
2. De Marco P, Merello E, Rossi A, Piatelli G, Cama A, Kibar Z, Capra V. FZD6 is a novel gene for human Neural Tube Defects. Hum Mutat. 2011 Nov 1. doi: 10.1002/humu.21643. [Epub ahead of print]
3. Biancheri R, Zara F, Rossi A, Mathot M, Nassogne MC, Yalcinkaya C, Erturk O, Tuysuz B, Di Rocco M, Gazzerro E, Bugiani M, van Spaendonk R, Sistermans EA, Minetti C, van der Knaap MS, Wolf NI. Hypomyelination and congenital cataract: broadening the clinical phenotype. Arch Neurol. 2011 Sep;68(9):1191-4.
4. Briguglio M, Pinelli L, Giordano L, Ferraris A, Germano E, Micheletti S, Severino MS, Bernardini L, Loddo S, Tortorella G, Ormitti F, Gasparotti R, Cbcd-Sg TC, Rossi A, Valente EM. Pontine Tegmental Cap Dysplasia: developmental and cognitive outcome in three adolescent patients. Orphanet J Rare Dis. 2011 Jun 8;6(1):36.
5. Tappino B, Biancheri R, Mort M, Regis S, Corsolini F, Rossi A, Stroppiano M, Lualdi S, Fiumara A, Bembi B, Di Rocco M, Cooper DN, Filocamo M. Identification and characterization

of 15 novel GALC gene mutations causing Krabbe disease. Hum Mutat. 2010 Dec;31(12):E1894-914.

6. Cassandrini D, Biancheri R, Tessa A, Di Rocco M, Di Capua M, Bruno C, Denora PS, Sartori S, Rossi A, Nozza P, Emma F, Mezzano P, Politi MR, Laverda AM, Zara F, Pavone L, Simonati A, Leuzzi V, Santorelli FM, Bertini E. Pontocerebellar hypoplasia: Clinical, pathologic, and genetic studies. Neurology. 2010 Oct 19;75(16):1459-64.
7. Rossi A, Gandolfo C, Morana G, Severino M, Garrè ML, Cama A. New MR sequences (diffusion, perfusion, spectroscopy) in brain tumours. Pediatr Radiol. 2010 Jun;40(6):999-1009.
8. Severino M, Schwartz ES, Thurnher MM, Rydland J, Nikas I, Rossi A. Congenital tumors of the central nervous system. Neuroradiology. 2010 Jun;52(6):531-48.
9. Morana G, Biancheri R, Di Rocco M, Filocamo M, Marazzi MG, Pessagno A, Rossi A. Enhancing cranial nerves and cauda equina: an emerging magnetic resonance imaging pattern in metachromatic leukodystrophy and Krabbe disease. Neuropediatrics. 2009 Dec;40(6):291-4.
10. De Grandis E, Di Rocco M, Pessagno A, Veneselli E, Rossi A. MR Imaging Findings in 2 Cases of Late Infantile GM1 Gangliosidosis. AJNR Am J Neuroradiol. 2009 Aug;30(7):1325-7.

PATHOLOGIC ANATOMY

DIRECTOR: Claudio Gambini

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Fabiana Malaguti
Katia Mazzocco
Daniela Murgia
Francesca Negri
Paolo Nozza
Andrea Rossi
Giulio Roggero
Cesarina Savioli
Angela Rita Sementa
Martina Verroca

MAIN RESEARCH ACTIVITIES YEAR 2011

- Study of histological, immunohistochemical and biomolecular aspects of cases of neuroblastic tumor associated with opsoclonus-myoclonus syndrome
- Immunocytochemical study with anti-GD2 of medullary disease in children with neuroblastoma at onset, during and after treatment, in collaboration with other European centres
- N-Myc and 1p deletion study on a series of neuroblastic tumors in adults and adolescents
- Pathologic, biomolecular and genetic study on CNS tumors
- Anatomo-functional study of genes involved in neural tube formation in affected and healthy fetuses
- Pediatric adrenocortical tumors: morphological and immunohistochemical diagnostic criteria. Case series from the Italian Registry of Rare Pediatric Tumors
- Study of the characteristics of human NB cells infiltrating the bone marrow
- International study on a case series of NB with INPC group genotype-immunophenotype discordance.

RESEARCH PROGRAMME YEAR 2012

- Study of spontaneous abortion in the first trimester. Correlation between histo-morphological aspects and chromosomal anomalies determined with FISH and cytofluorimetry.
- Study on an Italian case series from the NB registry with NB at onset in adolescents and adults with biomolecular characterization.
- Study on an italian case series from the NB registry with congenital NB: morphological and biomolecular aspects
- Study of atypical Spitz tumors.
- Study of minimal residual disease in patients with neuroblastoma (at onset and in various disease phases) by immunocytochemical study with anti-GD2 antibody on samples of bone marrow aspirate, peripheral blood, and apheretic collections.
- Clinico-pathological immunohistochemical study and molecular characterization of mixed tumors/myoepitheliomas, bone juxtacortical tumors.
- Study on glucide metabolism during pregnancy: screening, diagnosis, etiopathogenesis, maternal and fetal follow-up; newborn management.
- Study of telomere length and telomerasic activity in oncologic and metabolic diseases.

MAJOR COLLABORATIONS

- SIOPEN-R-NET (European Society of Paediatric Oncology Neuroblastoma Research Network). Creation of a network for telematic sharing of main diagnostic aspects of cases characterized by higher complexity, rarity and/or therapeutic and scientific impact among participating centres:
  Univ. Clinic of Pathology, Wahringer Gurtel 18-20, A-1090 Vienna, Dott. Gabriele Amann. Dept. of Pathology Rikshospitalet, Sognsvannsveien 20, N-0027 Oslo, Dott. Klaus Beiske Histopathology Pathology Dept. St. James's University Hospital, Beckett Street UK, Leeds LS9 7TF, Dott. Catherine Culinane
  Departamento de patologia, Facultad de medicina, Avda Blasco Ibanez 17, E-46010 Valencia, Dott. Samuel Navarro
  Service de Pathologie, Hopital Robert Debré, EA3102 Université Paris 7, 48 Boulevard Sérurier F – 75019 Paris, Prof. Michel Peuchmaur
- University of Padova and Anatomic Pathology Institute: soft tissue tumors and rare childhood tumors. Laboratory of Oncology: biological-molecular study of rhabdomyosarcoma and Ewing/PNET tumors
- Anatomic Pathology unit of Pini Orthopedic Institute of Milano: bone tumors
- King's College, University of London: liver disease.
- St. John's Hospital, University of London: skin disease.

- National Cancer Institute of Milan: pediatric renal tumors
- Anatomic Pathology, Dept. Experimental Medicine, Rome, Prof. F. Giangaspero: Oncologic neuropathology.
- Istitut fur Neuropathologie Sigmund-Freud-Strabe Bonn, Deutschland, Prof. T. Pietsch: Neuropathology.
- Childrens Hospital of Los Angeles, Dept. of Pathology, Prof. Hiro Shimada, Coordinator of INPC (International Neuroblastoma Pathology Committee).

MAIN PUBLICATIONS YEARS 2009-2011

1. Garrè ML, Cama A, Bagnasco F, Morana G, Giangaspero F, Brisigotti M, Gambini, C, Forni M, Rossi A, Haupt R, Nozza P, Barra S, Piatelli G, Viglizzo G, Capra V, Bruno W, Pastorino L, Massimino M, Tumolo M, Fidani P, Dallorso S, Schumacher RF, Milanaccio C, Pietsch T.
   Medulloblastoma variants: age-dependent occurrence and relation to Gorlin syndrome--a new clinical perspective.
   Clin Cancer Res. 2009 Apr 1;15(7):2463-71.
2. Pezzolo A, Rossi E, Gimelli S, Parodi F, Negri F, Conte M, Pistorio A, Sementa A, Pistoia V, Zuffardi O, Gambini C.
   Presence of 1q gain and absence of 7p gain are new predictors of local or metastatic relapse in localized resectable neuroblastoma.
   Neuro Oncol. 2009 Apr;11(2):192-200. Epub 2008 Oct 15.
3. Alaggio R, Cecchetto G, Bisogno G, Gambini C, Calabrò ML, Inserra A, Boldrini R, Salvo GL, G d'Amore ES, Dall'igna P.
   Inflammatory myofibroblastic tumors in childhood: a report from the Italian Cooperative Group studies.
   Cancer. 2009 Oct 22.
4. Passoni L, Longo L, Collini P, Coluccia AM, Bozzi F, Podda M, Gregorio A, Gambini C, Garaventa A, Pistoia V, Del Grosso F, Tonini GP, Cheng M, Gambacorti-Passerini C, Anichini A, Fossati-Bellani F, Di Nicola M, Luksch R.
   Mutation-independent anaplastic lymphoma kinase overexpression in poor prognosis neuroblastoma patients.
   Cancer Res. 2009 Sep 15;69(18):7338-46.
5. Gimelli S, Beri S, Drabkin HA, Gambini C, Gregorio A, Fiorio P, Zuffardi O, Gemmill RM, Giorda R, Gimelli G.
   The tumor suppressor gene TRC8/RNF139 is disrupted by a constitutional balanced translocation t(8;22)(q24.13;q11.21) in a young girl with dysgerminoma.
   Mol Cancer. 2009 Jul 30;8:52.
6. Haupt R, Garaventa A, Gambini C, Parodi S, Cangemi G, casale F, Viscardi E, Bianchi M, Prete A, Jenkner A, Luksch R, Di Catlado A, Favre C, D'Angelo P, Zanazzo GA, Arcamone G, Izzi GC, Gigliotti AR, Pastore G, De Bernardi B.
   Improved survival of childhood neuroblastoma between 1979 and 2005: a report of the Italian Neuroblastoma Regristry.
   Journal of Clincial Oncology 2009.
7. Maria Valeria Corrias, Claudio Gambini, Andrea Gregorio, Michela Croce, Gaia Barisione, Claudia Cossu, Armando Rossello, Silvano Ferrini and Marina Fabbi
   Different subcellular localization of ALCAM molecules in neuroblastoma: Association with relapse
   Cellular Oncology 32 (2010) 77–86 77 DOI 10.3233/CLO-2009-0494 IOS Press.
8. Riccardo Haupt, Alberto Garaventa, Claudio Gambini, Stefano Parodi, Giuliana Cangemi, Fiorina Casale, Elisabetta Viscardi, Maurizio Bianchi, Arcangelo Prete, Alessandro Jenkner, Roberto Luksch, Andrea Di Cataldo, Claudio Favre, Paolo D'Angelo, Giulio Andrea Zanazzo, Giampaolo Arcamone, Gian Carlo Izzi, Anna Rita Gigliotti, Guido Pastore, and Bruno De Bernardi
   Improved Survival of Children With Neuroblastoma Between 1979 and 2005: A Report of the Italian Neuroblastoma Registry
   Journal of clinical oncology.
9. Rita Alaggio, Giovanni Cecchetto, Gianni Bisogno, Claudio Gambini, Maria Luisa Calabro, Alessandro Inserra, Renata Boldrini, Gian Luca De Salvo, Emanuele D'Amore, Patrizia Dall'Igna
   Inflammatory Myofibroblastic Tumors in Childhood A Report From the Italian Cooperative Group Studies
   Cancer January 1, 2010.
10. Francesca Schena, Claudio Gambini, Andrea Gregorio, Manuela Mosconi, Daniele Reverberi, Marco Gattorno, Simona Casazza, Antonio Uccelli, Lorenzo Moretta, Alberto Martini and Elisabetta Traggia
    Derived Interferon-Dependent Inhibition of B Cell Activation by Bone Marrow Mesenchymal Stem Cells in a Murine Model of Systemic Lupus Erythematosus
    ARTHRITIS & RHEUMATISM Vol. 62, No. 9, September 2010, pp 2776–2786
    DOI 10.1002/art.27560 © 2010, American College of Rheumatology.

RADIOLOGY

DIRECTOR: Gian Michele Magnano

STAFF
Maria Beatrice Damasio
Mirella Ghiorzi
Claudio Giuseppe Granata
Giorgio Lucigrai
Francesca Magnaguagno
Anna Marzoli
Francesca Nardi
Francesca Rizzo
Nicola Stagnaro
Maura Maria Valle
Elisabetta Vignale

MAIN RESEARCH ACTIVITIES YEAR 2011

- New imaging techniques in the evaluation of chronic rheumatic diseases in children
- MR urography with functional evaluation of kidney activity in children with nephrourologic diseases

RESEARCH PROGRAM YEAR 2012

- New imaging techniques in the evaluation of chronic rheumatic diseases in children (continuation)
- MR urography with functional evaluation of kidney activity in children with nephrourologic diseases (continuation)

MAJOR COLLABORATIONS

- Prof. Andrew Taylor (UCL, Professor in Cardiovascular Imaging), Cardiac-MRI unit of Great Ormond Street Hospital (GOSH) , London
- Siemens collaboration project: IVU and optimization of radiation dose in pediatric patients
- Prof A. Dacher, Department of Diagnostic Imaging Rouen University de France: MR Urography with functional evaluation
- Participation in Euronet PHL-C1 add on study on WholeBody Magnetic Resonance Imaging in Hodgkin Lymphoma (Coordinator Rutger J. Nievelstein, Utrecht, NL)
- Member of the commission of SIOPEN (International Society of Paediatric Oncology European Neuroblastoma) dedicated to writing, implementation and diffusion of Neuroblastoma Diagnostic Imaging Guidelines
- Member of ESPR (European Society of Pediatric Radiology) oncologic task force
- Member of European Excellence Network on Pediatric Radiology Research of ESPR (European Society of Pediatric Radiology)
- Member of ESPR Uroradiology Force (Coordinator Prof Michael Riccabona)

MAIN PUBLICATIONS YEARS 2009-2011

1. Development and preliminary validation of a paediatric-targeted MRI scoring system for the assessment of disease activity and damage in juvenile idiopathic arthritis
   Clara Malattia, Maria Beatrice Damasio, Angela Pistorio, Maka Ioseliani, Iris Vilca, Maura Valle, Nicolino Ruperto, Stefania Viola, Antonella Buoncompagni, Gian Michele Magnano, Angelo Ravelli, Paolo Tomà, Alberto Martini
   Ann Rheum Dis (2011);70:440–446

2. Invasive mould infections in newborns and children
Elio Castagnola, Maura Faraci, Francesca Fioredda, Loredana Amoroso, Francesco Risso, Alessia Franceschi, Roberto Bandettini, Gian Michele Magnano, Alessio Pini Prato, Chiara Gardella, Serena Arrigo, Marco Gattorno, Giorgio Piaggio, Antonella Ciucci, Ines Lorenzi, Anna Loy, Riccardo Haupt
Early Human Development xxx (2011) xxx–xxx
EHD-03392; No of Pages 3 © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.earlhumdev.2011.01.015

3. Multislice CT in congenital bronchopulmonary malformationsin children
La TC multistrato nello studio delle malformazioni congenite broncopolmonari in età pediatrica
P. Tomà, F. Rizzo, N. Stagnaro, G. Magnano, C. Granata
Radiol med (2011) 116:133–151

4. HHV-8-related visceral Kaposi_s sarcoma following allogeneic HSCT: Report of a pediatric case and literature review
Ilaria Sala, Maura Faraci, Gian M.Magnano, Angela Sementa, Eddi di Marco, Alberto Garaventa, Concetta Micalizzi, Edoardo Lanino, Giuseppe Morreale, Cristina Moroni and Elio Castagnola
Pediatr Transplantation (2011): 15: E8–E11

5. Paediatric musculoskeletal US beyond the hip joint
Carlo Martinoli, Maura Valle, Clara Malattia, Maria Beatrice Damasio, Alberto Tagliafico
Pediatr Radiol (2011) 41 (Suppl 1):S113–S124

6. Guidelines for Imaging and Staging of Neuroblastic Tumors: Consensus Report from the International Neuroblastoma Risk Group Project
Hervé J. Brisse, M. Beth McCarville, Claudio Granata, K. Barbara Krug
Radiology. (2011) Oct;261(1):243-57. Epub 2011 May 17.

7. The paediatric wrist revisited: redefining MR fi ndings in healthy children
Lil-Sofi, Ording Müller, D Avenarius, B Damasio, O P Eldevik, C Malattia
Ann Rheum Dis (2011);70:605–610

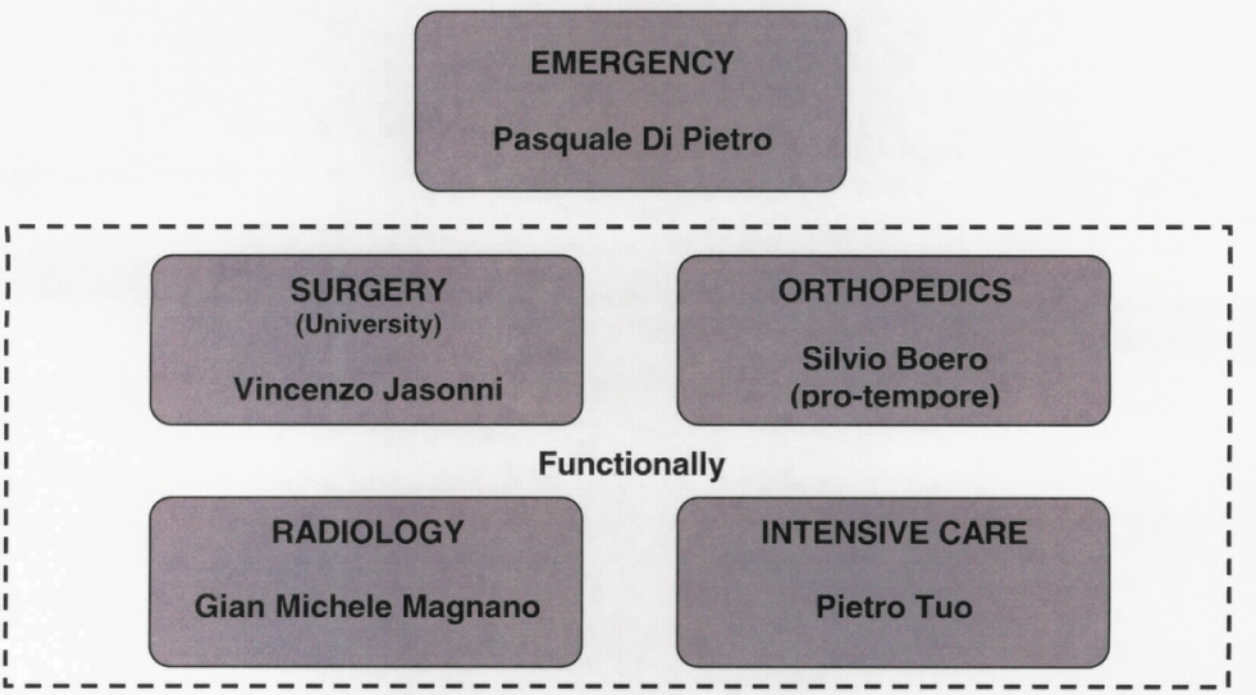
8. Gaslini's tracheal team: preliminary experience after one year of paediatric airway reconstructive surgery
Michele Torre, Marcello Carlucci, Stefano Avanzini, Vincenzo Jasonni, Philippe Monnier, Vincenzo Tarantino, Roberto D'Agostino, Renato Vallarino, Mirta Della Rocca, Andrea Moscatelli, Anna Dehò, Lucio Zannini, Nicola Stagnaro, Oliviero Sacco, Serena Panigada7 and Pietro Tuo
Italian Journal of Pediatrics (2011), 37:51

9. Coxarthritis as the presenting symptom of Gaucher disease type 1
Brisca G, Di Rocco M, Picco P, Damasio MB, Martini A.
Arthritis. (2011):361279. Epub 2011 Mar 30.

10. Computerized tomography in pediatric oncology
Granata C, Magnano G.
Eur J Radiol. (2011) Dec 29. [Epub ahead of print]

EMERGENCY

Dr. Pasquale Di Pietro



EMERGENCY

DIRECTOR: Pasquale Di Pietro

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Ornella Bellagamba
Simona Costabel
Carla Debbia
Maria Cristina Diana
Silvia Fontanazza
Piero Gianiorio
Mario Lattere (seconded to another unit)
Ilaria Negro
Antonella Palmieri
Emanuela Piccotti
Daniela Pirlo
Salvatore Renna
Marta Romanengo
Barbara Tubino
Marta Vandone
Giovanna Villa

MAIN RESEARCH ACTIVITIES YEAR 2011

- pharmacovigilance: national research project on the safe use of drugs in paediatric age
- ALTE/SIDS: national research project, regional project (ALTE/SIDS prevention campaign)
- regional research project on child abuse
- sedation and pain management in the Emergency Department (national multicentre study)
- advanced simulation in emergency medicine
- registry on thrombosis in children (national multicentre study)
- clinical trial on efficacy and safety of an alcohol-free formulation of 0.15% benzydamine spray in children with sore throat
- oral ondansetron versus domperidone for symptomatic treatment of vomiting during acute gastroenteritis in children: multicentre randomized controlled trial (AIFA)
- prevention of domestic accidents in children: national project on epidemiologic surveillance

RESEARCH PROGRAM YEAR 2012

- pharmacovigilance: national research project on the safe use of drugs in paediatric age
- ALTE/SIDS: national research project, regional project (SIDS prevention campaign)
- regional research project on child abuse
- sedation and pain management in the Emergency Department (national multicentre study)
- advanced simulation in emergency medicine
- registry on thrombosis in paediatric age (national multicentre study)
- oral ondansetron versus domperidone for symptomatic treatment of vomiting during acute gastroenteritis in children: multicentre randomized controlled trial
- prevention of domestic accidents in children
- capnographic monitoring in respiratory emergencies/use of ET CO2 as triage tool to predict acidosis among children with gastroenteritis
- prevention of domestic accidents in children

MAJOR COLLABORATIONS

- Istituto Superiore di Sanità (pharmacovigilance)
- AIFA (clinical trials)
- Children's Hospital – Boston (sedation and pain management in ED, advanced simulation, capnographic monitoring)

- Genetics Department, G. Gaslini Children's Hospital, Genoa; NICU, Meyer Institute, Florence; Department of Paediatrics, Varese; SIDS Center Turin, Genetics Department, Parma; Pneumology Bambin Gesù Hospital, Rome (ALTE/SIDS)
- Regina Margherita Hospital, Turin; Meyer Institute, Florence; Bambin Gesù Hospital, Rome; IRCCS Burlo Garofalo, Trieste; Santobono Hospital, Naples; Paediatrics Department, Padua; Paediatrics Department, Bari; Salesi Hospital, Ancona (sedation and pain management in ED)
- Paediatrics Department, Padua (pharmacovigilance)
- Paediatrics Departments, Bari, Milan and Padua; Regina Margherita Hospital, Turin; Meyer Institute, Florence; Bambin Gesù Hospital, Rome; Santobono Hospital, Naples (register on thrombosis in paediatric age)

MAIN PUBLICATIONS YEARS 2009-2011

1. Ansaldi F, de Florentis D, Canepa P, Bandettini R, Diana MC, Martini M, Durando P, Icardi G. Epidemiological changes after PCV7 implementation in Italy. Perspective for new vaccines. Hum Vaccin. 2011 Jan-Feb; 7 Suppl: 7: 211-6. Review.
2. Marchetti F, Maestro A, Rovere F, Zanon D, Arrighini A, Bertolani P, Biban P, Da Dalt L, Di Pietro P, Renna S, Guala A, Mannelli F, Pazzaglia A, Messi G, Perri F, Reale A, Urbino AF, Valletta E, Vitale A, Zangardi T, Tondelli MT, Clavenna A, Bonati M, Ronfani L. Oral ondansetron versus domperidone for symptomatic treatment of vomiting during acute gastroenteritis in children: multicentre randomized controlled trial. BMC Pediatr. 2011 Feb 10;11:15.
3. Panatto D, Amicizia D, Giacchino R, Tacchella A, Natalizia AR, Melioli G, Bandettini R, Di Pietro P. Diana MC, Gasparini R. Burden of rotavirus infections in Liguria, northern Italy: hospitalisation and potential saving by vaccination. Eur J Clin Microbiol Infect Dis. 2011 Aug; 30 (8): 957-64. Epub 2011 Feb 4.
4. Italian Multicenter Study Group for Drug and Vaccine Safety in Children. Effectiveness and safety of the A-H1N1 vaccine in children: a hospital-based case–control study. BMJ Open. 2011; 1(2): e000167.
5. De Florentiis D, Parodi V, Orsi A, Rossi A, Altomonte F, Canepa P, Ceravolo A,Valle L, Zancolli M, Piccotti E, Renna S, Macrina G, Martini M, Durando P, Padrone D, Moscatelli P, Orengo G, Icardi G, Ansaldi F. Impact of influenza during the post-pandemic season: epidemiological picture from syndromic and virological surveillance. J Prev Med Hyg. 2011 Sep;52(3):134-6.
6. Palmieri A, Riccardi S, Bergamino L, Ciccone MO, Fornoni L, Piccotti E, Di Pietro P. Apparent life threatening event (ALTE): the role of the training in the follow-up. Minerva Pediatr. 2011 Apr;63(2):139-48.
7. Marchisio P, Bellussi L, Di Mauro G, Doria M, Felisati G, Longhi R, Novelli A, Speciale A, Mansi N, Principi N. Acute otitis media: From diagnosis to prevention. Summary of the Italian guideline. International Journal of Pediatric Otorhinolaryngology 74 (2010) 1209–1216.
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OBSTETRICS-NEONATOLOGY

NEONATAL INTENSIVE CARE

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MAIN RESEARCH ACTIVITIES YEAR 2011

Delivering optimal care to premature babies and in particular very low birth babies is the mission of the unit also from the research point of view. The main research areas are and will remain neurological disease, neuroprotection and respiratory problems affecting preterm babies. Elegant research will be continued also in the field of hydrops fetalis and the study of the lymphatic system also in premature infants.
Research was focused on the diagnosis of subtle brain lesions with magnetic resonance imaging and on the stabilization of extremely preterm babies (starting from the respiratory function) at a crucial time when preterm babies are more prone to develop acquired perinatal brain lesions. Direct research will be performed also in the field of the visual performances of premature babies as a validated tool to predict neurological prognosis and to investigate different therapeutic strategies with a very short term neurological follow-up. A revised and shorter version of neurological clinical examination will be compared with conventional examination and with MRI images of the maturing preterm brain.

RESEARCH PROGRAM YEAR 2012

The field of neuroprotection will be directly addressed through different critical approaches with specific RCT, some with Gaslini as Principal Investigator (the use of caffeine at higher doses in extremely preterm babies compared to conventional dosage already used for prevention of apnea in prematurity; optimization of endotracheal suction during the first days of life in the very low birth weight babies) and others associated with already existing RCT (e.g. sustained lung inflation during the initial breathing, optimization of the kind of ventilation with weaning strategies and in particular ROP prevention through direct pharmacological approach - Proposal for FP7 HEALTH.2012.2.4.4-1, Preclinical and/or clinical development of substances with a clear potential as orphan drugs with this title: New approach to preventative treatment of the blinding disease Retinopathy of Prematurity (ROP), called **PREVENT-ROP).**
Visual function in the preterm and ex-preterm babies will be better investigated with specific projects in collaboration with other centres like Gemelli hospital, Catholic University of Rome.
Specific studies will be started also for the research of the best therapeutic options for congenital lymphatic dysplasia.

MAJOR COLLABORATIONS

- Department of Neonatology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel
- We are building a joint research programme together with other neonatal intensive care units for the best treatment of respiratory diseases of preterm babies (Milano, Santiago, Miami)

- Prevent ROP study with Professor Ann Hellström as PI, The Sahlgrenska Academy at University of Gothenburg Institute of Neuroscience and Physiology, Department of Ophthalmology, The Queen Silvia Children's Hospital, 416 85 Gothenburg

MAIN PUBLICATIONS YEARS 2009-2011

1. The proper tidal volume target using volume guarantee ventilation in the course of neonatal respiratory distress syndrome: a crucial endpoint. Scopesi F, Risso FM, Sannia A, Traggiai C, Arioni C, Zullino E, Campone F, Mezzano P, Massocco D, Baldi F, Serra G. J Matern Fetal Neonatal Med. 2010 Jul;23(7):692-4. Review.
2. Misinterpreted signals during guarantee volume ventilation in the newborn. Scopesi F, Rolfe P. Pediatr Pulmonol. 2009 Aug;44(8):835-837.
3. Non-immune hydrops fetalis: A short review of etiology and pathophysiology. Bellini C, Hennekam RC. Am J Med Genet A. 2012.
4. Perinatal deaths and lymphatic system involvement: a diagnostic flow-chart applying immunohistochemical methods. Bellini C, Rutigliani M, Boccardo F, Campisi C, Fulcheri E, Bellini T, Bonioli E. Lymphology. 2011 Sep;44(3):131-3.
5. Germinal matrix hemorrhage: intraventricular hemorrhage in very-low-birth-weight infants: the independent role of inherited thrombophilia. Ramenghi LA, Fumagalli M, Groppo M, Consonni D, Gatti L, Bertazzi PA, Mannucci PM, Mosca F. Stroke. 2011 Jul;42(7):1889-93.
6. Magnetic resonance imaging of white matter diseases of prematurity. Rutherford MA, Supramaniam V, Ederies A, Chew A, Bassi L, Groppo M, Anjari M, Counsell S, Ramenghi LA. Neuroradiology. 2010 Jun;52(6):505-21.
7. Visual performance and brain structures in the developing brain of pre-term infants. Ramenghi LA, Ricci D, Mercuri E, Groppo M, De Carli A, Ometto A, Fumagalli M, Bassi L, Pisoni S, Cioni G, Mosca F. Early Hum Dev. 2010 Jul;86(1):73-5.
8. Assessment of brain tissue injury after moderate hypothermia in neonates with hypoxic-ischaemic encephalopathy: a nested substudy of a randomised controlled trial. Rutherford M, Ramenghi LA, Edwards AD, Brocklehurst P, Halliday H, Levene M, Strohm B, Thoresen M, Whitelaw A, Azzopardi D. Lancet Neurol. 2010 Jan;9(1):39-45.
9. Auxological and metabolic study in small for gestational age children during 2 years follow-up.Polo Perucchin P, Traggiai C, Calevo MG, Gastaldi R, Di Battista E, Amisano A, Lorini R. J Matern Fetal Neonatal Med. 2011 Feb;24(2):381-7.
10. Preterm and term newborn: primary investigations. Risso FM, Sannia A, Gazzolo D. J Matern Fetal Neonatal Med. 2012 2012 Mar 12. [Epub ahead of print].

OBSTETRICS AND GYNECOLOGY

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MAIN RESEARCH ACTIVITIES YEAR 2011

- RNA (RNA-based Noninvasive Aneuploidy) Study: an LTD (Laboratory Developed Test) for the detection of Down syndrome in early pregnancy
- Carbohydrate metabolism in pregnancy: screening, diagnosis, etiology, maternal and fetal follow-up, and management of the newborn
- Breast cancer and pregnancy (research project conducted in collaboration with National Cancer Institute, IST-Genova)

RESEARCH PROGRAM YEAR 2012

- Ultrasound diagnosis, intrauterine course, management and prognosis of prenatally diagnosed fetal and neonatal malformations
- Assessment of the gestational age of onset of fetal bone nuclei in relation to fetal and neonatal growth

MAJOR COLLABORATIONS

- Women & Infants Hospital, Rhode Island
- Wolfson Institute of Preventive Medicine, London - Professor Sir Nicholas Wald

MAIN PUBLICATIONS YEARS 2009-2011

1. Antenatal screening for Down's syndrome: Experience of Giannina Gaslini Children's Hospital (Genoa, Italy) from 2002 to 2010. Jovovich O, Perotti M, De Biasio P, Cozzani R. Clin Biochem. 2011 May;44(7):527-8. Epub 2011 Apr 27.
2. Congenital defects in assisted reproductive technology pregnancies. Sala P, Ferrero S, Buffi D, Pastorino D, Bertoldi S, Vaccari L, Bentivoglio G, Venturini PL, De Biasio P. Minerva Ginecol. 2011 Jun;63(3):227-35. English, Italian.
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4. Stepwise sequential screening for trisomy 21 in assisted reproduction pregnancies. Pastorino D, Canini S, Prefumo F, Buffi D, Pugliese M, Venturini PL, De Biasio P. J Matern Fetal Neonatal Med. 2009 Dec;22(12):1194-6.