

## Linea di ricerca 4

### EMATOLOGIA, ONCOLOGIA E TERAPIE CELLULARI

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#### Responsabili scientifici:

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#### Descrizione:

Le aree di ricerca trattate in questo settore, riguardano A) i tumori solidi e tumori del sangue pediatrici (es neuroblastoma e leucemie) B) e le patologie di origine non tumorale, C) la fisiopatologia del sistema ematopoietico e delle cellule staminali. I punti focali di indagine sono: la caratterizzazione dei meccanismi alla base delle recidive della malattia, dall'altra la messa a punto di protocolli terapeutici innovativi basati su terapie cellulari e farmaci biologici intelligenti, lo studio delle basi biologiche e la fisiopatologia come piattaforma per sviluppare terapie innovative. Le insufficienze midollari sono un gruppo eterogeneo di malattie genetiche congenite, causate da deficit nel numero di cellule del sangue. Sebbene la percentuale di guarigione da neoplasie del sangue va aumentando, alcune forme tendono a recidivare. Il trapianto di cellule staminali ematopoietiche (HSC) è raccomandato nei pazienti con forme severe di citopenia e nei pazienti leucemici più gravi e refrattari. Nel paziente trapiantato si instaura un complesso processo di ricostituzione immunologica che dà origine ad un sistema immunitario sano e funzionale. Il 30% dei pazienti affetti da neuroblastoma (NB) decede o va incontro a complicazioni tardive post-trattamento. E' quindi necessario trovare nuovi target terapeutici per i casi di NB refrattario mirati contro i meccanismi di resistenza alla terapia. Nell'ambito dei tumori pediatrici, è stato dimostrato che una parte importante di pazienti "guariti" sviluppano patologie degenerative. L'eterogeneità delle insufficienze midollari rende necessaria un'approfondita indagine dei geni responsabili di malattia e della relativa funzione. All'interno dei tumori risiedono cancer stem cells (CSC) resistenti alla chemioterapia. L'Istituto, sta cercando di identificare marcatori molecolari associati alle CSC del NB per elaborare strategie terapeutiche CSC-specifiche. Una percentuale significativa di pazienti guariti da tumore pediatrico sviluppa patologie degenerative, probabilmente associate a lesioni molecolari indotte dalla chemio-radioterapia. La loro identificazione potrebbe cambiare lo scenario terapeutico in questo tipo di patologie post-tumore. Poiché il trapianto di cellule ematopoietiche comporta espansione di queste cellule, lo studio delle variazioni del profilo trascrizionale dei geni delle HSC dopo trapianto (post-T) potrebbe rivelare informazioni importanti per espandere le stesse HSC per scopi terapeutici.

#### Obiettivi:

1. Sviluppo di nuovi approcci diagnostici e terapeutici nei casi più gravi di tumori solidi e di insufficienze midollari.
2. Identificazione di nuovi target nel NB.
3. Caratterizzazione delle alterazioni molecolari patogenetiche delle patologie degenerative post-tumore.
4. Caratterizzazione a livello molecolare della espansione delle HSC.

### **U.O.C. Laboratorio cellule staminali post-natali e terapie cellulari**

Direttore: Marina Podestà

“Ageing e Orologio Biologico - Ageing and biological clock”

“Sviluppo di strategie metaboliche nella terapia di patologie oncologiche, autoimmunitarie ed infiammatorie - Development of metabolic strategies in the therapy of oncologic, autoimmune, and inflammatory diseases”

“Transdifferenziazione dei linfociti T  $\gamma\delta$  in T  $\alpha\beta$ : una nuova strategia immunoterapeutica contro le leucemie acute pediatriche - Transdifferentiation of  $\gamma\delta$  T lymphocytes into  $\alpha\beta$  T cells: a new immunotherapeutic strategy against pediatric acute leukemias”

“Lo studio del ctDNA nella diagnosi e nel monitoraggio della resistenza alla terapia in pazienti con Neuroblastoma ad alto rischio: le basi della medicina di precisione in oncologia pediatrica - The study of ctDNA in the diagnosis and monitoring of resistance to therapy in patients with high-risk neuroblastoma: the foundations of precision medicine in pediatric oncology”

“Plasticità ed eterogeneità delle cellule staminali tumorali nel neuroblastoma umano - Plasticity and heterogeneity of tumor stem cells in human neuroblastoma”

### **U.O.C. Oncologia**

Direttore: Alberto Garaventa

“NEUROBLASTOMA: progetto di coordinamento della ricerca clinica e sperimentale in Italia 2018-2020 - NEUROBLASTOMA: project for coordination of clinical and experimental research in Italy in the period 2018-2020”

### **U.O.C. Ematologia**

Direttore: Carlo Dufour

“Marrow failure syndromes e citopenie autoimmuni - Marrow failure syndromes and autoimmune cytopenias

“Trials clinici e studi osservazionali in leucemie dell’infanzia - Clinical trials and observational studies in childhood leukemias”

### **U.O.C. Malattie Infettive**

Direttore: Elio Castagnola

“Gestione delle complicanze infettive nel paziente pediatrico complesso - Management of infectious complications in complex pediatric patients”

### **U.O.C. Immunoematologia e Medicina Trasfusionale**

Direttore: Gino Tripodi

“Selezione di popolazioni di soggetti sani stratificati per età, sesso e specifiche caratteristiche da utilizzare come campioni di controllo negli studi collaborativi con gruppi di ricerca - Selection of populations of healthy subjects stratified for age, sex, and specific characteristics to be used as controls in collaborative studies with research groups”

### **U.O.S.D. Laboratorio Terapie Sperimentali in Oncologia**

Direttore: Mirco Ponzoni

“Ricerca traslazionale sui tumori pediatrici - Translational research on pediatric tumors”

“Investigation of microbiome in children with Neuroblastoma to unravel potential roles in etiology and response to current therapy”

### **U.O.S.D. Centro di Trapianto di Midollo Osseo**

Direttore: Edoardo Lanino

“Trapianto allogenico di cellule staminali emopoietiche per malattie oncologiche e non in età pediatrica - Allogenic hematopoietic stem cell transplantation for oncologic and non oncologic diseases in pediatric age”

### **U.O.S.D. Centro di Emostasi e Trombosi**

Direttore: Angelo Claudio Molinari

“Studi clinici e biologici in bambini ed adolescenti emofilici con particolare attenzione al monitoraggio della artropatia emofilica nell'era dei concentrati ad emivita estesa e delle terapie non sostitutive - Clinical and biological studies in hemophilic children and adolescents with special focus on monitoring of hemophilic arthropathy in the era of extended half-life concentrates and non-substitution therapies”

“Stroke e trombosi in pediatria - Stroke and thrombosis in children”

### **U.O.S.D. Centro di Neuro-Oncologia**

Direttore: Maria Luisa Garrè

“Implementazione e reclutamento di pazienti per studi clinici interventistici in pazienti con tumori del Sistema Nervoso Centrale in età pediatrica - Implementation, patients recruitment and data analysis of controlled clinical trials (Phase I, Phase II, Phase III and IV) in patients with Central Nervous System Tumours”

“Implementazione e reclutamento di pazienti per studi clinici osservazionali in pazienti con tumori del Sistema Nervoso Centrale in età pediatrica - Implementation and case recruitment in Observational studies for pediatric patients affected by Central Nervous System Tumours”

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