ImmunoTools IT-Box-139 Award 2012

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CHARACTERIZATION OF T and B CELL SUBSETS IN PEDIATRIC PATIENTS AFFECTED BY SCLERODERMA AND GRAFT VERSUS HOST DISEASE

The Scleroderma disorders comprise a heterogeneous group of autoimmune conditions characterized by visceral involvement and linked by the presence of thickened, sclerotic skin lesions.
Chronic Graft Versus Host Disease (c-GVHD), a serious and frequent complication of allogenic hematopoietic stem cell transplantation, presents clinical features similar to those observed in systemic scleroderma patients, such as diffuse sclerodermatous skin lesions. The pathogenesis of these conditions is still unknown, but a genetic predisposition with concomitant environmental stimuli results in immune activation, vascular injury and collagen accumulation. Moreover, abnormalities in B cell functions are thought to play an important role in the pathogenesis of both diseases and could contribute to the induction of systemic autoimmunity independently of autoantibody production. In particular, the specific role of B-10 competent cells in autoimmune conditions has not been clearly defined, nonetheless some reports showed in Systemic Eritematous Lupus patients a defect of regulatory B cells in suppressing *in vitro* effector T lymphocytes.

Because of a detailed analysis of both B and T cell compartment in pediatric scleroderma and GVHD patients has not been performed so far , this PhD will entail further phenotypic and functional characterization of B and T subpopulations, with emphasis on B 10 competent cells.
We collected, in collaboration with the Pediatric Hospital G. Gaslini of Genoa, clinical data and samples (frozen lymphomononuclear cells and plasma) from 19 scleroderma and 18 c-GVHD pediatric patients. Using the antibodies provided by the ImmunoTools IT-BOX-139, flow cytometric phenotypic analysis will require a combination of:

a) CD19 CD24 CD38 CD21 and CD5 in order to define transitional B cell subsets (T1, T2 and T3),
b) CD19 IgD CD20 CD27 IgM to enumerate naïve B cells and plasma cell,

c) CD19 CD27 IgGIgA CD39 CD73 CD40, for the characterization of memory B cell subsets,
d) CD70 CD19 CD20 CD27 CD43 to analyse B 1 cells.
e) CD4 CD45RA CCR7 CD25 CD69 CD8, will allow the enumeration of naïve, cm, em CD4 as well as CD8 T cells and their activation status,
f) CD4 CD45RA CCR10 CCR4 CXCR3 CCR6 for the enumeration of T em subsets,
g) CD4 CD25 CD127 CD39 and CD73 to assess T reg cells
h) CD4 CD45RA CXCR5 CXCR3 CCR6 to enumerate T follicular helper cells
The best hope for continued progress lies in the development of innovative treatments, thanks to a better understanding of diseases pathogenesis.