

PhD program: International PhD Course in Molecular Medicine of the Vita-Salute San Raffaele University of Milano – 2016/2017

Section: Experimental and Clinical Medicine (ECM)

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<http://www.hsr.it/research/organization/institutes/diabetes-research-institute-hsr-dri/manuela-battaglia-2/>

UNIT name: "Immune Mediated Diseases: from pathogenesis to treatment"
(Diabetes Research Institute)

PH.D. PROJECT: T1D-neutrophils: "NET" gain in understanding T1D pathogenesis

Type 1 diabetes (T1D) – one of the most frequent chronic, life-debilitating, autoimmune diseases in humans – is commonly portrayed as an autoimmune disease, in which misguided T lymphocyte activities cause selective destruction of insulin-producing pancreatic b-cells. New findings suggest that the immunological picture might be more complex than previously imagined.

Studies performed in the last 20 years demonstrate that the role of neutrophils in immunity, inflammation, and thereafter extends considerably beyond the previously perceived limits. Recent studies in humans and mice, including ours, suggest that neutrophils play a hitherto unsuspected role also in T1D autoimmune pathogenesis.

Overall objective of this project is to define the pathogenic role of neutrophils and neutrophil extracellular traps (NETs) in T1D in humans. This will be realized through the achievements of the following specific aims:

- 1) To describe the distribution of neutrophils and NETs in the pancreas;
- 2) To investigate the interaction of neutrophils with other immune cells;
- 3) To understand the contributions of neutrophils and NETs in disease pathogenesis.

This ambitious goal will be accomplished thanks to our access to unique human samples from patients and matched controls. A broad approach and long-standing partnerships with experts in the field of innate immunity additionally make this project groundbreaking.

Key References

1. Valle, A., G.M. Giamporcaro, M. Scavini, A. Stabilini, P. Grogan, E. Bianconi, G. Sebastiani, M. Masini, N. Maugeri, L. Porretti, R. Bonfanti, F. Meschi, M. De Pellegrin, A. Lesma, S. Rossini, L. Piemonti, P. Marchetti, F. Dotta, E. Bosi, and M. Battaglia. "Reduced circulating neutrophils precedes and accompanies type 1 diabetes." *Diabetes* 2013, 62:2072-7
2. Diana, J., Y. Simoni, L. Furio, L. Beaudoin, B. Agerberth, F. Barrat, and A. Lehen. "Crosstalk between neutrophils, B-1a cells and plasmacytoid dendritic cells initiates autoimmune diabetes." *Nat Med* 2013, 19:65-73
3. Battaglia, M. "Neutrophils and type 1 autoimmune diabetes." *Current Opinion in Hematology* 2014, 21:8-15.