

**PhD Curriculum:** Experimental and Clinical Medicine

**Project Title:** Characterization of circulating biomarkers of tissue damage in T1D and other diseases

**Director of Studies:** Vito Lampasona

Type 1 Diabetes (T1D) is characterized by the autoimmune destruction of pancreatic islets beta cells. Circulating autoantibodies are currently used to diagnose disease and identify at risk subjects. Autoantibodies are good biomarkers of autoimmunity but cannot assess or quantify pancreatic beta cell damage. This project is aimed at improving our ability to track beta cell damage through circulating biomarkers. In particular we'll focus on the development of novel assays for the measurement of antibody responses to TSPAN7, a very recently identified autoantigen of T1D, in the hope that characterization of TSPAN7 autoantibodies might help in better staging of disease progression. In addition, we'll develop alternative assays based on ultrasensitive measurement by ddPCR of circulating nucleic acids of beta cell origin as potential biomarkers of tissue damage. Validation of the developed tools will take place using as models patient samples from diverse clinical settings like type 1 and type 2 diabetes, pancreatic islet allo- and auto-transplantation, and pancreatic cancer. Furthermore, the tools we are planning to develop might find potential applications in other clinical settings like tissue or solid organ allo-transplantation, in which tissue damage following an immune reaction is in need of constant monitoring, or in the case of oncological malignancies other than pancreatic cancer, that may nonetheless share some of its biological signatures.

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**Key references:**

1: McLaughlin KA, Richardson CC, Ravishankar A, Brigatti C, Liberati D, Lampasona V, Piemonti L, Morgan D, Feltbower RG, Christie MR. Identification of Tetraspanin-7 as a Target of Autoantibodies in Type 1 Diabetes. *Diabetes*. 2016 Mar 7. pii: db151058. [Epub ahead of print] PubMed PMID: 26953162.

2: Brambati C, Galbiati S, Xue E, Toffalori C, Crucitti L, Greco R, Sala E, Crippa A, Chiesa L, Soriani N, Mazzi B, Tresoldi C, Stanghellini MT, Peccatori J, Carrabba MG, Bernardi M, Ferrari M, Lampasona V, Ciceri F, Vago L. Droplet digital polymerase chain reaction for DNMT3A and IDH1/2 mutations to improve early detection of acute myeloid leukemia relapse after allogeneic hematopoietic stem cell transplantation. *Haematologica*. 2016 Apr;101(4):e157-61. doi: 10.3324/haematol.2015.135467. Epub 2015 Dec 24. PubMed PMID: 26703962.

3: Lampasona V, Passerini L, Barzaghi F, Lombardoni C, Bazzigaluppi E, Brigatti C, Bacchetta R, Bosi E. Autoantibodies to harmonin and villin are diagnostic markers in children with IPEX syndrome. *PLoS One*. 2013 Nov 8;8(11):e78664. doi:10.1371/journal.pone.0078664. eCollection 2013. PubMed PMID: 24250806; PubMed Central PMCID: PMC3826762.

4: Piemonti L, Everly MJ, Maffi P, Scavini M, Poli F, Nano R, Cardillo M, Melzi R, Mercalli A, Sordi V, Lampasona V, Espadas de Arias A, Scalamogna M, Bosi E, Bonifacio E, Secchi A, Terasaki PI. Alloantibody and autoantibody monitoring predicts islet transplantation outcome in human type 1

diabetes. *Diabetes*. 2013 May;62(5):1656-64. doi: 10.2337/db12-1258. Epub 2012 Dec 28.  
PubMed PMID: 23274902; PubMed Central PMCID: PMC3636624.