Recent advances in genome-wide association studies have generated hopes of better understanding of pathogenic processes of disease and more importantly, how it varies among different individuals to explain responders vs. non-responders and use this information to individualise therapeutics. However, germ line genetics have yielded variants of typically very small effect sizes (outside HLA), which, to date; have failed to convincingly predict response to various interventions. Autoimmunity is a special case because it is due to unchecked proliferation of a relatively small number of lymphocyte clones and more importantly, these clones can be distinguished from the rest of lymphocytes of the same type because they carry T-cell receptors that specifically recognise antigen. Moreover, these cells behave aberrantly for some reason that should be sought in their clonal genome and epigenome and is not necessarily present in the epigenome of the rest of the lymphocytes. I will present work on T-cells specifically isolated from the blood of children newly diagnosed with type-1 diabetes to highlight specific properties of the TCR rearrangements and the rest of the auto-reactive T-cell genome.

**Biography**

Constantin Polychronakos studied Medicine at the Aristotelian University in Greece, following which he moved to Canada and trained in Pediatric Endocrinology, followed by a research fellowship at the Polypeptide Hormone Laboratory at McGill University in Montreal. Since 1983 he is on faculty at McGill University (Full Professor since 2000). For the past three decades, his research is focused on the genetics and immunology of diabetes. He has played a central role (corresponding author) in the first GWAS for type 2 and one of the first two for type-1 diabetes. He has also done seminal work on the role of thymus in the immune self-tolerance to tissue-specific antigens like insulin and in one of the first uses of exon capture+NGS, he discovered RFX6 as the gene whose mutations abrogate the development of the endocrine pancreas.

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