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Immune profiling of human liver autoimmune diseases

Chronic liver diseases (CLDs) represent a rising global public health problem and include autoimmune and metabolic diseases such as autoimmune hepatitis (AIH) and primary sclerosing cholangitis (PSC) which target the liver parenchyma (AIH) or the bile ducts (PSC); and non-alcoholic steatohepatitis (NASH) which associates with abnormal lipid metabolism and fat deposition in the liver. An aggressive T cell-mediated immune reaction and associated destruction of liver tissue and fibrosis is a hallmark of AIH, PSC and NASH. Because a significant number of patients are diagnosed late and some patients fail to respond or develop resistance to steroidal immunosuppressive treatments, identification of immune therapeutic targets may be effective in treating late-stage CLDs. Despite the commonality of T cell infiltration in CLDs, it is currently unclear whether these diseases exhibit overlapping and/or distinct immune profiles especially at later stages. Towards this end, we analyzed the immune signatures of resected, paraffin-embedded liver specimens from AIH, PSC and NASH patients by RNAseq. Comparisons between normal and AIH, PSC or NASH liver tissues revealed that while specific genes were upregulated in all disease settings, distinct gene expression profiles could be deduced for each disease despite the presence of late-stage pathology. Expressions of genes regulating the cytokine/chemokine and innate/host-pathogen pathways were most significantly affected in AIH and PSC, but to a lesser extent in NASH. In summary, our results identify novel distinct, as well as overlapping immune components in AIH, PSC and NASH which can potentially serve as targets for treating individual or combined late-stage CLDs.

Biography

Konstantina Alexandropoulos completed her PhD from the City University of New York and Postdoctorate from The Rockefeller University and the Massachusetts Institute of Technology in the Laboratory of Nobel laureate Dr. David Baltimore. She was appointed Assistant Professor at the College of Physicians and Surgeons of Columbia University in 1997 and as an Associate Professor at the Icahn School of Medicine at Mount Sinai in 2008. She is the Head of the T-cell Autoimmunity and Inflammation Laboratory, has published more than 30 papers in reputed journals and has served on Editorial Boards of peer review journals.

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