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CD4+CD28null T lymphocytes from patients with myocardial infarction have distinct gene signatures, phenotype and function compared to conventional CD4+CD28+T cells

We have previously shown that CD4+CD28(null) (CD28null) T cells are a unique T lymphocyte subset with pro-inflammatory and cytolytic function. CD28null T cells increase in the circulation and atherosclerotic plaques of myocardial infarction (MI) patients. CD28 null T cells accumulate preferentially in unstable atherosclerotic plaques and promote atherosclerotic plaque rupture via release of their cytotoxic cargo and lysis of endothelial and vascular smooth muscle cells. MI patients with high CD28null T cell numbers have increased risk of recurrent severe coronary events and unfavourable prognosis. The precise mechanisms that regulate the inflammatory and cytolytic functions of CD28null T cells in MI remain elusive. We performed whole genome transcriptome analysis of CD28null and conventional CD28+ T cells from MI patients to identify differences in gene signatures between these two lymphocyte subsets. We found that CD28null T cells from MI patients had marked differences in gene programmes compared to conventional CD28+ T cells. Functional enrichment pathway analysis revealed the natural killer cell mediated cytotoxicity and chemokine signalling pathways as the most significantly up-regulated. We provide data confirming these changes at protein level and demonstrating their impact on the function of CD28null T lymphocytes. Our novel findings reveal that the distinct phenotypic and functional properties of CD28null T cells are regulated at transcriptional level and can identify novel molecular targets to modulate the deleterious function of this cell subset in MI patients.

Biography

Ingrid E Dumitriu pursued MD Degree and a PhD in Immunology from San Raffaele DIBIT Scientific Institute, Milan, Italy. She is a Reader (an Associate Professor) in Cardiovascular Immunology at St George's, University of London, London UK. She leads the Cardiovascular Immunology Research Group and has her research focused on the role of inflammation and immune cells in atherosclerosis and other cardiovascular diseases. She is a Nucleus Member of the European Society of Cardiology (ESC) Working Group on Atherosclerosis and Vascular Biology. She is also a Member of the ESC, European Atherosclerosis Society, British Society for Immunology, and ESC Working Group on Peripheral Circulation.

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