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Immune sensing of the fat tissue in obesity: The role of NK cells

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Obesity is an increasingly common health issue that predisposes people to metabolic disorders such as insulin resistance (IR), which can progress to diabetes mellitus type 2 (DM2). An important underlying cause of obesity-induced IR is chronic systemic inflammation derived from accumulating pro-inflammatory macrophages in visceral adipose tissue (VAT). Currently, it is unknown which signal initiates adipose tissue macrophage (ATM) activation in VAT. We find that a phenotypically distinct VAT-resident NK cells provide a crucial link between obesity-induced adipose tissue stress and ATM activation in VAT. Ligands for the NK cell-activating receptor Nkp46/Ncr1 are expressed in human and mouse VAT. Feeding with high-fat diet causes up regulation of Ncr1-ligands on adipocytes, leading to localized activation and cellular increase of NK cells. IFN γ produced by these cells drives early pro-inflammatory macrophage differentiation and promotes obesity-induced insulin resistance. Lack of NK cells, Ncr1 or IFN γ prevents macrophage activation in VAT and greatly ameliorates glucose tolerance and insulin sensitivity. Therapeutic blocking of Ncr1-signaling forestalls ATM activation. Our study identifies NK cells as key regulators of macrophage polarization and insulin resistance in response to obesity-induced adipose stress. The NK-ATM axis therefore provides an attractive new target for early treatment of patients with metabolic syndrome to prevent progression to DM2.

Biography

Bojan Polic graduated medicine in 1989 and received his Ph.D. in 1996 at the University Of Rijeka School Of Medicine. From 1997 till 2001 he did his postdoc in the group of prof. Klaus Rajewsky at the Institute of Genetics University of Cologne, Germany. In 2001 he established his research group dealing with Immunology at the Dept. of Histology and Embryology of the University Of Rijeka School Of Medicine. Since 2008 he is a full professor at the Department and was Vice-dean for research at the School (2008 – 2014). He has published more than 40 papers in reputed journals.

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