MOI Project 4

Regulation of KIR3DL1 gene expression and functional consequences for the antiviral activity of NK cells

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Innate cellular immunity via NK cells is essential for protection against viral infections. The function of NK cells is regulated by multiple inhibitory and activating receptors, including the so-called *killer cell immunoglobulin-like receptors* (KIRs). The ligands for most KIR receptors are specific HLA class I molecules, accordingly, depending on the KIR receptor, either inhibitory or activating signals are sent to the NK cell when HLA expression changes. The complex structure of the KIR gene locus, with different genes and multiple alleles, is still poorly understood in terms of its functional relevance in viral infections. The KIR3DL1 gene is 14.3kb in size and contains a total of 9 exons. Based on preliminary analyses of RNA sequencing data from NK cells, we hypothesize that in addition to the transcript for the full KIR3DL1 receptor, several splice variants are produced that either skip exon 5 or result in a truncated transcript without the coding region for the transmembrane domain. In initial targeted analyses of KIR3DL1pos NK cells, the existence of these two splice variants was confirmed by variant-specific PCR. This project will systematically investigate the splicing pattern of KIR3DL1, possible differences in the splicing of different KIR3DL1 alleles and the functional relevance of splice variants for the regulation of NK cell function.