Targeting CD70 in the treatment of B cell lymphoma

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Conclusions

- Human B cell lymphoma and multiple myeloma cell lines express high levels of CD70.
- CD70 and CD27 expression is inversely correlated suggesting an interaction between these molecules in vitro.
- Stimulation of CD70 with sCD27.Fc downregulates CD70 protein levels in CD27-negative cancer cells.
- sCD27.Fc may promote transcription of the immune suppressive cytokine IL-10.

Background

CD70 is a member of the TNF family that is typically only transiently expressed on several types of immune cells in settings of immune activation. In contrast, CD70 is highly and persistently expressed on a number of malignant cells, particularly on B cell lymphomas. This finding suggests a role for CD70 in promoting survival of these cells and makes this a highly attractive target for antibody therapy. Knowledge about the function of CD70 activation in cancers and its downstream signaling pathway(s), however, remains unknown and needs to be elucidated to understand the molecular consequences of targeting CD70 in patients.

Results

CD70 stimulation induces Il10 mRNA expression

Figure 3: Burkitt’s lymphoma cell lines BL2 and BJAB, which both express high levels of CD70, were stimulated with 1 µg/ml human CD27.Fc chimera and expression of Il10 mRNA was assessed at 24h by qRT-PCR.

Generation of CD70 knockout cells using CRISPR/Cas9

Figure 4: (A) Schematic representation of the two lentiviral constructs expressing constitutively active Cas9 or a Doxycycline-inducible sgRNA, respectively. (B) CD70 knockout efficiency after 3 days of Doxycycline treatment.

In the future, we will study the effect of CD70 deficiency on tumor growth and drug sensitivity in vivo and on gene expression profiles of these cancers.