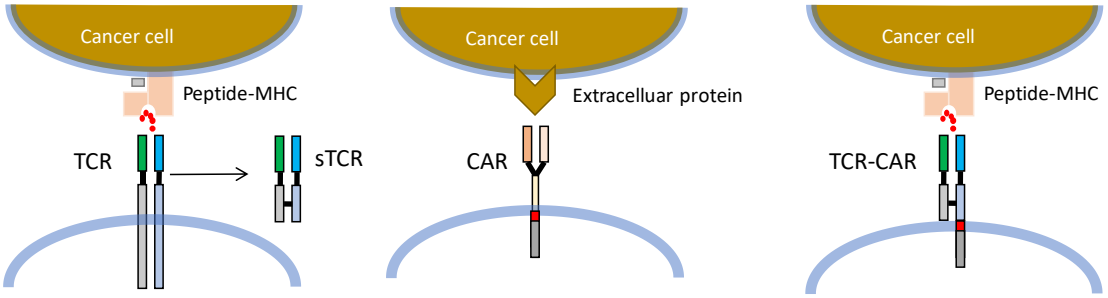
TCR-CAR: a TCR-based chimeric antigen receptor for redirection of NK cells

Executive summary
Chimeric antigen receptor (CAR) recognition is limited to membrane antigens, which represent around 10 % of the total proteins expressed, whereas TCRs (T-cell receptor) have the advantage of targeting any peptide resulting from cellular protein degradation. Scientists at Oslo University Hospital (Norway) have invented a novel receptor construct utilizing the target specificity of a TCR, wherein the signaling machinery is functional in both T-cells and NK-cells. This opens therapeutic avenues combining the killing efficiency of NK cells with the diversified target recognition of TCRs.



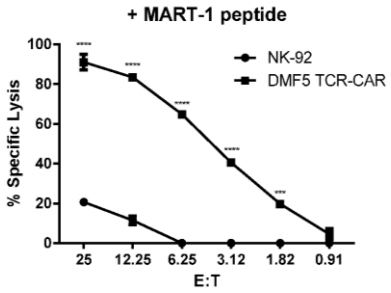
TCR: all proteins recognized (restricted to T cells)

CAR: only surface proteins are recognized (any effector cell)

TCR-CAR: all proteins are recognized (any effector cell)

Above: sTCR (a mammalian soluble TCR) molecules are fused to the signalling domain of a CAR molecule. This design combines the TCR recognition to the plasticity of the CAR signalling. The TCR-CAR enables specific redirection of NK-cell using TCRs.

Right: NK92 expressing TCR-CAR are efficient and specifically kill cancer targets. Target cells were incubated with native NK-92 or NK-92 expressing a therapeutic TCR designed as TCR-CAR constructs (in this case DMF5). Specific killing was detected at different effector to target ratios (E:T).



Business opportunity
The main applications of TCR-CAR is therapeutic use: anti-cancer adoptive cell transfer (ACT). The product may be transferred to effector cells (T cells or NK cells) by mRNA electroporation or viral transduction. The recognition of the target will depend on the peptide-MHC (pMHC) complex.

Technology/Advantage
The scientists have cloned, expressed and killed target cells in a specific manner using two different constructs to redirect T cells and the NK cell line NK-92 (ATCC strain). As a proof of concept they have used DMF5 TCR-CAR (HLA-A2-MART1 specific TCR) and Radium-1 TCR-CAR (HLA-A2-TGFbRII frameshift specific TCR), however the invention can be used for converting other TCRs into TCR-CARs as well, followed by subsequent introduction into T cells or NK cells.

IPR
PCT application filed March 5th 2018.

Development plans
Further optimization of the technology and verification of tumor cell killing and safety *in vivo*.

Business offer
Inven2 AS, the TTO at Oslo University Hospital seeks to out-license the IP.

Contact information:
Kristin Sandereid, Business Development Manager, (+47) 93 03 72 22, Kristin.sandereid@inven2.com