

Switch receptor for use in adoptive cell therapy

Scientists at Oslo University Hospital, led by Dr. med. Jon Amund Kyte, have developed a switch receptor (SwR), which turns immune suppressive TGFβ-signaling into a stimulatory signal for increased CAR T expansion and functionality. SwR is a platform technology that can be utilized in combination with any cell-based therapy modality (CAR, TCR, NK) impacted by the negative consequences of TGFβ signaling and for other biological targets and cancer types.

Business Opportunity

Therapy employing T cells modified with chimeric antigen receptors (CARs) is effective in hematological malignancies but not yet in solid tumors. CAR T cell activity in solid tumors is limited by immunosuppressive factors, including transforming growth factor β (TGFβ). The SwR is composed of the ligand-binding domain of TGFβ and the intracellular domain of IL2/15. This innovative design has been evaluated alongside CAR constructs targeting STEAP1 and HER2. STEAP1 is highly expressed in prostate cancer, Ewing's sarcoma, and other cancers, while HER2 is a tumor-associated antigen found in breast cancer, glioblastoma, and more. Inven2 is seeking licensees to the patented technology.

Technology Description

The SwR-STEAP1 CAR variant offers superior performance compared to the parent STEAP1 CAR in TGFβ-rich environments, demonstrating potent anti-tumor effects in prostate cancer models. SwR CAR T cells exhibit robust expansion, survival, and sustained functionality upon repeated antigen exposure. Similarly, the HER2 CAR with the switch receptor (JK89) has shown greater efficacy than the HER2 CAR alone (JK80). Before rechallenging, all mice treated with JK89 were tumor-free, compared to residual tumors in the JK80 group. Post-rechallenge, JK89-treated mice showed a significant reduction in tumor burden, underscoring the switch receptor's promise in enhancing tumor control across multiple solid cancers (see below). Notably, after rechallenge, JK89-treated mice continued to exhibit a lasting reduction in tumor burden, further demonstrating the switch receptor's durable anti-tumor effects and its promise in enhancing control across multiple solid cancers.

Category

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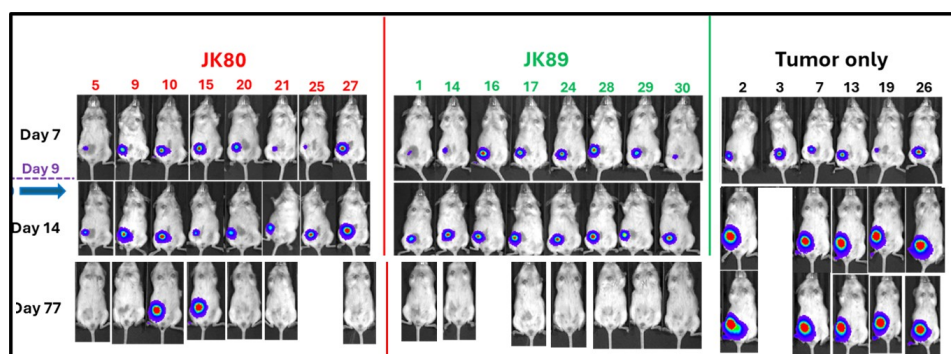


Fig.: HER2 CAR with the switch receptor (JK89) demonstrates greater efficacy than the HER2 CAR alone (JK80). Note one mouse in each group was sacrificed for reasons not related to tumor or CAR-T treatment.

Intellectual Property

The technology is the subject of filed patent application WO2024160976A1 pending in US and EPO.