19th International Conference on
European Immunology

June 23-24, 2025

Webinar

Improving cervical cancer immunotherapy: Safe and specific tumor targeting via the UniCAR system

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Cervical cancer (CC) is the second leading cause of cancer-related mortality in women worldwide. Despite advances in treatments such as chemotherapy, radiotherapy, and surgery, these therapies are often only effective in early stages, highlighting the need for novel and more effective therapeutic strategies. Chimeric antigen receptor (CAR) T-cell immunotherapies have demonstrated significant clinical efficacy, especially in treatment of hematological cancers. Nevertheless, their application is limited by the risk of severe, even life-threatening adverse effects. To improve safety, the Universal CAR (UniCAR) system was developed as a switchable platform. This system is characterized by T-cells engineered to express a CAR targeting the E5B9 epitope, derived from the nuclear La protein, and a target module (TM) capable of binding to both the UniCAR and the target cell. UniCAR T-cell activity depends entirely on the presence of the TM providing an on/off control mechanism. This study aimed to evaluate the UniCAR platform as a therapeutic strategy for cervical cancer. The Prostate Stem Cell Antigen (PSCA), an antigen, highly expressed by cervical tumor cells and associated with increased tumor invasiveness was targeted. Two PSCA-specific TMs were tested: one based on a single-chain variable fragment (scFv) and the other on an IgG4 backbone differing in molecular size and pharmacokinetics. Through in vitro analyses, we assessed the potential of the UniCAR system in a cervical cancer model. It was demonstrated that both TMs were able to bind to PSCA-expressing SiHa cells and redirect UniCAR T-cells thereby inducing effective killing in a concentration-dependent manner at picomolar levels. Furthermore, increased release of effector cytokines, including IL-2, IFN-γ, TNF-α and GM-CSF, are only secreted in the presence of the corresponding TMs and target cells. Taken together, these in vitro experiments suggest that the UniCAR platform has the potential to serve as a highly specific immunotherapeutic strategy for CC treatment.

Biography

Nathalia Andrea Jones Cifuentes is a passionate biomedical researcher with a Master's degree in Microbiology and is currently a PhD candidate in Biomedical Sciences at the Universidad Industrial de Santander. She is currently a research intern at the Institute of Radiopharmaceutical Cancer Research -HZDR in Dresden, Germany. Her work focuses on cervical cancer immunotherapy using the UniCAR system and the development of novel therapeutic strategies against cancer. Nathalia is deeply committed to contributing to science and advancing cancer research, she combines her academic background and laboratory expertise to contribute to the development of more precise and effective treatments.

Received: May 12, 2025; **Accepted**: May 13, 2025; **Published**: June 24, 2025