Gene and Cell Therapy: Updates and Innovations

Dear Colleagues,
Gene and Cell Therapies continue transforming cancer treatment in clinic by offering new ways to target tumors and boost immune responses. EPO remains a leader in supporting this field through our dedicated preclinical models and delivery platforms.

Gene and Cell Therapies: Shaping the Future of Oncology

While surgery, chemotherapy, and radiotherapy remain central to cancer treatment, gene and cell therapies have emerged as clinically relevant alternatives. Today, nearly two-thirds of global gene and cell therapy trials focus on cancer. At EPO, these cutting-edge approaches are supported through robust pre-clinical services for both in vitro and in vivo testing.

These therapies work by enhancing anti-tumor immunity or directly targeting tumor cells to inhibit growth, prevent metastasis, induce cell death, or resensitize tumors to conventional therapies. Strategies include T-cell engineering (TCR or CAR T cells), gene editing, RNA-based gene suppression (shRNA, siRNA, miRNA, AS-ODNs), suicide gene therapy, and oncolytic virotherapy.

Advancing Gene and Cell Therapy at EPO

With decades of experience, EPO has contributed to numerous projects involving cytokine delivery, RNA-based therapies, suicide genes, and virotherapy. Recent studies at EPO demonstrated significant anti-tumor effects of clostridium enterotoxin gene therapy in colon and pancreatic cancer models. These efforts utilize advanced in vivo delivery methods, including LNPs, electroporation, jet-injection, and viral vectors (retroviral, lentiviral).

We also conduct TCR and CAR T cell studies to assess anti-tumor activity in CDX and PDX models. We have generated real-time efficacy data *in vivo* using luciferase-tagged leukemic and lymphoma models. And we are exploring CAR NK cell therapies in neuroblastoma models, expanding the spectrum of cellular immunotherapies.

Additionally, EPO supports the production of gene-modified T and NK cells using lentiviral or gammaretroviral transduction. And we complement our Gene and Cell Therapy studies through *in vitro* assays include real-time cytotoxicity testing with Incucyte® and cytokine profiling via flow cytometry.

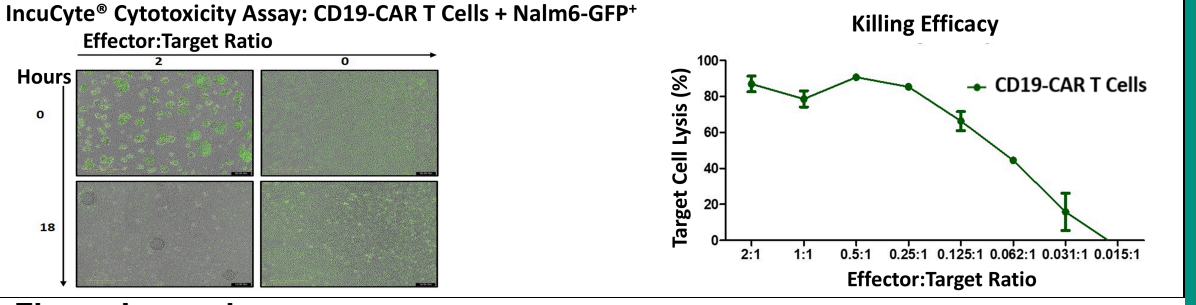

Figure Legend

CD19-CAR T cells were co-cultured with 5 × 10^4 GFP-expressing Nalm6 cells at varying effector-to-target (E:T) ratios and monitored using the live-cell imaging IncuCyte® system. GFP-positive (green) objects were quantified over time to assess cytotoxic activity.

Related Selected Publications, which used EPO models and service

- **Blood (2024):** CRISPR-mediated integration of ζ-deficient CARs into CD3ζ enabled potent antitumor activity in T and NK cells, supporting off-the-shelf CAR-T/NK therapies with reduced GvHD risk and physiological CAR regulation. https://pubmed.ncbi.nlm.nih.gov/38493479/
- **Cancers (2021):** Claudin-targeted suicide gene therapy using Clostridium perfringens enterotoxin was evaluated in pancreatic cancer PDX models at EPO-Berlin, demonstrating strong oncoleaking-mediated tumor eradication and synergy with chemotherapy. https://pubmed.ncbi.nlm.nih.gov/34503203/
- **Eur J Pharm Sci (2021):** RIP-encoding suicide nanoplasmids were evaluated in vitro and in EPO-supported neuroblastoma models, showing antitumor efficacy and tolerability—marking the first in vivo application of nanoplasmids for RIP-based gene therapy. https://pubmed.ncbi.nlm.nih.gov/34958884/
- **J Immunother Cancer (2021):** A mutation-specific TCR targeting MyD88 L265P enabled selective killing of lymphoma cells in vitro and in vivo, supporting precision-engineered TCR-T therapy for B-cell malignancies. https://pubmed.ncbi.nlm.nih.gov/34330762/
- **Cancers (2021):** CD28-based CAR T cells showed superior trafficking, expansion, and antitumor efficacy over 4-1BB CARs in neuroblastoma and ovarian carcinoma models using a mouse-in-mouse system at EPO-Berlin. https://pubmed.ncbi.nlm.nih.gov/33801448/
- **J Control Release (2018):** A saporin suicide gene delivered by sapofectosid-enhanced nanoplexes showed antitumor activity and good tolerability in EPO-supported neuroblastoma PDX models. https://pubmed.ncbi.nlm.nih.gov/29481823/
- **BMC Cancer (2017):** A translation-optimized CPE vector achieved rapid claudin-3/-4-dependent cytotoxicity and selective tumor necrosis in colon cancer PDX models at EPO-Berlin. https://pubmed.ncbi.nlm.nih.gov/28193196/
- **Mol Oncol (2014):** MIDGE® vectors encoding TNF-α enhanced chemosensitivity and significantly inhibited tumor growth in A375 and melanoma PDX models at EPO-Berlin, supporting clinical development. https://pubmed.ncbi.nlm.nih.gov/24503218/
- **Hum Gene Ther Methods (2012):** Intratumoral MIDGE®-TNF-α jet-injection yielded high tumor-specific uptake and rapid systemic clearance, supporting safety and tumor-localized gene expression in nonviral gene therapy. https://pubmed.ncbi.nlm.nih.gov/22924532/
- **Mol Ther (2008):** Jet-injection of shRNA plasmids reversed MDR1-mediated resistance in drug-resistant tumors, restoring doxorubicin sensitivity in vivo in a clinically relevant nonviral delivery approach. https://pubmed.ncbi.nlm.nih.gov/17878902/

For more information, contact Dr. Dennis Kobelt to learn how we can support your Gene and Cell Therapy program.

Best regards,
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