Abstracts

VIRAL/GENE THERAPY AND OTHER NOVEL THERAPIES

THER-01. AWAKENING THE IMMUNE SYSTEM WITH AN IMMUNO-ONCOLOGIC VIRUS AS A THERAPEUTIC STRATEGY FOR DIPGs
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Diffuse intrinsic pontine glioma (DIPG) is an aggressive brain tumour, being the leading cause of paediatric death caused by cancer. Despite all the advances made regarding effective therapies, the survival is dismal. Our lab has engineered the oncolytic virus Delta-24-ART armed with the costimulatory ligand 41BBL in order to increase the antitumoral effect of the adenovirus. 41BBL is a co-stimulatory protein that promotes the expansion of activated T cells and the generation and maintenance of CD8 T memory cells. Therefore, we propose the use of Delta-24-ART as a therapeutic approach for DIPG tumours. We observed that Delta-24-ART is able to infect and replicate in NPS1 and PDGFB-driven, two DIPG murine cell lines, having pulmonic valvular stenosis, has been investigated at the molecular level. Screening of mutations in the entire coding sequence of PTPN11, having germline SOS1 mutations may not be at increased risk of developing anti-glioma memory in long-term survivors. Mechanistic experiments, showed an increase of T cell infiltration (mainly CD8), decrease of proliferating cells and a reduction of the number of vessels in FFPE brain samples in deceased mice. We are currently performing comprehensive studies in the therapeutic window. In summary, our data suggest that Delta-24-ART is safe and induces a potent antitumor immune response in DIPG models mainly based in the activation of CD8 lymphocytes recruited by the viral activity.

THER-02. EVALUATION OF THE ONCOLOGY VIRUS DELTA24-RGD AS AN ANTI-TUMOR AGENT IN PRECLINICAL MODELS OF LOCALIZED AND DESEMINATED AT/RT
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Current therapies for atypical teratoid/rhabdoid tumors (AT/RTs) are suboptimal, resulting in a 2-year OS below 20% and the development of severe side effects. Therefore, we need to explore alternative therapeutic approaches for this disease. Since the virus Delta24-RGD has already demonstrated its efficacy and safety as a therapeutic agent for human brain tumours, including pediatric patients, here we propose to evaluate the anti-tumor effect of Delta24-RGD in AT/RT. In vitro, Delta24-RGD infects and replicates in AT/RT cultures following occlusion by obtaining, obtaining IgG values below 1 pFU/ cell. In vivo, a single local injection of Delta-24-RGD in three intrathecical AT/RT models (BT-12, CHLA-06; and CHLA-266) extended significantly the median OS (50 to 78 days BT-12; 21 to 31 days CHLA-06; 64 to 110 days CHLA-266). Delta-24-RGD also increased the survival of mice bearing supratentorial CHLA-266 tumors (from 93 to 132 days). Next, we evaluated the efficacy of Delta24-RGD in a model mimicking metastatic disease through intraventricular injection of BT-12-luciferase cells. Administration of Delta24-RGD inhibited tumor growth and development of metastases, leading to an increased OS and nearly 70% of long-term survivors. The interaction between Delta24-RGD thermore, 41BBL is expressed in the membranes of the infected cells and results with immunogenic cell death as shown by the different DAMPs. Injection of Delta-24-ART in DIPG model was safe, showed no sign of toxicity and Delta-24-ART significantly increase the median overall survival, generating anti-glioma memory in long-term survivors. Mechanistic experiments, showed an increase of T cell infiltration (mainly CD8), decrease of proliferating cells and a reduction of the number of vessels in FFPE brain samples in deceased mice. We are currently performing comprehensive studies in the therapeutic window. In summary, our data suggest that Delta-24-ART is safe and induces a potent antitumor immune response in DIPG models mainly based in the activation of CD8 lymphocytes recruited by the viral activity.

THER-03. IN VITRO EVALUATION OF THE EFFECT OF CANNABIDIOIL ON PAEDIATRIC BRAIN TUMOUR CELL LINES USING A PULSED TREATMENT REGIME
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Paediatric brain tumours are the second most common cancer after haemato- logical malignancies. Intermittent dosing regimens are typical for chemo-