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Non viral gene therapy for pancreatic cancer, from preclinical models to phase II clinical trial

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To date, pancreatic adenocarcinoma (PDAC) can't be diagnosed early. Consequently, a majority of patient (80%) display an advanced disease that results in a low resection rate leading to a dismal overall median survival of 4 to 6 months. This lecture will address how preclinical findings can be translated into clinical applications for treating pancreatic tumors in patients using gene therapy. Attendees of this lecture will be familiarized with the need for rigorous and stringent testing of candidate therapeutics in relevant preclinical models. Consequently, the discussion will include the description of the anticancerous genes activity, the non viral vector efficacy, the route of administration in patients and the manufacturing of the gene therapy product. In addition, we will discuss on how to carry out ancillary studies to identify non invasive diagnostic biomarkers predictive and/or indicative of treatment response and follow-up, to select clinical trial participants and/or to tailor therapy for individual patient, to create a clear prescription path for gene therapy in the forthcoming phase II clinical trial.

Biography

Pierre Cordelier has studied pancreatic cancer cell proliferation and gene therapy for more than 15 years, during which time he has authored more than 50 peer-reviewed papers. He is currently the principal investigator of a INSERM research group in the Cancer Research Centre of Toulouse in Toulouse, France and the Vice-President of French Society of Gene and Cell Therapy. He is the Scientific Director of the first phase I-II gene therapy trial for pancreatic cancer using non viral vectors. He is now developing viral vectors for the therapy and exploring the use of microRNA as early molecular markers/targets for cancer.

Cascade primed (CAPRI) immune cells destruct cancer cells *in vitro* and in patients: Dissection of the CAPRI method and results of clinical case series

Rudolf Wank
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The CAPRI therapy is a novel adoptive cell therapy (ACT). It surpasses other ACT methods by its technical simplicity, the efficacy and broad applicability. The priming procedure employs solely peripheral blood monocytic cells (PBMC) of the respective cancer patient without isolation of subpopulations. A quartette of immune cells, namely monocytes, dendritic cells, helper T cells and cytotoxic T cells remain in contact with each other during all activation steps. The cancer-immunogenic information for naïve T cells comes from monocytes. Monocytes need to be activated to display the specific cancer information. For this T cells were activated in the PBMC cultures with OKT3 antibodies to activate the monocytes. However, OKT3/CD3-stimulation induces downregulation of the antigen (αβ)-TCR of the OKT3-stimulated T cells. Therefore, PBMC with naïve/unstimulated T cells have to be added. Already after 24 h, the priming procedure is finished and yields highly efficient CAPRI cells, probably for each type of cancer. A five-year survival analysis showed that breast cancer patients with distant metastases (M1, N=42), treated with CAPRI cells in an adjuvant fashion, survived on average 53 months whereas breast cancer patients from the Munich Tumor center in the same tumor stage without CAPRI cell treatment survived 31 months.Case series with non-metastatic breast cancer or non-small-cell lung cancer (NSCLC) showed similar favorable results. Very remarkable is the maintenance of life quality in the patients.

Biography

Rudolf Wank has focused on problems in immunogenetics and immunology for nearly four decades. After receiving the license to practice medicine in Munich, Germany, he spent five years in the USA as scientist at the University of Madison, Wisconsin and at the Sloan Kettering Cancer Institute. He became professor of immunology at the University of Munich and concentrated on the genetics of the immune response. Eight years ago he established the Immunotherapy Research Centerin Munich, which undertakes to combine the treatment of patients with the best of science.