P03.05 VACCINE IMMUNOTHERAPY AGAINST HUMAN ENDOGENOUS RETROVIRUS: A FOCUS ON ANTI-HERV-K ANTIBODIES

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Background Immunotherapies have managed to cover the needs of cancer patients that traditional therapies could not treat. Despite the improvement, broadly acting and highly effective therapies capable of eliminating human cancers without mutated antigens still need to be developed. In this regard, virus-like-vaccine (VLV) technology together with the selection of a cancer specific but ubiquitous antigen can be the key to a successful immunotherapy. VLVs combine the benefits of adenoviral vectors and virus-like-particles (VLPs), leading to the activation of both B- and T-cell responses. Human endogenous retroviruses (HERV) are remnants of ancient viral infections that got integrated into our genome millions of years ago, comprising now the 8% of it. HERVs are usually silenced in healthy tissues but are overexpressed in various cancer types, making them good antigen candidates. HERV-K is the most widely studied HERV, and evidence of HERV-K expression is particularly strong in breast cancer. There are currently no curative therapies for advanced breast cancer, thus our research has been focused on the putative effect of our cancer vaccine in advanced breast cancer.
Materials and Methods This project seeks to describe the effects of HERV-K specific humoral immunity on breast cancer progression. Expression of HERV-K protein in a wide range of breast cancer cell lines was initially investigated. We optimized proliferation, cell migration and invasion, and colony formation assays to explore the role of HERV-K in the phenotype of breast cancer cells. These are then subjected to treatment with commercial and in vivo generated antibodies against HERV-K, protease inhibitors, and agents that block putative HERV-K interaction partners.
Results HERV-K was shown to be present in a wide panel of breast cancer cell lines of various HR, ER, and HER2 status. The project is still ongoing, and I will be analyzing data with this cell lines over the next four months, showing the oncogenic phenotype of HERV-K. Additionally, I will be assessing the effect of our vaccine derived antibodies in tackling the immunosuppressive properties of HERV-K in T-cell and NK, as well as in the involvement of antigen presentation and T-cell activation.
Conclusions This project will reveal whether HERV-K is a valuable target for VLVs in advanced and recurrent breast cancer

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P03.06 TUMOR ASSOCIATED ANTIGENS AND PATHOGEN ANTIGENS: FRIENDS OR FOES

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Background The host's immune system develops in equilibrium with both cellular self-antigens and non-self antigens derived from microorganisms (e.g. viruses and microbiota) which enter the body during lifetime. In addition, during the years, a tumor may arise presenting to the immune system an additional pool of non-self antigens, namely tumor antigens (Tumor Associated Antigens, TAAs; Tumor Specific Antigens, TSAs). Here we offer a new perspective, proposing that a molecular mimicry between the two classes of non-self antigens may play a role in cancer development and progression.
Methods In the present study we looked for homology between published TAAs and non-self microorganism-derived epitopes. Bioinformatics analyses and ex vivo immunological validations have been performed.
Results Several of such homologies have been found. Moreover, structural similarities between paired TAAs and microorganism peptides as well as comparable patterns of contact with HLA and TCR α and β chains have been observed. Moreover, cross-reacting T cells have been identified by tetramer and IFN-γ ELISpot assays.
Conclusions The two classes of non-self antigens may converge, eliciting cross-reacting CD8+ T cell responses which possibly drive the fate of cancer development and progression. An established anti-microorganism T cell memory may turn out to be an anti-cancer T cell memory, able to control the growth of a cancer developed during the lifetime if the expressed TAA is similar to the microorganism-derived epitope. This may ultimately represent a relevant selective advantage for cancer patients and may lead to a novel preventive anti-cancer vaccine strategy.

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P03.07 TOWARDS HERV-H ENV PROTEIN BASED TUMOR STRATIFICATION AND INTERVENTION STRATEGIES

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Background The Envelope (Env) protein of the human endogenous retrovirus H (HERV-H) was shown to be overexpressed in different kinds of cancer tissue, especially in colon cancer and head and neck cancer (1). Therefore, it is a potential target for cancer immunotherapy. Herein we aimed towards analyzing the potential impact of modifications in the HERV-H Env on its expression and immunogenicity with the ultimate