University of Fribourg / Faculty of Science and Medicine / Medicine Section

Mechanisms of T-cell recruitment into gastric tumors in CEA424-SV40 T Ag mice

Nathalie Steinhoff

Cancer immunotherapy has revolutionized the field of oncology by prolonging survival of patients. Although it is the first line treatment for many cancer indications, the efficacy is limited to a subset of cancer patients that have a favorable immune-contexture in the tumor. For the development and evaluation of successful therapies, also for patient subsets who do not respond to cancer immunotherapy so far, adequate preclinical models recapitulating the characteristics of the tumor microenvironment in humans, are required and need thorough characterization.

In order to provide a comprehensive picture of the immune and tumor cell contexture of commonly used pre-clinical models, we performed a thorough analysis of the baseline tumor microenvironment by several technologies. The multimodal approach allowed us to classify the gastric cancer model CEA424-SV40 T Ag x CEACAM5 as immune-desert tumors in comparison to several widely used syngeneic cell line-derived models from different indications representing different sub-types of tumor immune contexture.

To highlight suitable models for certain patient subsets, to underline their translational relevance and to find promising approaches for non-inflamed, hard-to-treat tumors, we tested cancer immunotherapeutical approaches in this relevant gastric cancer model.

Overall, we could show that the models of CEA424-SV40 T Ag and CEA424-SV40 T Ag x CEACAM5 are suitable gastric cancer models to test cancer immunotherapies for tumors exhibiting an immune-desert phenotype associated with poor prognosis and challenging to eradicate. Moreover, we could show effective therapeutic treatment classes that could help the design of clinical studies in patients with gastric carcinomas.

Jury:

Prof. Carole Bourquin (thesis supervisor)

Dr. Sara Colombetti (co-thesis supervisor Roche)

Prof. Jens Stein (internal co-examiner, co-thesis supervisor)

Prof. Etienne Meylan (external co-examiner)

Prof. Curzio Rüegg (president of the jury)