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MAIN FIELDS OF RESEARCH; ABSTRACT

One of my projects focuses on cancer-associated cachexia.
Cancer-associated cachexia is a severe disorder characterized by progressive loss of muscle mass with or without loss of adipose tissue. Cachexia is an often neglected condition even though it is estimated that almost half of all cancer patients develop cachexia syndrome at some point during disease progression. It has not only a dramatic impact on the patient's quality of life, but it is also associated with poor responses to treatment, hence decreasing the patient's chance of survival. Several different pathways and multiple mechanisms have been reported to be involved in the development of Cachexia, however the role of tumor secreted factors in the establishment of this syndrome remain elusive. With this project, we want to decipher Melanoma secreted triggers that are responsible for the induction and maintenance of this disease.
First, we use the C2C12 immortalized mouse myoblast cell line to screen for cachectogenic melanoma cell lines *in vitro*. By co-culturing C2C12 cells together with different melanoma cell lines, we will be able to assess whether myotube differentiation and myotube formation of C2C12 cells is impaired – an *in vitro* read out for cancer cachexia. The co-culture growth medium of the selected melanoma cell lines will further be analyzed via an unbiased mass spectrometry proteomic approach, to find candidate proteins secreted by cancer cells, which possibly induce cachexia-like syndromes in the C2C12 cell line. To confirm the cachectogenic potential of specific cell lines, xenografts of patient-derived melanoma cell lines will be performed in nude mice. The mice will be monitored for tumor growth, weight loss, food intake and changes in their body composition (lean, fat) via EchoMRI. By using CRISPR/CAS9 technology, we will generate knock outs of newly identified, potentially cachectogenic genes in human melanoma cell lines. Those cell lines will again be analyzed in co-culture experiments *in vitro* and with xenograph experiments *in vivo*.
Identification of new tumor-secreted factors causing Cachexia will give valuable insights into how cancer cells communicate with their surrounding microenvironment and how they force the patient's body into a cachectic condition. These findings could point to new treatment strategies to prevent cancer-induced weight loss and increase the overall survival of cancer patients suffering from cachexia.
The second project I am interested in is about CD271 (NGFR) and its role in melanoma invasion and metastasis formation. The nerve growth factor receptor CD271, which normally can be found on neural crest stem cells (NCSC) was also identified as a marker for melanoma-initiating cells and plays a crucial role in the regulation of phenotype switching in melanoma. It has been found via RNAseq that upregulation of CD271 induces changes in the melanoma cells transcriptome, specifically in cholesterol biosynthesis genes. My goal is it, again with an unbiased mass spectrometry proteomic approach, to determine the CD271 specific secretome, which will lead to the identification of factors responsible for melanoma invasion and metastasis.

SPECIAL TECHNIQUES AND EQUIPMENT

Cell culture, LC-MS, Protein purification, mouse models, murine and human biopsies, immunohistochemical stainings, Invasion assays….

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cancer biology
phd program