Name of research institute or organization:

Institute of Veterinary Physiology, University of Zurich

Title of project:

The impact of high altitude on cancer

Project leader and team:

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Project description:

High altitude represents a challenging environment that requires precise adaptation of the human body. Of note, even "adapted" highlanders (e.g. the South American Quechua) might develop severe high altitude related diseases like chronic mountain sickness (CMS). It is surprising, nevertheless, to find that humans populating such an inhospitable environment display reduced cancer mortality compared to those living at low altitude and that this effect is independent of ethnicity and socio-economical environment. Although the reasons and the underlying mechanisms remain a matter of speculation, it seems very likely that the systemic adaptation to hypoxia activates pathways that prevent cancer formation and/or delay tumor growth. Elucidating these mechanisms will lead to the development of new (hypoxia-based) therapeutic approaches and related drugs and may be a valuable contribution to fight cancer.
In our project we analyze the impact of acute exposure to high altitude and isobaric hypoxia (Zurich, hypoxia chamber) on cancer progression, chemotherapy efficacy and tumor metabolism in comparison to low altitude. To test our hypothesis, we generated allograft mouse models with murine lung and breast cancer cells and kept these mice either at low altitude (Zurich, 400m), at high altitude (Jungfraujoch research station, 3580m) or in an isobaric hypoxia chamber (Zurich).

Our analyses are ongoing and so far the following conclusions can be made:

i) no difference in tumor growth of the primary tumor
ii) tumors at JFJ might respond better to chemotherapy (to be verified)
iii) mitochondrial respiration in tumors of mice kept at JFJ is reduced (in complex II)
iv) anemia of cancer, comorbidity and a poor prognosis factor, can be rescued in the lung cancer model, but not in the breast cancer model in JFJ or hypoxia exposed mice

Still ongoing analyses:

i) metabolomics – analyzing the changes of different metabolites
ii) histology (blood vessel formation [tumor perfusion] and quantifying the size of hypoxic tumor areas [tumor hypoxia correlates with aggressiveness])
iii) metastasis in liver and lung (repetition animal experiment with labeled cells in 2017)

Key words:
Cancer, chemotherapy, oxygen, metabolism, anemia

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