Integral Analysis of Pancreatic and Prostate Cancer Energy Metabolism for Clinical Diagnosis and Therapeutics

Summary

Living cells need a constant supply of chemical energy, which they produce by converting food-sourced fuels into usable cellular energy carrier molecules. Cellular energy metabolism was proposed to play a central role in cancer development nearly a hundred years ago. Mitochondria are the power stations of cells and are responsible for most such energy conversion processes. The primary function of mitochondria is the production of ATP via cellular respiration. The hypothesis of this project is that novel biomarkers for the cancer prevention and treatment can be unveiled from the altered energy metabolism of cancer cells. The main objective is to identify which ATP supplier pathway (glycolysis or oxidative phosphorylation) exerts the main control on prostate and pancreatic cancer growth and metastasis, and hence whether these pathways may provide new sensitive cancer biomarkers.

Research field:	Biomedicine and health technology
Supervisor:	Dr. Tuuli Käämbre
Availability:	This position is available.
Offered by:	National Institute Of Chemical Physics And Biophysics
Application deadline:	Applications are accepted between June 01, 2023 00:00 and June 30, 2023 23:59 (Europe/Zurich)

Description

Profound alterations occur in mitochondria that are related with bioenergetic mechanisms during carcinogenesis, resulting in changes in tissue oxygen content and the balance between different energy conversion pathways. This is unsurprising since maintaining malignant growth inevitably requires substantial changes in cellular energy management. Consequently, the functional status of mitochondria plays a pivotal role in the cancerous transformation of cells, and understanding these mechanisms will shine a light on new molecular targets for the development of novel cancer therapies. The general objective of the present topic is to identify which ATP supplier (glycolysis or oxidative phosphorylation) exerts the main control on pancreas and prostate cancer growth, metastasis, and hence whether these pathways may provide new sensitive cancer biomarkers. By applying integral analysis, including not only the changes in RNA and protein, but also function determination, it may be achievable to fully understand how a biological function or behavior is regulated, and by doing this, it may be possible to be manipulated for therapeutic purposes. The both cancers are complex and multi-factorial diseases, where an integrated "omics" approach is more viable. Most of this information on cancer glycolysis has been elucidated in bi-dimensional cancer cell cultures. However, data from tri-dimensional cancer models like microspheroids and from actual human tumor samples are lacking, but they are deemed essential for accurately understanding the behavior of tumor cells. This topic will examine both cancer microspheroids and human tumor samples searching for novel glycolytic biomarkers either at the level of protein or mRNA contents, or enzyme activities, specific metabolites and pathway fluxes.

The results of the first specific research objective of the present topic aim to elucidate which energy metabolism pathway predominates for ATP supply. It may also lead to improve the selection of the most appropriate probes for PET scans based on the metabolic profile of each type of cancer as alternative to the typical 18FDG (glycolytic) probe. Moreover, the unveiled predominant energy metabolism pathway may become an alternative chemotherapeutic target.

The energy transport pathways and associated systems in a well-defined prostate and pancreatic cancer patient population have not been previously studied, so this is a unique topic. This project enables linking basic research with applied research and to provide an output for it. As molecular systems bioenergetics is an interdisciplinary field, the project will develop the capabilities of several strategic research areas.

Supervisors:

Main supervisor: Dr. Tuuli Käämbre
Co-supervisor: Prof. Dr. Rafael Moreno-Sanchez

Responsibilities and (foreseen) tasks

- Cancer cell cultures or handling and processing of post-operative surgical material
- Determine protein contents by Western blotting, and metabolite contents, enzyme activities and Pathway fluxes by spectrophotometry and respirometry
- Determine metastatic features (migration, invasiveness, epithelial-mesenchymal transition)
- Participates in work planning and data publication

Applicants should fulfill the following requirements:

- A master's degree in biology, biochemistry, biomedicine or graduation from the faculty of medicine
- English language skills, both spoken and written, are required
- Writing and analytical skills
- Capacity to work both as an independent researcher and as part of an international team

The following experience is beneficial:

- Light microscopy, confocal fluorescence microscopy
- Working with cells
- Knowledge of enzymology

We offer:

- 4-year PhD position on a unique topic throughout Europe
- The chance to do high-level research in the supportive research Prof. Tuuli Käämbre, international team
- Opportunities for conference visits, research stays and networking with other universities and research centers.

About the department

- National Institute of Chemical Physics and Biophysics (NICPB) acts in the benefit of knowledge-based Estonia. Laboratory of Chemical Biology, the laboratory from National Institute of Chemical Physics and Biophysics, joins excellent scientists with various backgrounds on chemistry, physics, medicine, biochemistry and system biology. Dr. Kaambre´s group works closely with the North Estonia Medical Centre to have access to human tumor and control tissue samples. Their expertise in the management of these tissue samples is fundamental for the successful development of this part of the project. It has to be emphasized that the use of clinical biological samples is of the utmost importance for Translational Medicine to verify and challenge the in vitro results with what occurs in the real medical situation.
- The laboratory joins excellent scientists with various backgrounds on chemistry, physics, medicine, biochemistry and system biology. The laboratory is a member of MitoGlobal Network - a world-wide information platform for scientific mitochondrial organizations and mitochondrial research consortia.

Additional information

For further information, please contact with the research professor Tuuli Käämbre; e-mail: tuuli.kaambre@kbfi.ee; Tel: +372 56159541

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