Application for 1 year Faculty Scholarship

Application form may not exceed 1 page. Please fill out the form in Danish or English, and send it to phd@health.sdu.dk with documentation for financing attached in a separate file. For application deadlines, please see www.sdu.dk/healthphd

Name: *Michael Friberg Bruun Nielsen*

Master Degree/kandidatgrad (include year): *Cand.scient. Biomedicine, SDU, Odense (2012)*

Main supervisor: *Clinical Associate Professor, Consultant pathologist, MD, Ph.D. Sönke Detlefsen*

Department/institute and research unit: *Department of Pathology, OUH, in close collaboration with the Department of Surgery, HPB Section, OUH. Research unit: Institute of Clinical Research, SDU.*

Project title: *Pancreatic stellate cells: characterization of the immune phenotype in the normal human pancreas and pancretic cancer*

Abstract of project (no more than 200 words):

About 1.000 new cases of pancreatic cancer (PC) are diagnosed each year in Denmark. The median survival is only 7 months. Surgical resection offers the only chance of long term survival, but less than 20% are candidates for surgery. PC is histologically characterized by scar tissue ("desmoplasia") that accounts for up to 80% of the cancer nodule. Desmoplasia and the cells producing it facilitate spread of the cancer and protect it against therapy. Cancer-associated fibroblasts (CAFs) are responsible for the production of desmoplasia in PC, and the most important cellular source for CAFs is the pancreatic stellate cell (PSC). During development of PC, PSCs transform into CAFs. No significant progress in the survival has been achieved during the last 20 years, where several combinations of chemotherapeutic drugs directed against the cancer cells have been used. Therapies directed against the desmoplasia have the potential for a paradigm shift in the treatment of PC. At present, no specific biomarkers for PSCs and CAFs have been identified, and it is our aim to identify such biomarkers, because this will enable the development of new drugs. Our preliminary results indicate that we may bridge the gap between local tumor biology and the clinical treatment strategy in PC patients.

Financial information:

First year salary financed by: *Scholarship, Faculty of Health Sciences, SDU.*

Second year salary financed by: *Ph.D. stipend from the Ph.D. fund of OUH.*

Third year salary financed by: *Department of Pathology, OUH.*

Running costs excluding salary (amount and donor): *Total running costs are estimated to 151.000kr. 100.000kr have been awarded by Aase and Ejnar Danielsens Fond.*

Your publications:

Peer-reviewed articles in scientific journals (max. 3):

***Nielsen MF**, Mortensen MB, Detlefsen S. The impact of desmoplasia and stellate cells on pancreatic cancer. [In Danish]. Ugeskr Laeger. 2015 [Epub ahead of print: August 17, 2015]*

*Damgaard D, **Nielsen MF**, Gaunsbaek MQ, Palarasah Y, Svane- Knudsen V, Nielsen CH. Smoking is associated with increased levels of extracellular peptidylarginine deiminase 2 (PAD2) in the lungs. Clin Exp Rheumatol. 2015 May-Jun;33(3):405-8*

*Eriksen MB, **Nielsen MF**, Brusgaard K, Tan Q, Andersen MS, Glintborg D, et al. Genetic alterations within the DENND1A gene in patients with polycystic ovary syndrome (PCOS). PLoS One 2013;8(9):e77186.*

Poster and/or abstract in connection with international conferences (max. 3):

Other relevant publications (max. 3):

*Damgaard D, Jensen BM, Palarasah Y, **Nielsen MF**, Adhikari KB, Schnoor HJ, Juel-Berg N, Poulsen LK, Fomsgaard IS, Nielsen CH. Dietary exposure to benzoxazinoids enhances bacteria-induced monokine responses by peripheral blood mononuclear cells. Mol Nutr Food Res. 2015. [Epub ahead of print: August 10, 2015]*

*Damgaard D, Senolt L, **Nielsen MF**, Pruijn G, Nielsen CH. Demonstration of extracellular peptidylarginine deiminase (PAD) activity in synovial fluid of patients with rheumatoid arthritis using a novel assay for citrullination of fibrinogen. Arthritis Res Ther 2014 Dec 5;16(6):498.*

*Eriksen MB, Glintborg D, **Nielsen MF**, Jakobsen MA, Brusgaard K, Tan Q, et al. Testosterone treatment increases androgen receptor and aromatase gene expression in myotubes from patients with PCOS and controls, but does not induce insulin resistance. Biochem Biophys Res Commun 2014 Aug 14. 4 of 20*

Odense Universityhospitals Research Board

Application R22-A1133
- **Free Research Fund**

Sönke Detlefsen

Position:

Department: / Institution:

Amount applied for: 230.500

July 1, 2014 - June 30, 2018

Project title
Cancer-associated fibroblasts and stellate cells: potential for a change in pancreatic cancer treatment?

Kategori
Department of Pathology

Brief description of the project
About 1.000 new cases of pancreatic cancer (PC) are diagnosed in Denmark on a yearly basis. Fewer than 20% of the patients are offered potential curative operation and less than a third of the patients are alive after 12 months. Hence, the disease is extremely aggressive and sadly no significant progress in pancreatic cancer treatment has been achieved in the last decades. The most prominent feature distinguishing pancreatic cancer from other cancer types is the excessive amounts of scar tissue ("desmoplasia") that surround the cancer cells. Desmoplastic tissue and the cells producing it facilitate spread of the cancer and protect the cancer against therapy.

Cancer-associated fibroblasts (CAFs) are responsible for the production of desmoplasia in pancreatic cancer, and the most important source of CAFs are the resting ("quiescent") pancreatic stellate cells (qPSCs), which in the normal pancreas store vitamin A. During PC progression, PSCs become activated (aPSCs) and proliferate, resulting in an increase in CAF numbers with excessive production of desmoplasia.

At present, no specific biomarkers for PSCs and CAFs in the human pancreas have been identified. However, it is important to find ways to specifically identify these cells, since this would enable the development of therapeutic drugs directed against the specific molecules expressed by PSCs and CAFs. For that reason, the purpose of this project is to find ways to identify these cells, to describe what happens when normal tissue becomes cancerous and to test the effect of chemo- and radiation therapy on them. The last point aims to improve and individualize the pancreatic cancer treatment. This study will likely contribute to the initiation of a paradigm shift in pancreatic cancer therapy, as it provides the basis for a treatment in which not only the cancer cells will be targeted, but also the microenvironment that protects the cancer cells and initiates their tissue invasion.

The specific aims of this study are:
1) To identify specific biomarkers for qPSCs in the normal human pancreas.
2) To identify specific biomarkers for CAFs in pancreatic cancer.
3) To examine the effect of chemo- and radiation therapy on CAFs in cell cultures and human patients.
4) To identify prognostically and therapeutically relevant subtypes of CAFs in pancreatic cancer.