Joint MD/PhD Fellowships Groningen-Oldenburg

Outline PhD Project

Working title of project	**Investigating Rac-1 in Therapy Resistance and Immune Infiltration in Pancreatic Cancer**
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Short Summary of PhD project (mx. 500 words), incl. research question(s), methods, approx. schedule (incl. times in Groningen/Oldenburg)

This Joint PhD project endeavors to address a critical aspect of pancreatic cancer biology: therapy resistance in the context of immune infiltration, with a specific emphasis on the role of Rac-1. The project recognizes the urgency of understanding the molecular mechanisms underlying the resistance of pancreatic cancer to therapeutic interventions, particularly those involving the immune system.

Introduction to Rac-1:

Rac-1, a pivotal member of the Rho GTPase family, stands at the intersection of cellular signaling pathways crucial for cancer progression. This project places Rac-1 under scrutiny, acknowledging its multifaceted roles in cellular processes, with a keen focus on its potential contribution to therapy resistance and immune evasion in pancreatic cancer.

Research Questions:

Rac-1-Mediated Therapy Resistance: Explore how Rac-1 activation may contribute to therapy resistance in pancreatic cancer, specifically in the context of immune-based treatments.

Impact of Rac-1 on Immune Infiltration: Investigate the role of Rac-1 in shaping the immune microenvironment, understanding its influence on the recruitment and function of immune cells within the pancreatic tumor.

Methods:

The project employs a comprehensive set of methodologies to address the research questions:

Molecular Biology Techniques (e.g. qPCR): Assess the expression profile of genes associated with Rac-1 activation in therapy-resistant pancreatic cancer, providing insights into the molecular mechanisms involved.

Immunofluorescence of Tissue Samples: Utilize advanced imaging techniques to analyze the spatial distribution of Rac-1 and key immune markers in pancreatic cancer tissues, identifying potential correlations with therapy resistance.

Functional Studies in Ex Vivo Models (Tumor Organoids): Employ tumor organoids to model the complex tumor microenvironment and assess the impact of Rac-1 on therapy response and immune cell interactions.

Cell-Based Assays: Investigate the functional consequences of Rac-1 activation on immune cell behavior and response to therapeutic agents, providing a cellular perspective on therapy resistance.

Animal Experiments: Utilize in vivo models to validate findings from cell-based assays and ex vivo studies, offering a holistic understanding of the interplay between Rac-1, therapy resistance, and immune infiltration.

Schedule of the project (36 month):

Months 1-12: Initiate the project by setting up a patient cohort in both Groningen and Oldenburg, with a focus on collecting clinical data and biospecimens from therapy-resistant cases.

Months 13-24: Conduct molecular and cellular studies in Groningen, emphasizing the role of Rac-1 in therapy resistance. Investigate its impact on immune cell recruitment and function within the tumor microenvironment.

Months 25-36: Shift the focus to Oldenburg for advanced imaging and functional studies, exploring the spatial and dynamic aspects of Rac-1 activation in therapy-resistant pancreatic cancer.

This Joint PhD project not only contributes to advancing our understanding of therapy resistance in pancreatic cancer but also seeks to unravel the intricacies of Rac-1's involvement in orchestrating immune evasion strategies. By deciphering these mechanisms, the project aims to pave the way for innovative therapeutic strategies that can overcome immune resistance in the treatment of pancreatic cancer.

PhD Candidate Profile/desired qualifications

We are seeking a dynamic PhD candidate with a master's degree in Molecular Biology, Cancer Biology, or related fields. The ideal candidate should have research experience in cancer biology, molecular techniques, and a keen interest in pancreatic cancer or immune-related studies. Proficiency in qPCR, immunofluorescence, and cell-based assays is desired, along with experience in tumor organoid and animal models. Strong analytical skills, effective communication, and the ability to work collaboratively in an interdisciplinary setting are crucial. This position offers an exciting opportunity to contribute to cutting-edge research at the interface of cancer and immunology. Apply if you are a motivated researcher ready to unravel the mysteries of therapy resistance in pancreatic cancer.