ED414
Proposition of doctorate for 3 years
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Please send your CV, motivation letter, and 2 reference letters to:
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Subject: **Characterizing inter-organ communication between heart and tumors**

Supervisor of the thesis

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Localization of the study

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Summary of the thesis subject

Recent meta-analyses and epidemiological studies demonstrate that Heart Failure (HF) and cancer are tightly linked. Indeed, HF patients have a higher risk to develop cancer below age 55, especially lung, breast and colon cancers. Approximately 20-30% of cancer patients develop cardiac disease not only as a consequence of cardiotoxicity induced by anticancer drugs, but also because tumor cells release soluble factors (secretoms) leading to cardiac dysfunction. Co-occurrence of both diseases causes a major clinical burden and has a strong impact on the quality of life and survival rates. A better understanding and early diagnosis of HF and cancer development are critical to deliver timely and targeted prevention strategies.

Hypothesis: Over the past several decades, understanding of how non-coding RNAs (ncRNAs) contribute to normal homeostasis and disease pathogenesis has increased exponentially, illuminating novel classes of RNA molecules with diverse functional roles. Firalis is pioneering the long non-coding RNAs (lncRNAs) as biomarkers in HF, and we hypothesized that some lncRNAs as secretomes can be involved in a bidirectional link between heart failure and cancer.

Project objectives: 1**/** To unravel whether circulating ncRNAs is functional in the pathogenesis and associated with outcome or phenotype in order to enable a new understanding of HF and cancer interaction pathways at the molecular levels, utilizing preclinical models (cancer and cardiac Organoids and mice PDX lung and breast cancer models). We will also use state-of-the-art techniques, in particular 3D cell cultures on nanomatrix, antibody arrays on conditioned mediums, transfections (adeno/Lentivirus), genetic invalidations (cre-loxP, siRNA technologies), protein chips and other molecular biology and physiology techniques.
2/ To identify disease-specific biomarkers (ncRNAs) in the cancer and heart failure patient blood samples (e.g., **FIMICS**, ELISA test), in collaboration with Firalis.

Expected results: This will enable not only identify a novel pathway involved in development of cancer in HF patients, but also early diagnostic tool(s), for prediction of cancer in HF patients in the future.

Wished skills:
The student should have background knowledge on molecular cellular biology and good level of English. The candidate should be a very dynamic, motivated person and a team worker.

Expertise which will be acquired during the training:
Gaining expertise in molecular and cell biology and physiology, including a certification in experimentation of animals, experience in biomarker development and clinical validation together with professional experience at a biotechnology company.

References:
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2. Sturgeon KM et al.A population-based study of cardiovascular disease mortality in US cancer patients. European Heart Journal, Volume 40, Issue 48, 21 December 2019, Pages 3889–3897, https://doi.org/10.1093/eurheartj/ehz766
3. Nebigil CG et Chan M. HF2Cancer: Exploring Bidirectional Interaction Between Cardiovascular diseases and cancer. https://www.frontiersin.org/research-topics/ 23719/hf2cancer-exploring-bidirectional-interaction-between-cardiovasculardiseases-and-cancer
4. FIMICS Targeted quantification of cardiac enriched long non-coding RNAs. https://drive.google.com/file/d/1hFhhbKssCXChVZWUq0JweVhq6GP8BJRx/view
5. Tancin Lambert A, Kong XY, Ratajczak-Tretel B, Atar D, Russell D, Skjelland M, Bjerkeli V, Skagen K, Coq M, Schordan E, Firat H, Halvorsen B, Aamodt AH. Biomarkers Associated With Atrial Fibrillation in Patients With Ischemic Stroke: A Pilot Study From the NOR-FIB Study. Cerebrovasc Dis Extra. 2020;10(1):11-20. doi: 10.1159/000504529