



PhD Project: Constructing mathematical models that predict therapy responses in colorectal cancer.

A PhD position is now available in Systems Biology Ireland, University College Dublin. The project involves the patient-specific mathematical modelling of cancer signalling dynamics for improved patient stratification in colorectal cancer and is part of the EU research consortium COLOSSUS also involving biotech companies and several clinical partners. Envisioned start date: August/September 2019.

Location: Systems Biology Ireland, UCD School of Medicine, University College Dublin, Dublin, Ireland.

Supervisor: Dr Dirk Fey – SBI Group Leader Cancer Dynamics and Modelling.

Project Background & Description:

Biomarkers are cornerstones of clinical medicine, and personalized medicine, in particular, is highly dependent on reliable and highly accurate biomarkers for individualized diagnosis and treatment choice. Modern omics technologies, such as genome sequencing, allow molecular profiling of individual patients with unprecedented resolution, but biomarkers based on these technologies often lack the dynamic element to follow the progression of a disease or response to therapy. In this project we will develop computational models of cancer signalling networks as a new conceptual approach to biomarker discovery and design¹. Being able to integrate a large amount of information, including dynamic information, computational models can simulate disease evolution and response to therapy with high sensitivity and specificity. By populating these models with personal data, they can be highly individualized and will provide a powerful new tool in the armory of personalized medicine.

The main goal in this project is an highly integrated computational model for prediction of clinical outcome in colorectal cancer. To achieve this we need to understand the time-dependent input/output relationships of the underlying signalling network, and the processes that shape them. To that end, we will employ both mathematical modelling and experimentation. In particular, we will construct mathematical models of these signalling networks in terms of ordinary differential equations, apply a from us developed patient-specific modelling technology^{2,3}. The initial model construction will be guided by multi-omics high-throughput data from tumour samples available through the COLOSSUS consortium; mathematical modelling and analysis is the main responsibility of the PhD student; experimental validation using cell cultures will be performed internally in SBI; and clinical validation through COLOSSUS partners.

Candidate requirements:

- Master degree in systems biology, engineering, mathematics, computer science, physics, or equivalent.
- Experience with mathematical modelling using ordinary differential equations.
- Knowledge of biological systems, in particular cancer and cell signalling, is preferable.
- Motivation, passion, and ability to work in an interdisciplinary research environment.

Stipends & fees: The successful candidate will receive a tax-free stipend of €18,500 per annum their registration fees (EU) will be covered. The position is funded for four years, and part of UCD's Structured PhD Programme in Computational and Systems Biology.

Application procedure: Please sent a Cover Letter & CV as soon as possible to Dr Dirk Fey, dirk.fey@ucd.ie. Informal inquiries to the same email are welcome.

Closing date: Applications will be reviewed as received. Closing date: 30/06/2019

Further information:

Systems Biology Ireland is a world-leading interdisciplinary research centre designing new therapeutic approaches to cancer by integrating dry and wet lab work: <http://www.ucd.ie/sbi/>

University College Dublin is a research intensive university located in Dublin, and Ireland's largest university: <http://www.ucd.ie/>

Fey group - Cancer Dynamics and Modelling: <http://www.ucd.ie/sbi/research/researchgroups/feygroup/>

COLOSSUS is an EU-funded H2020 project that aims to provide new and more effective ways to classify patients with a specific type of colorectal cancer (MSS RAS mt mCRC). The ultimate goal is to deliver a personalised medicine approach for patients with MSS RAS mt mCRC that is currently not available: <https://www.colossusproject.eu/>. Research web page: <https://www.colossusproject.eu/researchers/>

References:

1. Kolch, W. & Fey, D. Personalized Computational Models as Biomarkers. *Journal Personalised Medicine* **7**(2017).
2. Fey, D., Kuehn, A. & Kholodenko, B.N. On the personalised modelling of cancer signalling. *IFAC-PapersOnLine* **49**, 312-317 (2016).
3. Fey, D., *et al.* Signaling pathway models as biomarkers: Patient-specific simulations of JNK activity predict the survival of neuroblastoma patients. *Science Signaling* **8**, ra130 (2015).