Postdoctoral Training Fellow in Tumour-host metabolic interactions

This is a **full-time**, **fixed term (4 years)** position on Crick terms and conditions of employment.

The research group

We are a lab of three postdocs and four PhD students (three experimentalists, one computational) who are exploring the fundamental mechanisms that regulate metabolism and how disruption of these mechanisms contributes to cancer development. We are using the insights from our work to propose new ways to diagnose, treat and prevent tumours, in particular liver cancer. To this end, we are studying how glucose metabolism is controlled at the cellular level with a focus on allosteric enzyme mechanisms and redox regulation. We are also investigating the interplay between the metabolism of tumours and host tissue, which is also the focus of this project. For our investigations, we collaborate closely with computational biologists and use state-of-the-art, metabolomics, computational modelling and biochemical methods.

Further information about the group can be found at: http://www.crick.ac.uk/dimitrios-anastasiou

Project summary

Human liver cancer cases are projected to increase significantly in the near future, however, there is a paucity in effective therapies. Among its broader investigations in cancer metabolism, Dr. Anastasiou's lab aims to identify new molecular targets for the treatment and prevention of liver cancer. Towards this goal, we are using mouse models of hepatocellular carcinoma with a focus on understanding how metabolic changes in the tumour and the host contribute to tumorigenesis. In recent unpublished work, we have shown that mice with hepatocellular carcinoma exhibit systemic metabolic changes that are similar to those found in human patients. We have uncovered evidence that these changes are driven both directly by tumours and indirectly by hepatic non-parenchymal cells. In this context, the successful candidate will lead an independent project that complements ongoing work in the lab to (i) identify the signals from cancer and immune cells that drive whole-body metabolic reprogramming, and (ii) assess the effects of host metabolic reprogramming on tumorigenesis.

The successful candidate will use genetic engineering to knockout candidate genes (discovered from our past work) in mice, or in primary cultured cells. He/she will then assess the effects of these knockouts on hepatic function using stable isotope tracers and *in vivo* magnetic resonance spectroscopy (MRS) or *ex vivo* mass spectrometry and NMR-based metabolomics. Depending on expertise and scientific interests of the post holder, some of the specific aims could include, but are not be limited to:

- Elucidating the cell-autonomous mechanisms that regulate glucose metabolism in the liver during cancer development
- Investigating the role of immune cell metabolism in liver functions
- Using proteomics and metabolomics to discover new pathways that induce host tissue reprogramming in liver cancer

Key experience and competencies

Postdoctoral Training Fellows are expected to lead their own projects and collaborate within the lab and externally. The ability to work in a team is essential. The post holder should also embody and demonstrate our core Crick values: bold, imaginative, open, dynamic and collegial, in addition to the following:

Essential
- PhD (or in the final stages of PhD submission) in biochemistry, cell biology, cancer biology, physiology, endocrinology or related discipline
- Good knowledge and hands-on experience with mouse cancer models, *or* genetic engineering (CRISPR/Cas9, lenti-/retro-viral transduction) of primary cultured cells, or advanced cell culture methods (3D, spheroid, co-culture)
- Experience in common laboratory methods (cloning, western blotting, tissue culture)
- Track record of writing papers as evidenced by publications or submitted manuscripts in peer-reviewed journals
- Ability to work independently and also capable of interacting within a group
- Efficient use of working time; Takes responsibility for carrying out research project
- Ability to synthesise scientific information into logical arguments; Can work with day-to-day independence
- Good oral and written communication skills evidenced by data presentation at scientific meetings

Desirable
- Experience in metabolomics
- Experience in transcriptional analysis of mouse disease models
- Knowledge of data analysis using basic computer programming (R, Python, Matlab)