UK Functional Genomics Capability Build
Call for project proposals

GSK has issued a call for proposals for collaborative research in functional genomics including synthetic lethality linked to GSK strategic priorities and leveraging key UK Life Sciences Infrastructure. This call is open to group leaders from the University of Oxford. Funding is available for two years in the first instance, with the aim of taking successful collaborations further depending on project outcomes.

*UK Life Sciences Infrastructure includes for example the UK Biobank, NIHR-Bioresource, HDR-UK Digital Innovation Hubs and Genomics England 100K Genomes Project (see 2020 LSIS update). *GSK has provided support and investment to establish this infrastructure and is keen to leverage this investment.*

This call aims to enable GSK to build relationships and capability in this area with a view to determining where to focus our UK FxG investments in the longer term. **We are seeking ambitious ideas that can transform our understanding of how genetics influences disease and enable the identification of novel and high quality genetically validated targets**. Multi-disciplinary bids involving more than one academic group would be welcomed. Proposals do not need to be fully defined at the outline stage – ideas that are of interest can be further developed at the second stage of the call.

Functional Genomics comprises a set of technologies and analytical methods used to measure and perturb at scale to determine the function of genes and genomes. At GSK, these technologies are especially applied to the understanding of human disease mechanisms and the identification of novel high quality and genetically validated targets.

Many genetic signals (~80%) from genetic studies such as GWAS, map to non-coding regions of the genome, presenting challenges in linking common and rare variants to the causal disease gene and ultimately to a function (the so-called variant to function (V2F) challenge). This makes it difficult to confirm potential new drug targets, slowing down the development of effective therapies and reducing the number of successful clinical trials.

Synthetic lethality describes a concept of context restricted gene essentiality that has been used, for example, to identify novel tumour cell specific therapeutic targets in oncology[1]. The historical lack of scalable methods to probe gene function has left this a relatively untapped space. Rapid recent advances in functional genomic technologies and complex disease models have created significant opportunities for target discovery of synthetic lethal targets or more broadly to run gene modifier large scale screens.

Context: GSK R&D Strategy

GSK is strengthening its pipeline through a focus on oncology and immunology underpinned by significant investments in human genetics (e.g. 23andMe), advanced functional genomics technologies and Artificial Intelligence/Machine Learning (AI/ML – see www.gsk.ai) to help identify the most promising new medicines.

To maximise the probability of success of our genetics- and genomics-informed oncology and immunology-centred R&D strategy, we have a strategic focus on increasing the depth and breadth of our understanding of cancer and immune biology as it relates to normal physiology, disease mechanisms, response to infection

and potential therapeutic approaches. The success of this strategy will be enabled in part by collaborations with trusted clinical and academic collaborators, selected based on world-class expertise and access to high-quality relevant patient samples.

GSK is looking to build on its internal capabilities and existing partnerships by establishing programmes of research associated with four key areas:

1. Patient centric research - Linking genomic variants to cell-specific function and disease mechanisms requires comprehensive analysis of genome regulation across **a range of cell types and tissues from large numbers of patients**. Access to appropriate cellular resources (primary cells, IPS capabilities and organoids) is a core requirement of a successful FxG campaign. Such resources may include primary cells or patient-derived iPSCs, organoids from both "healthy" individuals and patients at key disease stages (e.g. IBD flare). These should be linked to longitudinal medical records.

2. Technologies enabling further understanding of molecular phenotype - There is no shortage of common variants associated with a wide number of different diseases. The real obstacle is turning this information into a better understanding of mechanisms that might be targeted to provide therapeutic benefit. **We are seeking unbiased novel approaches in order to perform deep molecular profiling e.g. single cell multi-'omics/cellular fingerprinting methodologies to translate information on genetic variants into insights into gene regulation and disease.**

3. Technologies associated with perturbation – The ability to intervene/perturb cellular systems via an increasing range of gene editing technologies and to measure the consequences via the application of bespoke functional readouts allows us to identify targets based on screening for disease relevant phenotypes and to validate mechanistic hypotheses.

4. Best in class data analysis capabilities – FxG approaches generate huge and complex data sets creating a need for reliable data science infrastructure to enable data interrogation using advanced analytics such as AI/ML. Seamless wet-dry lab integration is highly desirable to maximise value.

Note: Applicants must demonstrate how proposed projects will leverage key UK Life Sciences Infrastructure* to maximise potential research impact for patients. See accompanying video for further information.

What funding is available?

Funding will be provided for a two-year post-doctoral post and appropriate PI time, plus reasonable consumables. There may be an opportunity to extend the post depending on project outcomes.

Application Process

- Please complete the short **non-confidential** **Expression of Interest Form** and submit to Charlotte Bell, Business Partnerships Manager, by 28 August 2020 charlotte.bell@medsci.ox.ac.uk
- Note that proposals do not need to be fully defined at the Expression of Interest stage – ideas that are of interest can be further developed at the second stage of the call. All applications will be reviewed and shortlisted by a GSK expert panel.

- Prior to submitting your EoI please discuss any issues related to potential IP/freedom to operate restrictions with Charlotte Bell.
- Shortlisted applicants will be informed by 14 September 2020 at the latest and will be partnered with a GSK scientist to further develop the proposal for presentation to the Joint Steering Committee in late September (Date TBC).

Timelines

Call Opens (Expression of Interest Stage): We are encouraging applications to come in throughout July and August so that interested academics can have conversations with GSK discuss potential proposals and seek feedback.	Monday 13 July
Call Closes (Expressions of Interest stage)	Friday 28 August, 5pm
Applicants informed of shortlisting outcome. Those who are invited to the second stage are then connected with GSK scientists to work up a proposal in the form of a presentation to be made at the Oxford-GSK Joint Steering Committee.	Monday 14 September
Oxford-GSK Joint Steering Committee Meeting JSC Meeting Applicants invited to a time slot within the meeting to give a 10-15 minute presentation, jointly with the GSK scientist, and field questions from the committee.	Friday 9 October (between 10-12.30pm)
Applicants informed of final outcomes	Mid-October
Finalisation of workplan/budget and commencement of contracting process	From October (aimed for completion in December)
Projects start	January 2021

Additional Guidance

- Please click through to a video narrated by Tony Wood, SVP Medicinal Science and Technology, GSK R&D for additional information on the call https://www.medsci.ox.ac.uk/research/internal/funding-directory/uk-functional-genomics-capability-build#how-to-apply
- Please refer to the Frequently Asked Questions (FAQ) document on the link above
- If you still have questions or wish to discuss your proposal further, Charlotte will put you in contact with Victoria Higgins, Senior Director, UK Academic Alliance Management, GSK for an informal discussion before submission.

[1]Behan, F.M. et al., Nature 568, 511–516 (2019)