**Project title**

COVID-19 constellation of symptoms: role of SARS-CoV-2 cellular tropism and entry

**About the project**

SARS-CoV-2 is the aetiological agent of COVID-19 and the cause of the first pandemic in our modern and globalised world. COVID-19 has a significantly variable clinical presentation with symptoms and risk factors involving the respiratory system, but also the intestine, the olfactory bulb and the vascular system.

However, it is currently not clear if the symptoms are directly caused by the virus infecting a variety of tissues/cells and/or if the symptoms are caused by the host immune response.

Therefore, the project aims at investigating:

1. the cellular tropism of SARS-CoV-2 in respiratory, intestinal and endothelial cell lines and primary cells
2. the entry route (endocytosis/fusion at plasma membrane) of SARS-CoV-2 in susceptible cells
3. the role of naturally occurring variants of the Spike glycoprotein in tropism and entry

SARS-CoV-2 is a single stranded positive-sense enveloped RNA virus, classified in the *Coronaviridae* family. Cellular tropism for enveloped viruses in mainly determined by the interaction of the Spike (S) glycoprotein with a host cell protein expressed at the plasma membrane (i.e. receptor).

For SARS-CoV-2, the human angiotensin converting enzyme 2 (ACE2) has been identified as the primary attachment receptor. ACE2 is expressed in several organs such as lung, heart, kidney, intestine and also endothelial cells.

However, for entry and replication to occur other conditions need to be met, including that S is cleaved at a furin-like site. So far, a plasma membrane-resident protease and a late endosomal protease have been identified, but it is not clear to what extent the protease(s) affects tropism.

Additionally, for a productive infection, engagement of S glycoprotein with its receptor must be followed by virus internalisation either by endocytosis or fusion at the plasma membrane. Currently for coronaviruses, both major routes have been documented, but discrepancies exist depending on the cell system used and, even for the same virus, more than one pathway has been identified depending on the cell line used in the experiment.

Thanks to available expertise, there will be scope to investigate infection and by-standard effect in *in vitro* systems that mimic the respiratory and endothelial systems (air-liquid interface; *ex vivo* cells/tissues).

Overall, you will deliver the fundamental research to shed light on the fundamental virology aspects of SARS-CoV-2 that underpin the complexity and severity of the pandemic of COVID-19.

**Skills development**

You will become proficient in molecular biology and virology and cellular biology, including working in Containment Level 3. You will be able to design and deliver strategies to manipulate viral entry, endocytosis and protein processing. You will develop awareness of how fundamental virology is informed by clinical manifestations and can provide direction for therapeutic repurposing or development.

**Funding notes**

Students will receive a stipend and will have 3.5 years of fees paid for them. This fully-funded PhD studentship (3.5 years) is open to UK/EU/Overseas students and students from Lower and Middle Income Countries on the [DAC list of ODA recipients](http://www.oecd.org/dac/financing-sustainable-development/development-finance-standards/daclist.htm) are particularly encouraged to apply.

**References**

**How to apply**

This project suits a self-motivated person with a strong will to learn and deliver.

Minimum academic requirement is 2:1 Honours degree (or the overseas equivalent) and a Master’s qualification in an appropriate discipline will be a distinct advantage. You will also have hands-on experience in virology and/or molecular biology and/or protein expression in the context of a research laboratory (e.g. final year project; summer/year placement; MSc dissertation).

You will have a strong interest in virology and its impact in global health, coupled with a pro-active attitude to problem-solving.

You will have excellent written and verbal communication skills in English. Applicants whose first language is not English are expected to meet the [minimum University](https://www.sgul.ac.uk/study/life-at-st-georges/international-student-support/english-language-requirements) requirements for postgraduate studies e.g. 6.5 [IELTS](https://www.ielts.org/about-the-test/how-ielts-is-scored), with higher scores being a distinct advantage.

Please send the application form and the reference forms to researchdegrees@sgul.ac.uk by Sunday 9th August 2020

**Contact for information**

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