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| **Research Theme: Cell Biology; Neuroscience; Immunology** |
| **PhD Research Project Title: The role of stress granules in human microglial function** |
| **Scholarship category (Please indicate the type of scholarship for this project):**  **Grant Scholarship NTU Central RSS** |
| **Principal Investigator/Supervisor: Claudio Bussi** |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background:** Although the detrimental effects of neuronal dysfunction in neurodegeneration are well-documented, the contributions of microglia—the immune sentinels of the central nervous system—to brain health and disease progression demand further exploration. We recently uncovered a previously unknown role of stress granules (SGs), which are membrane-less organelles that form in response to cellular stress, in the stabilization and repair of damaged lysosomes in human macrophages (Bussi, et al., Nature 2023), a critical process that may be compromised in neurodegenerative diseases. This project aims to further investigate the components and functions of SGs in microglial cells under various physiological stressors, hypothesizing that the functionality of SGs is closely linked to their protein composition and cellular trigger. Although previous research has shown that SGs can stabilize ruptured lysosomal membranes, the molecular and structural determinants underlying SGs interactions with lysosomes and other membrane-bound organelles, such as mitochondria and the endoplasmic reticulum, remain unknown. This research proposal aims to determine if biomolecular condensate-mediated stabilization of damaged membranes is a universal or context-specific mechanism, identifying the proteins involved and assessing their functional outcomes. Furthermore, the proposal seeks to clarify the complex mechanisms regulating the formation and degradation of SGs and biomolecular condensates, with a focus on aging and metabolic changes.  **b) Proposed work:** The successful candidate will work with human microglial cell lines and iPSC-derived microglial cells (Drager et al., Nature Neuroscience 2022) and implement cutting edge technologies such as, organelle proteomics, flow cytometry, extracellular flux analysis, super-resolution live cell imaging and gene engineering.  **c) Preferred skills**: molecular cloning, experience with confocal and/or super-resolution microscopy, good knowledge of any language for statistical computing and graphics (e.g., R), experience with stem cells or iPSC culture would be a big plus but nor indispensable. |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:** [**claudio.bussi@crick.ac.uk**](mailto:claudio.bussi@crick.ac.uk)**;** [**https://www.bussilab.com/**](https://www.bussilab.com/) |
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