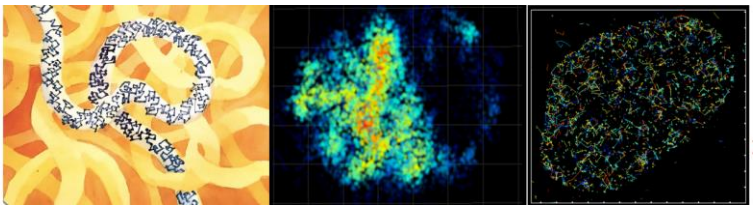

3 to 6 months Master 2 internship in experimental biophysics (starting from February 2023)

Title of the research topic	Dynamics of DNA repair at super resolution
Laboratory	Laboratory of Computational and Quantitative Biology (LCQB), UMR 7238 CNRS, Sorbonne University, 75005 Paris
Master supervisor	Judith Miné-Hattab
e-mail	Judith.mine-@curie.fr

Scientific Project:

Our genome is constantly damaged by a variety of exogenous and endogenous agents. Among the various forms of DNA damage, double-strand breaks (DSBs) are the most cytotoxic and genotoxic for the cell. Eukaryotic organisms use several mechanisms to repair DSBs among them non-homologous end-joining (NHEJ) and homologous recombination (HR). Here, **we investigate the molecular mechanisms of HR proteins inside cells at the single molecule level in human cells**. In response to DSB, repair proteins colocalize from diffuse distribution to repair foci located at the damaged DNA site. An enduring question in the DNA damage field is how do repair proteins find their correct target and accumulate within repair foci: how do they diffuse before DNA damage, during focus formation and inside such a repair focus? Despite their functional importance, the physical nature of repair sub-compartments remains largely unknown.

To answer these questions, we use **single particle tracking** (SPT) and **PALM** (Photo Activable Localization Microscopy) approaches allowing us to assess the physical properties underlying repair foci formation and decipher the internal structure of these condensates. Watching how proteins move and interact within a living cell is crucial for better understanding their biological mechanisms. In addition, more recently we have developed a unique set-up combining laser micro-irradiation and single molecule microscopy. This technique allows us to induce DNA damage directly on cells and to follow the mobility of individual proteins by SPT as soon as a few seconds after irradiation. During the internship, we will use this set-up in living human cells to address how the mobility of repair proteins is affected a few seconds after UV-induced DNA damage.

Reference:

Heltberg Mathias et al. ***eLife***, 10:e69181, **2021**; Judith Miné-Hattab et al., ***eLife***, 10: e60577, **2021**.

The Master internship could open to the possibility of a PhD thesis on this topic.

Techniques used: Fluorescent microscopy, super-resolution microscopy, advanced image analysis, cell biology, human cells culture.