Title of Project:	Visualizing protein function and malfunction in live cells: Application of super-resolution fluorescence microscopy to biologically and bio-medically important processes.
Cell Mechanism Supervisor Name	Lynne Regan
Quantitative Supervisor Name	Mathew Horrocks

Summary of project
An overarching goal of modern cell biology to determine the spatiotemporal behavior of all macromolecules and their complexes within live cells. Super-resolution microscopy plays a vital role in this endeavor. We have invented a simple yet powerful new way to perform super-resolution fluorescence microscopy. Our method is non-perturbing, it is spatially & temporally controllable, and it can be performed in live cells. The method involves fusing a protein of interest to a short peptide, and achieving the labeling via interaction of this peptide with a peptide-binding module-fluorescent protein fusion. We have already demonstrated that the method works well, and have applied it extensively in yeast. We now propose to apply this novel method to study TAR DNA-binding protein 43 (TDP-43) whose aggregation is associated with Amyotrophic Lateral Sclerosis (ALS). Studying the aggregation of TDP-43 has proven to be exceedingly challenging, particularly in cells, in part because direct fusion of TDP-43 to a fluorescent protein significantly perturbs its activity. The rotation project will involve manipulating and studying the TDP-43 protein in yeast. Working in yeast will ensure that the student is exposed to many different cellular and quantitative/physical methods during the course of a short rotation. The thesis version of this project would evolve to also study this process in mammalian cells. This project will provide the student with excellent interdisciplinary mentorship and the student will work alongside others with related interests and diverse undergraduate backgrounds.

What quantitative skills will the student acquire or develop during their PhD project?
The supervisors of this project will combine their expertise in protein structure/design (Regan), cell biology (Regan), neuroscience (Horrocks) and super-resolution microscopy techniques (Horrocks). Skills that will be developed include cell and molecular biology techniques, cell culture, gene editing, advanced microscopy (single-molecule and super-resolution), data analysis and coding.