**TITLE**

Transport of Pseudomonas Exotoxin A to the nucleus in Nuclear Envelope-Associated Endosomes

**ABSTRACT**

Endocytosis of cargo follows three pathways: recycling to the cell surface, retrograde trafficking via the golgi apparatus or degradation in lysosomes. Pseudomonas exotoxin A binds the cell surface receptor LRP1. It is internalised through endocytosis and typically traffics through from the golgi to the ER and cytoplasm. However, Pseudomonas Exotoxin A can follow a fourth pathway, translocating directly from the cell surface to the nucleus, skipping golgi trafficking where packaging and sorting of the cargo to their subcellular destination normally occurs. The toxin translocates to the nucleus in vesicles called Nuclear Envelope-Associated Endosomes (NAEs); these vesicles are derived from early endosomes. NAEs dock at the nucleus, fuse with the nuclear envelope and discharge their content into the nucleus.

My project involves using fluorescent imaging to visualise NAEs in live and fixed cells. I will carry out co-localisation studies to characterise NAEs and find out which cargo follow these pathways and whether there are specific markers or Rabs present on these vesicles. A large-scale siRNA screen will be carried out to help understand the pathway these vesicles follow to associate with the nucleus and fuse with the envelope.