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The characterisation of EphA1 receptors and their potential role in late onset Alzheimer's disease

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A recent genome wide association study identified new late onset Alzheimer's disease (LOAD) susceptibility loci, including the erythropoietin-producing-hepatocellular-carcinoma receptor (EphA1) gene that encodes EphA1; a membrane inserted tyrosine-kinase. EphA1 interaction with its ligand can lead to cell-to-cell adhesion or cell-to-cell repulsion, thought to contribute to the development of LOAD. Research suggests EphA1 signal termination may be caused by a disinterring and metalloproteinase domain-containing protein (ADAM). Therefore, we aimed to determine the effects of ephrinA1 and phorbol-12-myristate-13-acetate (PMA), an ADAM activator, on EphA1 localization. The expression and subcellular distribution of EphA1 in HEK-293 cells was determined following engagement with either its high affinity ephrinA1-ligand or PMA, using western blotting and immunocytochemistry. Antibodies against the EphA1 C-terminus were used to analyze the subcellular localization of EphA1 in intact cells by indirect immunofluorescent staining. To determine whether EphA1 undergoes constitutive or ligand-induced ectodomain proteolysis, EphA1 species in cell lysates and conditioned media were analyzed by western blotting. Immuno cyto-chemical staining shows the EphA1 C-terminus is internalized over three hours of ephrinA1-exposure, but not following PMA-exposure. Qualitative analysis of western blot data shows ephrinA1, but not PMA, causes the release of a cleaved protein fragment of ~75kDa from EphA1 expressing cells into the media. These findings suggest that EphA1 is internalized and degraded on exposure to its ephrinA1-ligand; consistent with current research that describes Eph receptor cleavage and ectodomain shedding following exposure to their respective ephrin ligands. Development of these findings may reveal a biomarker or therapeutic target for patients with EphA1 variant LOAD.

Biography

Louise Rogers completed my Medical Degree at Cardiff University in 2018. During this time, She also achieved a First-Class Honors in a Science in Pharmacology Intercalated Degree. She is currently working as a Foundation Year 1 Doctor in the Oxford University Health Trust where she has applied skills to Acute General Medicine, Psychiatry and Surgical Emergency settings. She hopes to complete Foundation Year 2 training in the UK before experiencing international healthcare settings and then returning to the UK to complete my consultant training.

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