New treatments for age related macular degeneration

Vascular Endothelial Growth Factor (VEGF) is a fundamental regulator of angiogenesis (new vessels formation from pre-established vessels). It is responsible for pathological blood vessel growth and increased micro-vessel permeability in many diseases including ocular pathologies such as wet age related macular degeneration (wAMD) and diabetic retinopathy (DR). VEGF comprises two families of isoforms generated by alternative mRNA splicing, the conventional VEGF isoform family members ($VEGF_{xxx}$ - dominant member $VEGF_{165}$) are pro-angiogenic, and a sister family ($VEGF_{xxx}b$ - dominant member $VEGF_{165}b$) that are anti-angiogenic. Alternative splicing is regulated at the cellular level, and switches during the angiogenesis in a process regulated by the kinase SRPK1. We recently identified drug targets and existing compounds that control the balance of VEGF alternative splicing. These compounds target a key series of molecules in the VEGF alternative splicing regulatory pathway. We have now gone further and identified novel small molecular weight SRPK1 inhibitors and SRPK1 inhibitors that can be given topically as eye drops to inhibit angiogenesis in in vivo models of wAMD without adverse effects in rodents. This project will characterise the pharmacology, safety, pharmacokinetics and efficacy of these new compounds, to use this information to develop efficacious compounds and understand the pharmacology of these compounds.

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Band: High Cost research

Theme: Ophthalmology

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