BMC Pharmacology

Poster presentation

Open Access

A novel role for cGMP-specific phosphodiesterase, PDE6, in active transport of cGMP

Jonathan P Day*[1], Miles D Houslay[2] and Shireen-A Davies[1]

Address: [1]Institute of Biomedical and Life Sciences, Division of Molecular Genetics, University of Glasgow, Glasgow G11 6NU, UK and [2]Division of Biochemistry and Molecular Biology, University of Glasgow, Glasgow G11 6NU, UK

Email: Jonathan P Day* - 0007468d@student.gla.ac.uk

* Corresponding author

from 2nd International Conference of cGMP Generators, Effectors and Therapeutic Implications
Potsdam, Germany, 10–12 June, 2005

Published: 16 June 2005

BMC Pharmacology 2005, **5**(Suppl 1):P11 doi:10.1186/1471-2210-5-S1-P11

Efflux of cyclic nucleotides via active transport in many cell types has been documented for many decades. However, the only route of cyclic nucleotide breakdown is via the action of specific phosphodiesterases (PDEs). The mammalian cGMP-specific phosphodiesterase, PDE6, was established as a retinal-specific enzyme. By contrast, the close Drosophila PDE6 homologue is functionally expressed in Drosophila Malpighian (renal) tubules. Generation of transgenic Drosophila allowing targeted expression of tagged PDE6 to tubule Type I (principal) cells revealed localisation of PDE6 primarily at the apical membranes. As expected, such targeted over-expression of PDE6 resulted in elevated cGMP-PDE activity and in decreased cGMP content. Significantly, over-expression of PDE6 inhibits active transport and efflux of cGMP by tubules. This effect is specific to PDE6 action, as no effect on cGMP transport is observed in tubules from a bovine PDE5 transgenic line. Specific ablation of PDE6 via expression of a targeted PDE6 RNAi transgene in tubule principal cells results in significantly increased active transport of cGMP, thus proving a direct, cell-specific role for PDE6 in cGMP transport. Finally, pharmacological inhibition of PDE6 in wild-type tubules using the vertebrate cG-PDE inhibitor, Zaprinast, also results in stimulated cGMP transport. We provide the first demonstration of a novel role for non-retinal PDE6 in regulating cGMP transport and efflux in a fluid-transporting epithelium.