Author's response to reviews

Title: The asthma candidate gene NPSR1 mediates isoform specific downstream signalling

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Version: 2 Date: 26 October 2010

Author's response to reviews: see over
Dear Editors:

We would like to submit our manuscript “The asthma candidate gene NPSR1 mediates isoform specific downstream signalling” by Christina Orsmar Pietras et al. for consideration of possible publication in *BMC Pulmonary Medicine*.

Neuropeptide S Receptor 1 (NPSR1, earlier GPR154 or GPRA) has been implicated in human allergy and asthma and neurobehavioral phenotypes in rodents. In humans only, the gene undergoes alternative splicing resulting in two functional isoforms that are in part differentially expressed in healthy and asthmatic airways and white blood cells. Because of their differential expression in disease, it is highly relevant to understand the possibly different signalling properties of the isoforms. We report here that the NPSR1-A isoform signals overall stronger than B, with one notable exception, CD69, that may be of relevance in inflammatory processes, as it has been recently implicated in controlling allergic airway inflammation. We further show that both isoforms employ the cAMP/PKA, MAPK/JNK and MAPK/ERK pathways, although A in general with higher efficiency. The signalling difference was not simply due to kinase target differences in the carboxyterminal tail of the isoforms. We believe that these studies are of high interest of a number of readers of *BMC Pulmonary Medicine*.

All of the material presented is original and has not been submitted for publication elsewhere. All authors have read the manuscript and have approved its submission to *BMC Pulmonary Medicine*.

We look forward to your decision.

Juha Kere
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