PROTEINASE ACTIVATED RECEPTOR-2 AND AUTOPHAGY REGULATION IN AIRWAY EPITHELIA CELLS

Kirsty McCallum¹, Mariarca Bailo¹, Lynette Dunning¹, Marija Stankovic¹, Lorcan McGarvey², Mark Hollywood³, Carl S. Goodyear⁴, Anne Crilly¹, John C. Lockhart¹, Gary J. Litherland¹.

1: Institute of Biomedical and Environmental Health Research, Health and Life Science, University of the West of Scotland, Paisley, PA1 2BE, Scotland.
2: School of Pharmacy, Queen’s University, Belfast, Northern Ireland.
3: Smooth Muscle Research Centre, Dundalk Institute of Technology, Dundalk, Ireland.
4: Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, Scotland.

Lungs from patients with chronic obstructive pulmonary disease (COPD) display hallmarks of premature ageing including reduced autophagy, which contributes to cellular senescence. However, mechanisms underlying dysregulated lung autophagy remain unclear. While proteinase activated receptor-2 (PAR2) is a drug target for inflammatory conditions, with documented roles in lung pathology, a role for this receptor in lung ageing is yet unexplored.

To investigate this, primary human epithelial cells and epithelial cell lines were stimulated with PAR2 activators (SLIGKV, trypsin) and autophagy quantified using a fluorescent marker of autophagosomes (CYTO-ID detection kit). Western blotting to analyse expression of autophagy-related proteins was used to confirm findings. PAR2 expression was assessed by immunofluorescence.

We confirmed that PAR2 was on human airway epithelial cells. Autophagic vesicles were successfully detected and modulated by appropriate autophagy control stimuli. Stimulation of PAR2, assessed alone and in combination with inflammatory stimuli, resulted in modulation of the level of autophagic activity within airway epithelial cultures.

Our study provides the first data that suggests a role for PAR2 in the regulation of autophagy in lung airway epithelia. This further suggests a possible novel targetable mechanism underlying conditions such as COPD that feature premature lung ageing.