

Correspondence

Is substance P a nasal epithelial neuropeptide?

To the Editor:

The article by Larsson et al¹ and the accompanying editorial by Kulka² pose a number of very important and provocative questions. In the interest of clarity, we address these issues and provide perspective in this emerging field.

Substance P was first isolated as a sialogogic peptide from extracts of bovine central nervous system by Chang et al,³ who also characterized this peptide through amino acid sequencing.^{3,4} Since this discovery by Leeman, substance P expression has been identified in different organs and cells, including the central and peripheral nervous systems and immune system.⁵

The quest to find a mediator of innate immunity in the airway and other sites of microbial entry is ongoing. Numerous bacteria and viruses enter the respiratory tract through the nasal passages. Of note, substance P and its cognate receptor, neurokinin-1, are mediators of immune activation, suppression, and inflammation.^{5,6}

The detection and identification of cell sources of substance P and neuropeptides remains complex. Specificity controls and functional assays are essential and necessitate valid active and inactive antagonists.⁶ It is well known that large quantities of substance P are present in ganglia, neurons, and the nervous system. However, any claims related to substance P and neurokinin-1 receptor detection in biopsy specimens, *ex vivo* cellular systems, and multiply passaged cells require application of multiple detection systems at the DNA, RNA, and protein levels.

Larsson et al¹ describe the detection of substance P release from murine trigeminal ganglion neurons, mouse nasal epithelial cells, and primary human nasal epithelial cells. They claim that nasal epithelial cells released detectable quantities of substance

P in the range of less than 1 pg/mL per 500,000 cells.¹ The ELISA kit used in these studies (Substance P EIA; Cayman Chemical, Ann Arbor, Mich) is a competitive assay with a detection range of 3.9 to 510 pg/mL. Studies using an additional confirmatory assay, such as single-molecule analysis, which measures femtomole (fg/mL) quantities, would have aided in further demonstrating expression levels of substance P in the nose. Future studies are required to demonstrate definitive detection of substance P and its cognate receptor neurokinin-1 in the nasal epithelium using high-sensitivity assays.

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