

Is the Dust Mite Allergen Der p1 Protozoal in Origin?

To the Editor:

The major allergen in house dust mites faeces, Der p1, is believed to have a role in digestion of the mite's main food supply (human epithelium). We postulate that the digestion of human epithelial scales by dust mites may rely on a symbiotic relationship between protozoa and mites, whereby the Der p1 required for mite digestion is produced by protozoa or other intestinal commensals rather than being of mite origin.

Der p1, a cysteine protease [1], affects matrix remodeling and immuno-regulation [2]. It is a potent inducer of proinflammatory cytokines, disrupts intercellular tight junctions and facilitates the transfer of allergens across the respiratory epithelial barrier [3].

There are important protozoal parallels. In parasitic organisms, including protozoa, cysteine proteases play important roles in pathogenic mechanisms including: cell invasion, immunoevasion, encystment, etc. Flagellated protozoa, including *Trichomonas vaginalis* and *Giardia lamblia*, display these phenomena when parasitizing human mucosal cavities. Cysteine proteases have been implicated as virulence factors utilized by *T. vaginalis*, including cytotoxicity by extracellular matrix proteins degradation [4], epithelial cell detachment and apoptosis [5]. *G. lamblia* cysteine proteases damage mucosa in giardiasis [6] and may increase antigen penetration [7].

The Der p1 gene, also called Peptidase 1 (mite), contains two active enzymes, a cysteine protease inhibitor and a C1A cysteine peptidase. Der p1's cysteine peptidase falls within the clan CA, family C1, sub-family C1A, which includes around 1300 sequenced enzymes (http://merops.sanger.ac.uk/cgi-bin/make_frame_file?id=c1a;action=tree). The C1A subfamily includes papin and cathepsin like enzymes that are distributed widely across many life forms including plants, nematodes, viruses, fungi, protozoa and mammals. The difference in protein sequence between different protozoal C1A enzymes, using tools such as BLAST, is not greater than the difference between Peptidase 1 and, for example, a C1A enzyme found in *Tetrahymena thermophila*. This moderately high level of sequence homology indicates that a protozoal origin for Der p1 cannot be excluded, although the sequence is not identical to that of any known protozoa.

The studies that identified the Der p1 protein structure/gene sequence used mite faeces or crushed samples of whole mites as their starting point [8]. They did not distinguish between gut contents and mite tissue and

cannot therefore exclude a protozoal origin for Der p1. In contrast, Der p5 has been identified in secretory granules of the midgut of epithelial cells of house dust mites indicating that it is of mite origin [9].

Protozoal forms have been found in intestinal extracts of dust mites [10]. Multiflagellated protozoa have also been demonstrated in the sputum of a proportion of asthmatics and we have previously postulated that the inhalation of mite faeces could introduce protozoa to the lungs.

It is conceivable, therefore, that Derp1 could be of protozoal, rather than of mite origin, as is currently assumed. This question is important because if it is found that Der p1 has a protozoal origin, then a number of existing anti-protozoal chemotherapeutic agents could be explored as treatments for Der p1 related allergic conditions.

References

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R. Martínez-Girón* & H. C. van Woerden†

*Protozoal Respiratory Pathology Research Unit.
Fundación INCLÍNICA,
Calvo Sotelo,
Oviedo, Spain;

and

†Division of Community Health Sciences, St George's
University of London,
Cranmer Terrace, London, UK

Correspondence to: Dr R. Martínez-Girón, Fundación
INCLÍNICA, Calvo Sotelo, 16-3º dcha, 33007-Oviedo,
Spain.

E-mail: rmartinezgiron@hotmail.com