Pollen found guilty

For the large proportion of the population that suffers the misery of hay-fever every year, the usual explanation has been that it is our immune system that should shoulder the blame for an overactive response to foreign, but harmless, pollen antigens. However, new work published in The Journal of Clinical Investigation shows that pollen can no longer be considered the innocent party and itself has an active role in inducing the airway inflammation that is responsible for symptoms.

Pollen antigens induce an adaptive immune response that leads to the recruitment of granulocytes, such as eosinophils and mast cells, to the airways. Granulocytes, in turn, contribute to the inflammatory response through the production of reactive oxygen species (ROS) by NADPH oxidase. Boldogh and colleagues now show that pollen also contains a plant NADPH oxidase that can cause oxidative stress in the absence of an adaptive immune response.

Fractionated extracts of ragweed pollen (RWE) were tested for their ability to reduce nitroblue tetrazolium (NBT) to generate ROS. The activity of the fractions that reduced NBT (pRWEOx) required NADPH substrate and was blocked by superoxide dismutase, which shows that ROS generation in the NBT assay is due to superoxides produced by a pollen NADPH oxidase.

RWE increased intracellular ROS levels in cultured epithelial cells and in the airway epithelium in a mouse model of airway challenge, and RWE and pRWEOx, but not fractions that lacked NADPH-oxidase activity (pRWEmix), led to increased levels of ROS and oxidative-stress markers in bronchoalveolar-lavage fluid. This occurred in mice that were deficient in mast cells, or in B cells and T cells, indicating that the ROS are generated by intrinsic pollen NADPH oxidases rather than by immune cells.

In wild-type mice, challenge with RWE resulted in recruitment of eosinophils and other inflammatory cells to the lungs, possibly through the production of CXC-chemokine ligand 8 (CXCL8), but challenge with heat-treated RWE (pRWEmix), which lacks NADPH-oxidase activity) recruited significantly fewer cells than did challenge with RWE. Addition of a surrogate ROS generator to pRWEmix reconstituted allergic airway inflammation, but the ROS generator alone could not induce inflammation.

The authors therefore suggest a two-signal model for the induction of allergic airway inflammation, in which signal 1 is the innate response generated by pollen NADPH oxidases (that is, oxidative stress) and signal 2 is the adaptive immune response to pollen antigens. Signal 1 is not sufficient to induce allergic inflammation in the absence of signal 2, but signal 1 has an important role in augmenting signal 2.