**Why do some asthmatics get ABPA and some bronchiectasis?**

Allergic Pulmonary Aspergillosis (ABPA) complicates asthma, cystic fibrosis and bronchiectasis. Affected patients develop an allergy to the spores of the *Aspergillus* moulds. ABPA often presents with shortness of breath, coughing and wheezing. If unrecognized or left untreated then in the long term ABPA can lead to permanent lung damage (fibrosis).

It is likely that its underlying cause is primarily genetic, with a 5% occurrence rate among family members. Many genes are involved, including those associated with recognition of *Aspergillus* in the lungs (surfactant, TLR3 and TLR9), processing by the immune system of *Aspergillus* proteins as ‘foreign’ (HLA) and triggering an exaggerated allergic response (cytokines). A couple of really important genetic links, which are not yet understood relate to cell to cell junctions and special action proteins called non-receptor tyrosine kinases. These tyrosine kinases regulate how cells adhere to each other and the communication channels within cells. It is likely that genetic differences in tyrosine kinases profoundly alter the immune response to *Aspergillus*, which in turn drives damaging inflammation in the airways. All aspects of how the tyrosine kinases work in airway cells, with and without *Aspergillus* present, will be experimentally investigated, culminating in an assessment of the specific genetic differences seen in patients with ABPA with the goal of improving diagnosis and effective treatment of ABPA sufferers.

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