Search for association between allergic diseases and 11p14 genetic variants: Indication of association with NELL1 gene.

Marie-Hélène Dizier (1), Michel Guilloud-Bataille (2), Patricia Jeannin (1), Isabella Annesi-Maesano (3), Jocelyne Just (4), Francine Kauffmann (5), Mark Lathrop (6), Emmanuelle Bouzigon (1), Florence Demenais (1)

(1) INSERM UMRS946, Univ Paris Diderot
(2) INSERM UMR-S535, Univ Paris Sud
(3) INSERM UMR-S 707, Paris
(4) Hôpital Trousseau, Paris
(5) INSERM UMR-S780, Univ Paris Sud
(6) CNG, CEA, Evry; CEPH, Paris

A previous genome-wide linkage scan conducted in French EGEA families (Epidemiological study on the Genetics and Environment of Asthma) detected the 11p14 region linked to three allergic diseases: asthma, atopic dermatitis and allergic rhinitis. Our aim was to further investigate this region using a panel of 306 SNPs genotyped in 365 EGEA families, spanning a 20 Mb region. To test for association of these SNPs and the three diseases, we used three different methods: two family-based tests (FBAT), the first one (FBAT1) applied to affected sibs only, the second one (FBAT2) to affected and unaffected sibs and logistic regression (LR) applied to all siblings while accounting for family dependence.

The strongest association signal was found between asthma and two adjacent SNPs, rs2282661 and rs95119 (r²=0.14) using FBAT1 (p=0.0002 and 0.008 respectively). One of these SNPs, rs2282661, showed also association using FBAT2 (p=0.002) and a marginal signal with LR (p=0.09). Using the parents of the nuclear families as an independent sample, we replicated the association of asthma with rs95119 (p=0.009). The two SNPs showing association belong to NELL1, a gene which encodes a protein that contains epidermal growth factor (EGF)-like repeats and is a potential candidate for allergic diseases. This gene has been recently found associated with Crohn’s disease which shares genetic determinants with asthma. Further analyses using multi-marker methods are underway to confirm our findings.