The **ANO3/MUC15** locus is associated with eczema in family samples ascertained through asthmatics

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A previous genome-wide linkage scan in 295 families of the French Epidemiological study on the Genetics and Environment of Asthma (EGEA) reported strong evidence of linkage of 11p14 to eczema. Our purpose was to conduct fine-scale mapping of the 11p14 region to identify the genetic variants associated with eczema and to investigate the influence of the mode of ascertainment of the data on the association outcomes. Association analyses were conducted in the EGEA discovery dataset using two statistical methods for internal validation: the family based association method (FBAT) and logistic regression. Replication of the EGEA findings was sought in French Canadian (SLSJ study) and UK (MRCA study) family samples, which similarly to EGEA, were ascertained through asthmatic subjects. We also tested for association in two German samples ascertained through subjects affected with eczema. We found significant association of eczema with 11p14 SNPs in the vicinity of the linkage peak in EGEA (p=10^{-4} for rs1050153 using FBAT, that reached the multiple testing-corrected threshold of 1.3x10^{-4}; p=0.003 using logistic regression). Pooled analysis of the three asthma-ascertained samples (EGEA, SLSJ, MRCA) showed strong improvement in the evidence for association (p=6x10^{-5} for rs293974 (OR=0.66), p=3x10^{-5} for rs1050153 (OR=1.5), p=6x10^{-5} for rs15783 (OR=0.69). No association was observed in the eczema-ascertained samples. The significant SNPs are located within the overlapping **ANO3** and **MUC15** genes. Several lines of evidence suggest that **MUC15** is a strong candidate for eczema. Further investigation is needed to confirm and better understand the role of **ANO3/MUC15** locus in eczema and its relationship with respect to asthma.