GENETICS

FINDING NEMO

17.04.2007

<u>ATG16L1</u> is now <u>confirmed</u> as a candidate gene for Crohns disease:

Specifically, the LD structure and association mapping around the most associated SNP [...] rs2241880 implicated a region on chromosome 2q37.1 containing a single gene known as ATG16 autophagy–related 16-like 1 (ATG16L1) [...] Logistic regression analyses conditional on A197T in the family-based samples indicated that this coding variant can fully explain the association signal to this locus; thus, we consider this to be the causal risk variant.

Excellent to have this replication, although the argument above cannot convince me that this already a causal variant.

ATG16L1 seems to be most abundant in CD4+ and CD8+ cells and knockdown of the gene will lead to loss of S. typhimurium autophagy. Does rs2241880 really induce a loss of function and how does it relate to TLR7 and NOD2/CARD15 signalling?

The authors of another <u>Nature</u> paper believe that there is a primary NF-kB signalling defect in the Toll-like receptor activation by intestinal bacteria – see also <u>KEGG</u> pathways. It will be much easier now to ask the right questions.

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