GENETICS

AUTOPHAGY

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Crohn`s disease is still a mystery. Associated gene variants have been described in CARD15, DLG5, SLC22A4, CARD4, TNFSF15, IL23R and many more genes that explain altogether less than one quarter of the disease risk. My friends in Kiel now add ATG16L1 to this list. They looked for nonsynonymous SNPs and voila rs2241880 (A/G*, T300A*) a new disease SNP is born.

What is remarkable in their study that the top 9 SNPs (as judged by significance in the range of 10^-14>p<10^-4) could NOT be replicated for whatever reason. I guess it would be even worse to see also panel C in this table. Expression of ATG16L1 is rather weak in the small intestine, not influenced by the reported SNP, not different in the gut of Crohns patients and not related to disease location. Genecards say that the subcellular location of ATG16L1 is close to a peripheral membrane protein complex known as preautophagosomal structure. Autophagy is an intracellular degradation system delivering cytoplasmic components to the lysosomes (L is not related to ligand or L1 transposon but indicates "like"). The gene has been tested so far in yeast and mouse. Unfortunately, information about ATG16L1 is scarce but there is some work on yeast ATG16 (which seems to miss the domain with the disease SNP).

Some authors believe that macroautophagy is process induced by nutrient starvation in eukaryotic cells, which could explain some of the Crohns' disease characteristics. Autophagy seems to have some developmental effect and may be related to even more diseases. It seems that there are now even more mysteries to solve, yea, yea.