

S006 Autophagy

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Crohn's disease (CD) and ulcerative colitis (UC) are debilitating, inflammatory diseases of the gastrointestinal tract, collectively known as the inflammatory bowel diseases (IBD). Among complex diseases, genetics has been particularly successful in the identification of genes for IBD, with recent efforts in genome-wide association bringing the total number of genes confirmed as associated to more than 40. One of the most unexpected findings that has come from Crohn's disease genome-wide association studies is that autophagy has an important role in disease pathogenesis. Autophagy involves the concerted action of cytoplasmic proteins that generate curved isolation membranes to envelop cytoplasm, cytoplasmic organelles and intracellular pathogens. Autophagy requires the action of two ubiquitin like conjugation (Atg5/12/16L1 and Atg8) systems. This relationship is supported by the finding that two genes involved in autophagic processes - *ATG16L1* and *IRGM* - were significantly associated with disease. Among the associated genes, recent studies have demonstrated that *ATG16L1* is essential for classic and microbe induced autophagy and this, along with association of variation at *IRGM* with CD, confirms that autophagy is a key process in CD susceptibility. We will review the functional implications of *ATG16L1* in murine models of colitis and human IBD. A bioinformatics and functional siRNA based approach to identify ancillary molecules involved in the autophagic process and their roles in different autophagic subtypes will also be presented.

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