Results The Nod2 signalling cascade is diverse. One protein identified, SHP-1, is a phosphatase known to control activation thresholds in immune cells. Another is HMGB1, an alarmin that can interact with beclin to facilitate autophagy. Nod2 also differentially phosphorylates L-plastin which is known to be involved in bacterial trafficking and engulfment.

Conclusion Phosphoproteomics casts light on how Nod2 signals, how this PRR might control DC maturation and inflammatory cytokine production, interact with the autophagy pathway and handle bacteria in DCs.

Competing interests None.

Keywords Crohn's disease, NOD2, phosphorylation, signalling.

OC-126 NOD2 SIGNALLING IN CROHN'S DISEASE

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Introduction NOD2 is an intracellular pattern recognition receptor that induces autophagy in human dendritic cells (DCs) in a manner important for bacterial handling and antigen presentation. Variants of NOD2 associated with terminal ileal Crohn's disease (CD) fail to induce autophagy normally on Nod2 stimulation and in turn display delayed bacterial handling and defective antigen presentation. We have used phosphoproteomics to map the Nod2 signalling cascade in human monocyte-derived DCs in order to identify proteins involved in Nod2 mediated autophagy and inflammatory pathway induction in these cells.

The aim of this study is to determine the molecular basis of Nod2 signalling and its effect on autophagy induction and DC maturation.

Methods Primary human monocytes expressing wild type (WT) NOD2 were used to generate monocyte derived DCs and the effect of stimulation of Nod2 with its ligand muramyl dipeptide (MDP) assessed using phosphoproteomics. Here phosphorylated proteins were extracted from cell lysates pre and post MDP triggering, off-gel fractionated and subject to mass spectrometry analysis by LC-MS/MS and Q-TOF. The function of differentially phosphorylated proteins on DC maturation, autophagy induction and bacterial handling was then investigated following knockdown with siRNAs.