

## WEEKLY GI RESEARCH WEBINAR

# "C1ORF106/INAVA - dual and competing functions for an IBD-risk gene enriched in barrier epithelial cells"



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The seminar will examine how the IBD-risk gene C1ORF106/INAVA acts in human intestinal epithelia to manage environmentally-induced cell stress, inflammation, and the integrity of mucosal surfaces. We found that INAVA exhibits dual activities mechanistically linking epithelial barrier function and inflammatory signaling by IL1 $\beta$ . This is driven by INAVA's signature Domain of Unknown Function DUF3338, which we newly defined as an enhancer of TRAF6-protein ubiquitination. Other ubiquitin-mediated cell-stress pathways are amplified by DUF3338, and these reactions appear to broadly affect the proteome via formation of macromolecular cytosolic INAVA-containing puncta - a form of liquid-liquid phase separation termed biomolecular condensate.

References: (1.) Luong PH, Hedl M, et al. INAVA-ARNO complexes bridge mucosal barrier function with inflammatory signaling. *elife*. 2018;7. Epub 2018/10/26. doi: 10.7554/eLife.385 (2.) Yan J, Hedl M, Abraham C. An inflammatory bowel disease-risk variant in INAVA decreases pattern recognition receptor-induced outcomes. *J Clin Invest*. 2017. doi: 10.1172/JCI86282. PubMed PMID: (3.) Mohanan V, Nakata T, et al. C1orf106 is a colitis risk gene that regulates stability of epithelial adherens junctions. *Science*. 2018;359(6380):1161-6. Epub 2018/02/09. doi: 10.1126/science.aan0814. PubMed PMID: 29420262.

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