Interaction between a virus and the Crohn’s disease gene ATG16L1
Crohn’s disease, a complex genetic disease

>30 genetic loci associated with increased susceptibility!
T300A variant of *ATG16L1* is associated with increased risk of acquiring Crohn’s disease

Generated *Atg16L1* ‘gene-trap’ mutant mice

![Atg16L1 protein expression](image)

*Atg16L1<sup>HM</sup>*

(HM = hypomorph)
Crohn’s patients

“Safe/Safe”

“Risk/Risk”

Paneth cells are abnormal

Atg16L1\textsuperscript{HM}
Murine Norovirus (MNV)

Closely related to human noroviruses that cause gastroenteritis.

Gastroenteritis is associated with increased risk of acquiring inflammatory bowel disease.


Norovirus infection is associated with inflammatory bowel disease.

3x10^7 PFU MNV

7 or 35 days

WT + MNV

HM + MNV

Blue = Nuclei  Red = Lysozyme

n > 5000 cell per condition

p < 0.001
Virus + susceptibility gene influence response to injury

WT + MNV

WT + MNV

HM

n ≥ 6 per condition
Virus + susceptibility gene influence response to DSS

**MNV CR6**

+ **7 days**

2.5% DSS

**HM + MNV CR6**

% Increase in muscle width

**Lymphoid aggregates**

WT HM WT HM

Uninfected MNV

WT HM WT HM

Uninfected MNV
can be prevented by Anti-TNFα or IFNγ or Antibiotics

Unlike CR6, CW3 does not trigger
Virus + Susceptibility Gene = Intestinal abnormalities in a Crohn’s disease model

ATG16L1 T300A

Trigger X

Crohn’s disease

Different Genotype

Trigger Y

Crohn’s disease
## Acknowledgements

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[the broad foundation](https://www.broadinstitute.org)