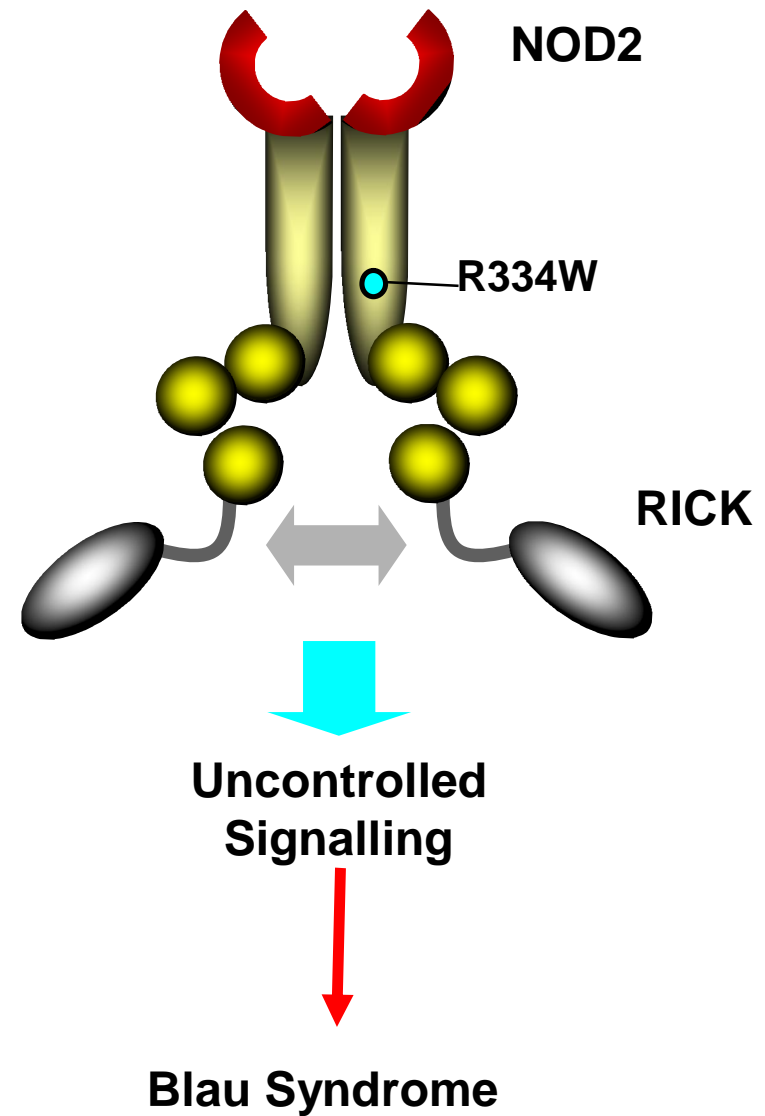
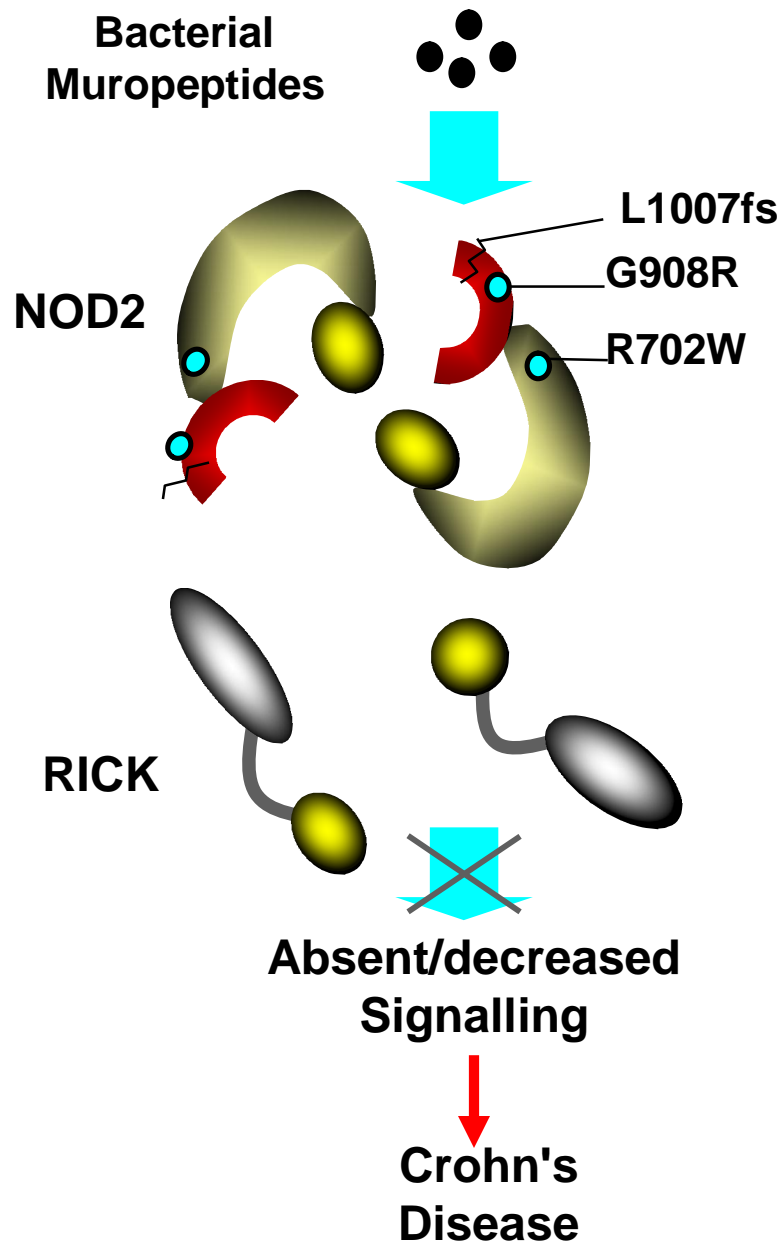


Host defense molecules

# Hypothetical Mechanisms of Disease in Patients with NOD2 mutations



**Nod2 mutations are associated with ileal disease**

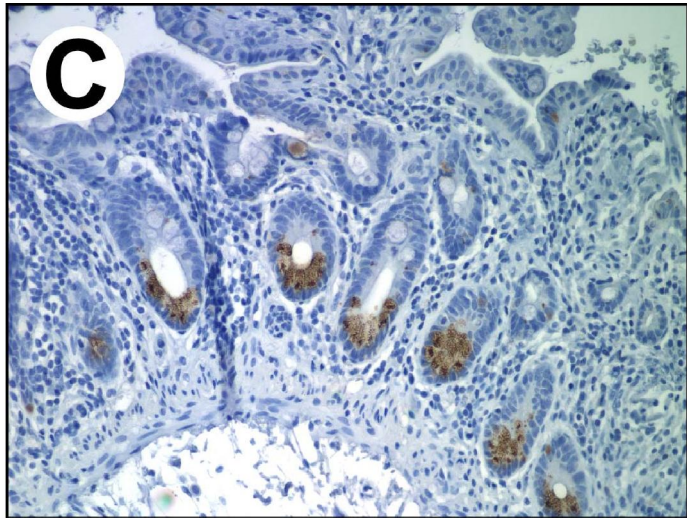
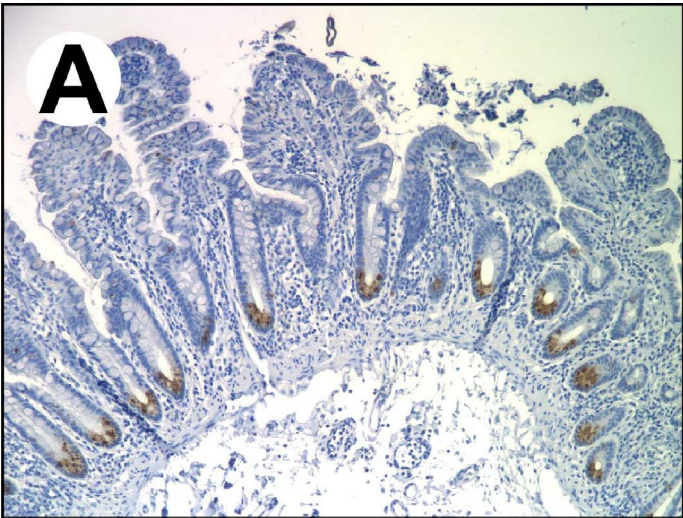
**Why?**

**Presence of particular pathogenic bacteria in the ileum?**

**Specific function of Nod2 in the ileum?**

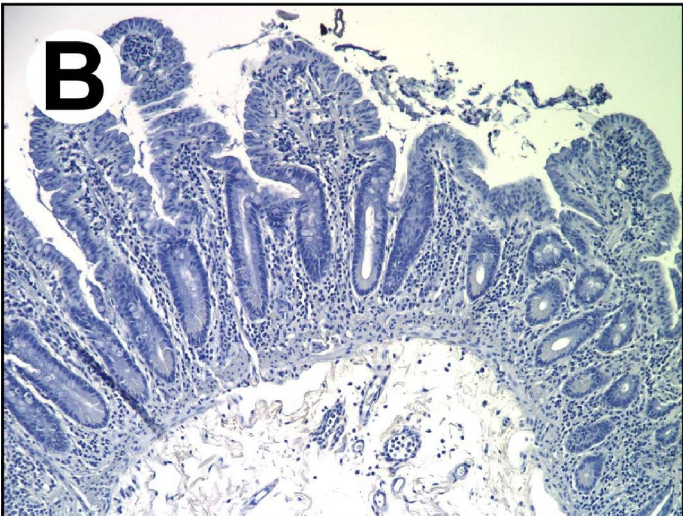
# Expression of Nod2 protein in Paneth cells

2D9



2D9

Control



2D9

Bacteria

Epithelium

Lamina propria

Gut lumen

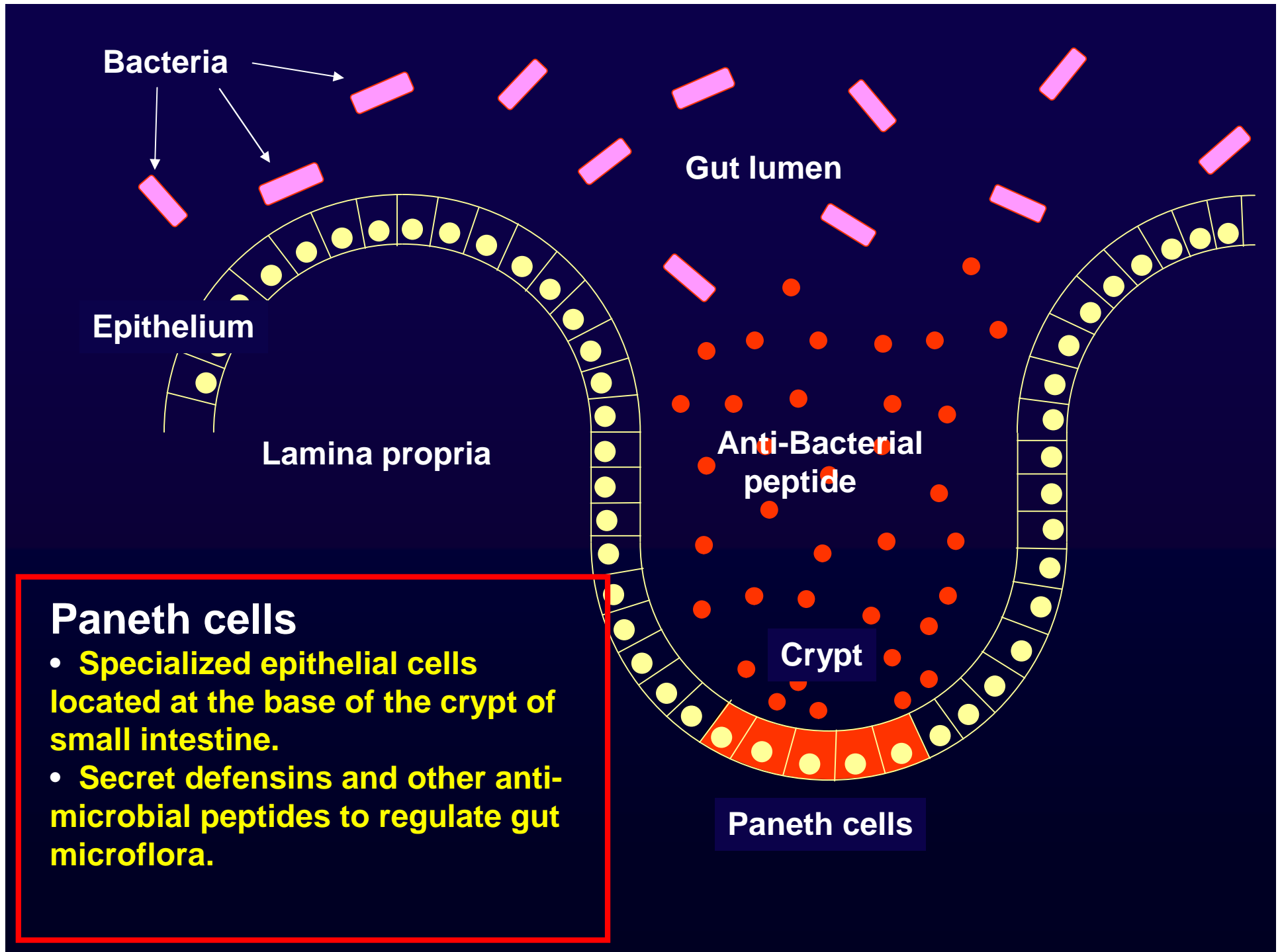
Anti-Bacterial peptide

Crypt

Paneth cells

## Paneth cells

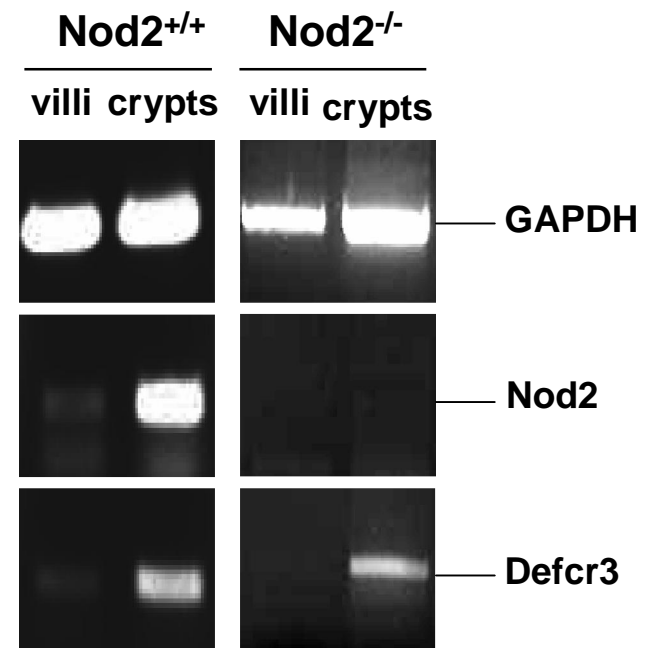
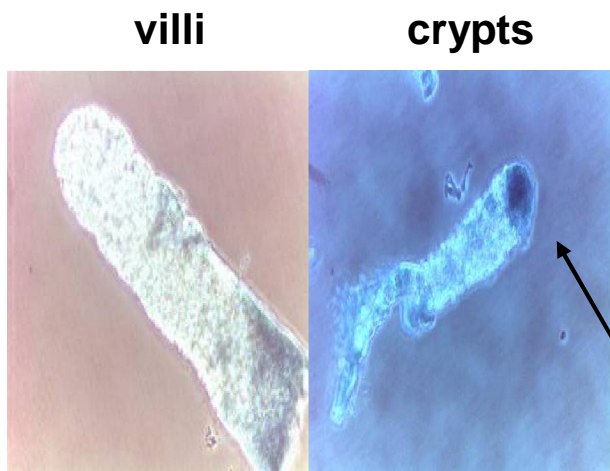
- **Specialized epithelial cells located at the base of the crypt of small intestine.**
- **Secret defensins and other anti-microbial peptides to regulate gut microflora.**



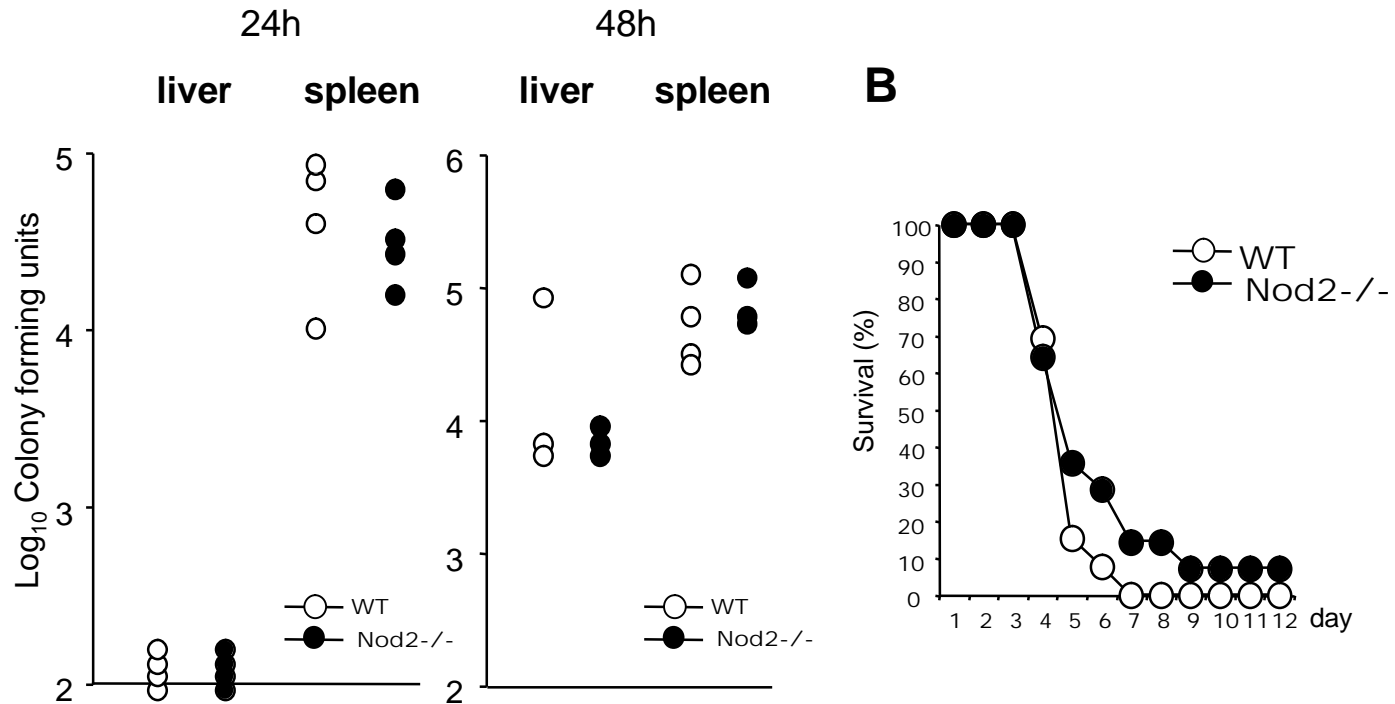
**Aim #1: Determine the role of NOD2 in the regulation of  $\alpha$ -defensin expression**

**Aim#2: Determine the role of NOD2 in the regulation of Paneth cell function**

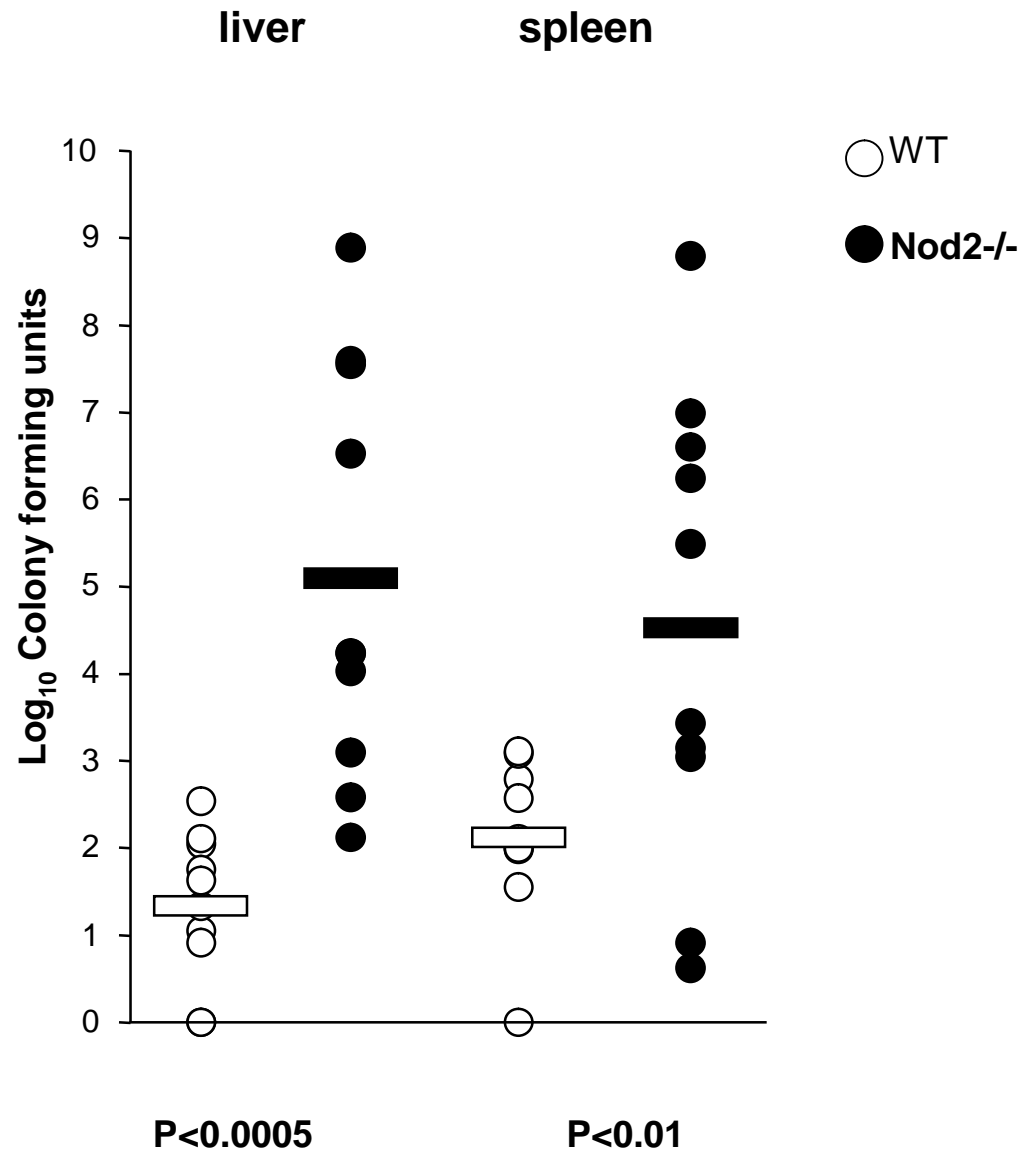
# Mouse Intestinal Crypts Express Nod2



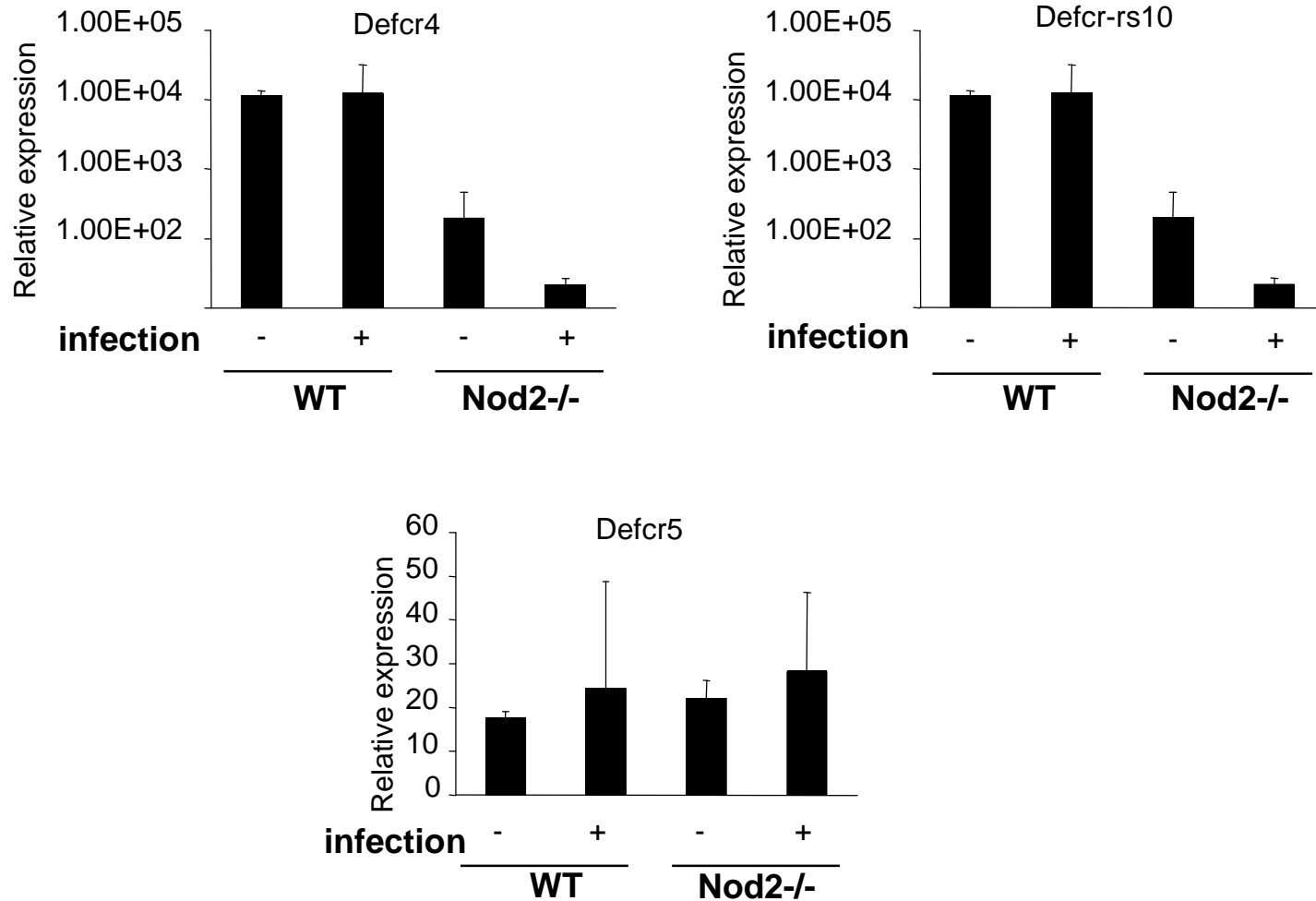
# No role for Nod2 in *Listeria* infection via IV or IP route

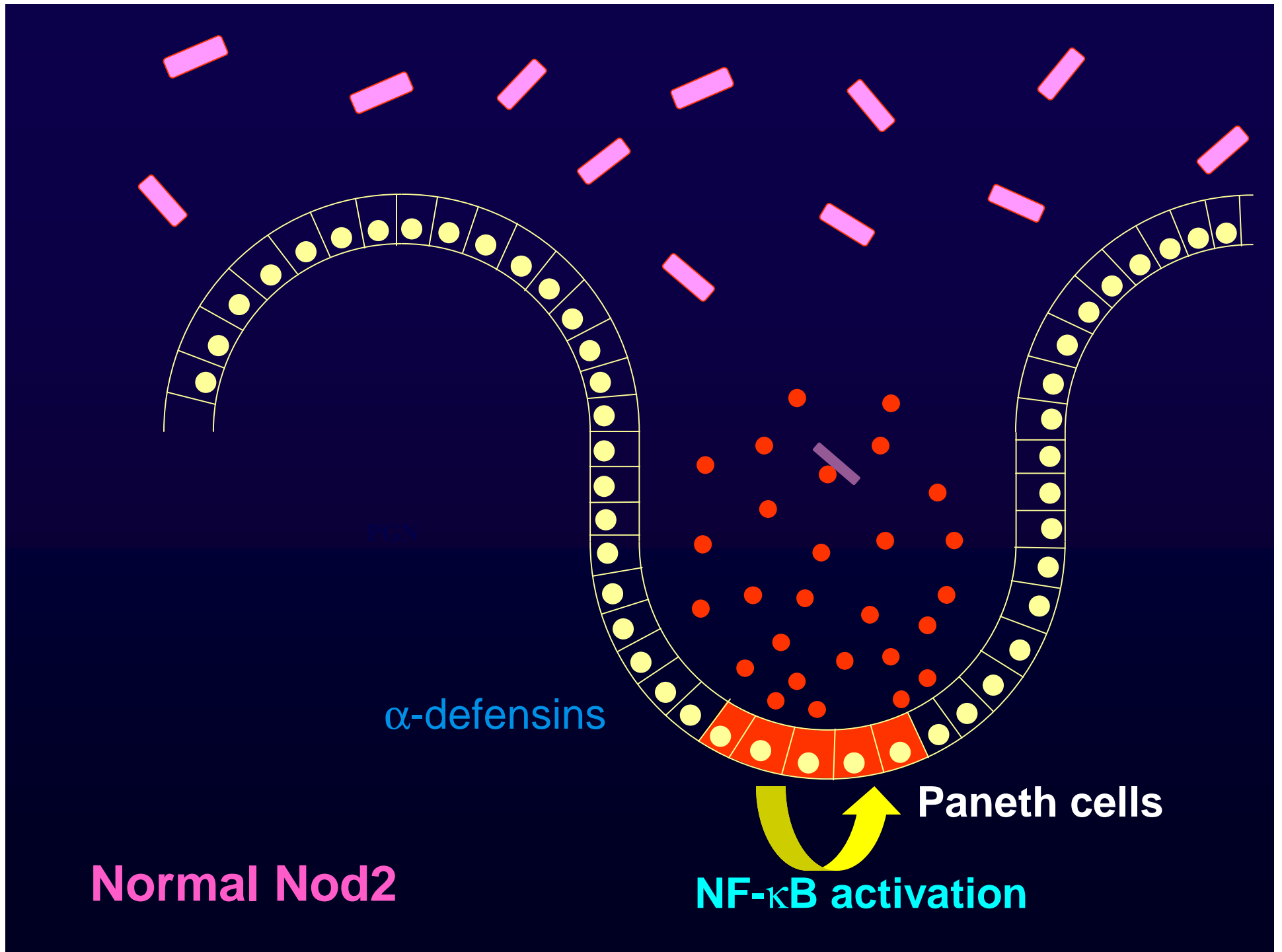


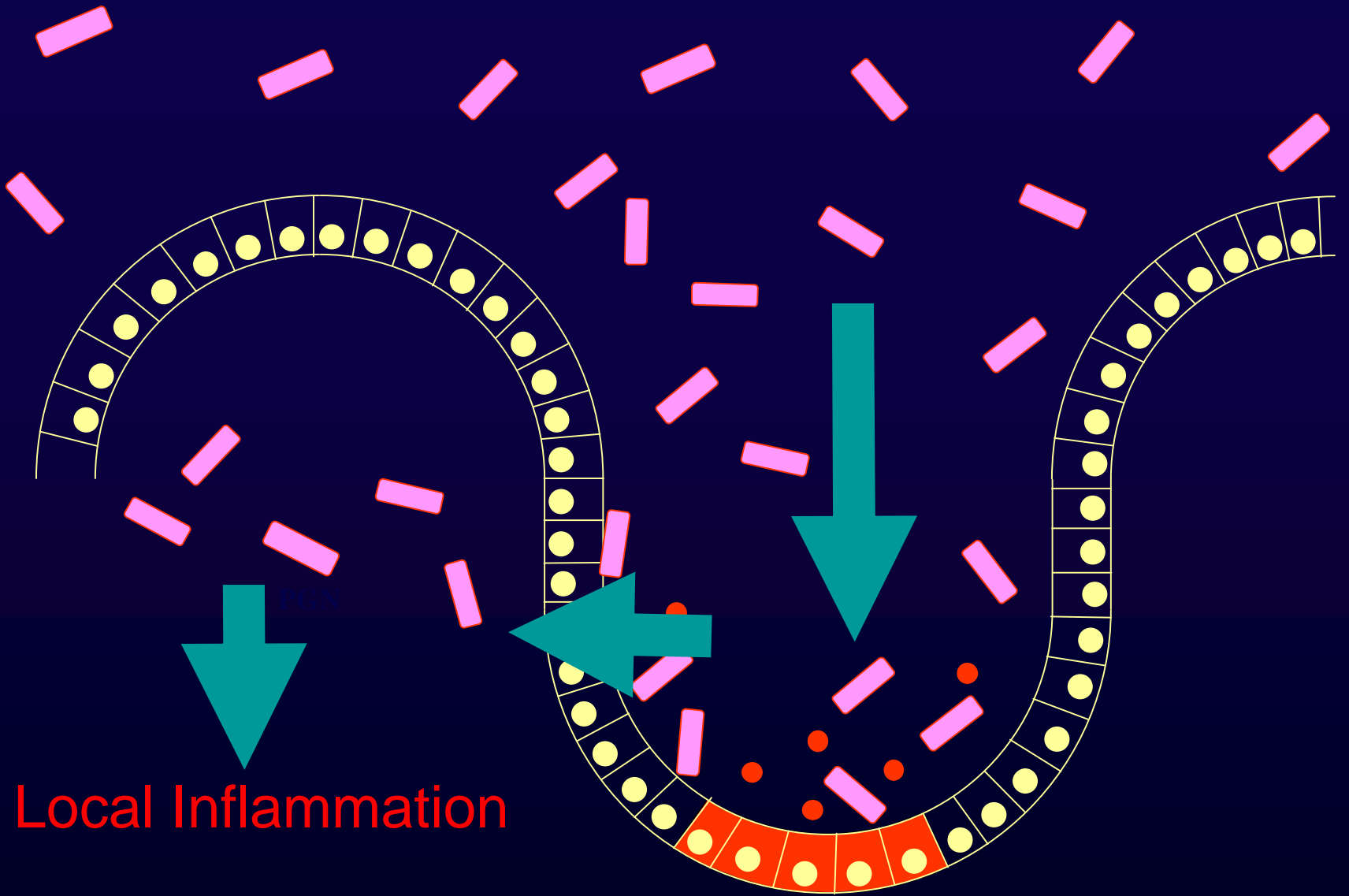
# Critical role for Nod2 in *Listeria* infection via oral route



# Nod2 regulates $\alpha$ -defensin expression in intestinal tissue







Local Inflammation

Paneth cells

Loss of Function of Nod2

**University of Michigan**

Mathias Chamillard

Naohiro Inohara

**Yale University**

Koichi Kobayashi

Richard Flavell