### Microbiota/Gut Epithelium Macromolecular Cross Talk

**Bacteroides thetaiotaomicron (Bt) is a dominant member of the mammalian gut microbiota that secretes Outer Membrane Vesicles (OMVs) into the external milieu. Bt may use OMVs as a mechanism for protein/nucleic acids delivery to host intestinal epithelial and immune cells.**

A eukaryotic-like BtMinpp enzyme is packaged into OMVs. BtMinpp-OMVs have dual roles, in providing dietary nutrients such as phosphate as well as in modifying host cell behaviour by modulating intracellular cell signalling. OMVs are internalised in vivo. Section of intestinal villi with cell nuclei stained blue and OMVs stained orange.

### OMV as Mucosal Delivery Vehicles

Engineering commensal bacteria to generate OMVs containing therapeutic proteins and vaccine antigens for delivery to mucosal sites such as GI-tract and upper respiratory tract.

- **Treatment of inflammatory bowel disease**
- **Induction of immune response**
- **Delivery of OMV to mucosal sites**
- **Intranasal vaccines**
- **Oral vaccines**

### HOMEOSTASIS

**omeostasis**

**Tolerance**

**Steady State**

**Inflammation**

**Dysbiosis**

**Eubiosis**

**Disease State**

**Intestinal Human Microbiota**

**The Gut-Brain Axis in Ageing and Neurodegenerative Disease**

**Healthily aged individual**

**Sporadic Alzheimer disease**

**Brain-Blood barrier permeability**

**Gut membrane permeability**

**systematic availability of:**

- Inflammatory molecules
- Cytokines
- Amyloid

### Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS) Research

The aetiology of ME/CFS is unknown, although there is evidence for an inappropriate immune response and GIT disturbances. We are investigating whether the intestinal microbiome, and in particular the virome, is altered in ME/CFS patients, and if microbial dysbiosis contribute to or explain the pathophysiology of the disease. We also aim to discover if microbial intolerance is intact and if patients generate abnormal immune responses to commensal microbes by self-reactive T and B cells.