

## **Gastric mucosoid cultures: a new model to investigate *Helicobacter pylori* infection and the host response**

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### Abstract:

The lining of the stomach is protected by a continuous epithelial cell layer with a glandular structure. This strong defense barrier can be colonized by *Helicobacter pylori*, inducing an acute inflammatory response that can become chronic if the pathogen is not eradicated. We have developed an innovative cultivation method for the epithelium of the stomach to generate “mucosoids”. These cultures display key characteristics of the mucosa, including the secretion of mucus at the apical surface.

Mucosoids represent primary stem cell-driven cultures that can be maintained for months. These highly polarized columnar epithelial layers encompass all gastric cell lineages including acid producing parietal cells. Their regeneration capacity is maintained by activation of the WNT/ $\beta$ -catenin signaling pathway, which stimulates proliferation of MUC6-producing cells, which would otherwise differentiate into a foveolar MUC5AC-producing phenotype. Co-cultivation with stromal cells from the lamina propria inhibits the  $\beta$ -catenin signaling pathway, inducing differentiation. Since the apical side of mucosoids is easily accessible and protected by a mucus layer, they represent an ideal model to mimic infection with pathogens like *Helicobacter pylori*. Infection of mucosoids revealed that the mucus is both a physical as well as a bactericidal barrier that only few bacteria are able to overcome. Furthermore, only upon activation of the  $\beta$ -catenin signaling pathway are the cells able to mount an inflammatory response. (Boccellato et al., GUT 2018). Mucosoids promise to be a useful drug-screening tool with an impact on personalized medicine.