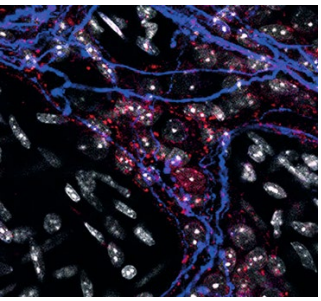


Credit: Enteric neurons stained for 5-HT (blue), 5-HT_4 receptor (red) and DNA (grey). Image courtesy of F. Bäckhed, University of Gothenburg, Sweden

induce neuronal 5-HT release in ENS neurons," says author Estelle Grasset.

Finally, expression of the 5-HT_4 receptor in the ENS was found to be dependent on the presence of the gut microbiota and treatment of colonized GF mice with a 5-HT_4 antagonist resulted in decreases in ENS neurons and the proportion of Nestin$^+$ neurons. Together, the data suggest that the gut microbiota stimulate 5-HT release after colonization, with 5-HT_4 receptor activation leading to ENS neuron maturation.

The investigators now want to determine which microbial factors trigger 5-HT production and 5-HT_4 activation in the ENS, and which neurons are involved. "One of the future goals is to map the neuronal targets of the gut microbiota in the ENS and correlate this to a disease phenotype in which the gut microbiota is modified," concludes Grasset.

Iain Dickson

ORIGINAL ARTICLE De Vadder, F. et al. Gut microbiota regulates maturation of the adult enteric serotonin networks. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1720017115 (2018)

> T cell recruitment was mediated by cross-dressing antigen presentation

showed enlarged lysosomal structures in IECs lacking STAT3. Subsequent experiments in these cells revealed that lysosomal membrane permeabilization (LMP), which releases proteases into the cytoplasm, improved effective antigen generation and the recruitment of CD8$^+$ T cells. Notably, T cell recruitment was mediated by cross-dressing antigen presentation, whereby antigen–MHCI complexes are transferred to dendritic cells directly.

Finally, LMP in STAT3-deficient IECs was found to be the result of increased mitophagy in these cells — the subsequent lysosomal accumulation of iron(II) increased production of reactive oxygen species, which was sufficient to induce LMP. In future work, Greten and colleagues plan to examine whether inhibiting STAT3 or triggering mitophagy could enhance immunotherapy effectiveness.

Hugh Thomas

ORIGINAL ARTICLE Ziegler, P. K. et al. Mitophagy in intestinal epithelial cells triggers adaptive immunity during tumorigenesis. *Cell* **174**, 88–101.e16 (2018)

SCREENING

Ingestible biosensors for gastrointestinal diagnosis

Haeme-sensitive biosensors constructed from genetically engineered probiotic bacteria can diagnose gastric bleeding in real-time in a pig model, according to a new study.

The human gastrointestinal tract is a challenging environment to access. Endoscopy, the modality most frequently used for this purpose, is invasive, costly and requires an expert practitioner to achieve optimal results. Advances in miniaturizing electronic devices have opened the door to using ingestible capsules to deliver various sensors to the gastrointestinal tract. However, despite the relative clinical success of capsule endoscopes, a number of hurdles have prevented the development of sensors able to measure molecular biomarkers noninvasively.

Biosensors, which use genetically engineered cells to detect levels of clinically relevant molecules, could offer a solution. "We realized that genetically engineered cells created by Tim Lu and his student Mark Mimee could be used as sensors in harsh and difficult-to-access environments," explains author Phillip Nadeau. "I had been working on ultra-low power wireless circuits with my advisor Anantha Chandrakasan, and we thought we might be able to combine the cells together with low power wireless readout electronics that could fit into a small device."

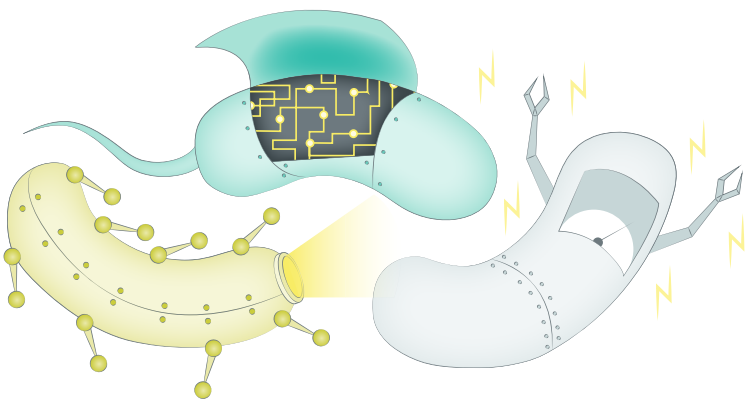
To create biosensors able to detect gastric bleeding, the researchers engineered a genetic construct consisting of bioluminescent reporter genes under the control of a promoter regulated by a haeme-responsive element. A gene encoding an outer-membrane haeme transporter was included in the construct to enable haeme internalization, and the entire gene circuit was introduced into a probiotic *Escherichia coli* strain.

Finally, these cells were incorporated into wells mounted in small ingestible capsules. "The resultant biosensors produce light in the presence of the target analyte and this luminescence can be detected by the electronic readout circuits in the capsule," says Mimee. "Custom-designed electronics can process the luminescence data and transmit it wirelessly from inside the body to a cellular phone." In a proof-of-concept study, the capsule was able to rapidly diagnose gastric bleeding in a porcine model — 100% sensitivity and specificity was achieved 2 h after device administration.

"We're developing additional biosensors that can detect disease-related biomolecules other than blood," concludes Mimee. "On the electronics front, we're working on further miniaturizing the device by combining several components into a single integrated circuit."

Hugh Thomas

ORIGINAL ARTICLE Mimee, M. et al. An ingestible bacterial-electronic system to monitor gastrointestinal health. *Science* **360**, 915–918 (2018)



Credit: Laura Marshall/Macmillan Publishers Limited