drawing conclusions about the evolutionary history of shared features. ■

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BIOTECHNOLOGY

Ultrasound approach tracks gut microbes

Monitoring microbes that live deep inside the gut is a challenge. Engineering bacteria to express structures that can be tracked by ultrasound offers a way to locate such cells *in vivo*, and might have clinical implications. SEE LETTER P.86

RICARD SOLÉ & NURIA CONDE-PUEYO

A microbial ecosystem exists inside you that is as rich and complex as the rainforest. Like the rainforest, this ecosystem contains inaccessible realms that are usually hidden from view. When trying to observe the living gut, a major problem is that light-based imaging techniques can monitor only a limited depth below the surface. However, on page 86, Bourdeau *et al.*[1] report an ultrasound approach for exploring this inner world that they use to map the *in vivo* location of specific microbial-cell populations. Some medical approaches currently in use or being developed introduce bacterial cells as a therapy for gut disease or cancer, so this ultrasound technique might be adapted for clinical use to determine whether such cells have reached the desired location.

Microbial communities have been coevolving with humans over millions of years[2], and they display notable spatial and temporal regularities in their organization. This natural ecosystem assembles at birth, develops, responds to perturbations and stress, and can sometimes collapse. Yet determining the laws and fragilities of life deep within the gut has been difficult, and even some of the best whole-body imaging techniques available can reveal structures at depths of only centimetres below the surface[3,4].

Bourdeau and colleagues offer an innovative solution. Ultrasound imaging has so far mainly been used to assess tissues, but the authors reveal that it can also be used to efficiently track populations of bacterial cells that have been genetically engineered to express what they term acoustic reporter genes. These encode components that form intracellular, protein-enclosed, gas-filled structures called gas vesicles, which are naturally present in many microorganisms, in which they control buoyancy in aqueous environments[5].

Ultrasound detection involves directing pulses of sound waves towards a sample and monitoring the reflected echoes, which are affected by density differences in the substances that the sound passes through. Gas vesicles scatter sound waves, and organisms containing them can be monitored using ultrasound[6]. Pressure pulses above a certain level cause gas-vesicle collapse; therefore, ultrasound signals that disappear after such pulses can be inferred to have originated from gas vesicles[6], an approach that could be used to enhance signal detection above background levels (Fig. 1).

There had been no previous tests to discover whether cells that do not normally form gas vesicles could be genetically engineered to do so, allowing such cells to be monitored by ultrasound. Bourdeau *et al.* engineered types of microorganism currently being used or developed as therapeutics to express gas-vesicle components. One of these microbes was a non-pathogenic strain of the bacterium *Escherichia coli* that is given to some people who have a gut infection[7]. Another was *Salmonella enterica* Typhimurium bacteria, which can invade

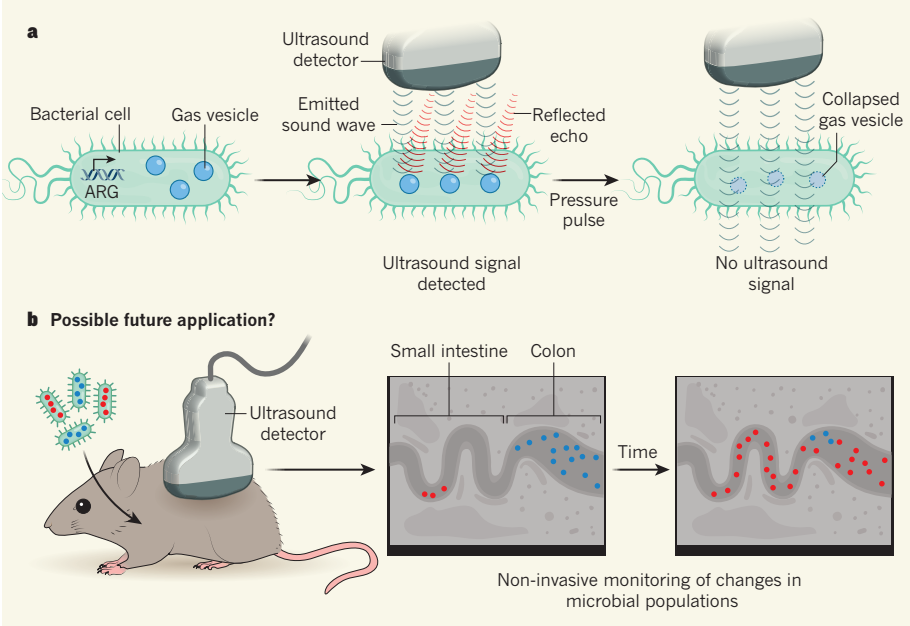

Figure 1 | Using ultrasound to monitor the *in vivo* dynamics of cell populations in space and time. **a**, Bourdeau *et al.*[1] genetically engineered bacteria to express what they term acoustic response genes (ARG), which encode the components of hollow structures called gas vesicles that scatter sound waves and generate an echo that can be detected by ultrasound. Pressure-pulse application causes gas-vesicle collapse and disappearance of the ultrasound signal, which can be used to improve signal detection when tracking the location of cells containing gas vesicles. This approach enables *in vivo* monitoring of a cell population deep within the mouse gut that cannot be tracked by light microscopy. **b**, The authors engineered two types of gas vesicle (red and blue) that collapse at different pressure-pulse levels, enabling cells containing these vesicles to be distinguished using ultrasound. One possible application of this work might be to introduce two bacterial strains that each contain one type of these gas vesicles into a mouse. This would enable non-invasive *in vivo* temporal and spatial monitoring of the dynamics of two distinct bacterial populations in the gut in regions such as the small intestine or colon.

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