tumours. Mouse models of tumour invasion by *S. enterica* Typhimurium are being investigated to determine the potential for using such bacteria to release tumour-killing drugs[8,9].

The authors introduced engineered bacteria that expressed gas vesicles into the mouse gut and showed that the ultrasound-imaging technique works efficiently even for highly diluted cellular populations — signals were detected for *E. coli* cells present at a concentration of 5×10^7 cells per millilitre. The authors also demonstrated that they could engineer bacterial strains that generate distinguishable ultrasound signals, enabling two different bacterial populations to be monitored simultaneously by using strains containing gas vesicles that collapse at different pressure-pulse levels.

The authors compared their ability to monitor the location of engineered bacteria using either ultrasound or a method that tracks bacteria expressing a light-emitting molecule, using strains that live in a deep internal gut region that is difficult to visualize by optical methods. The ultrasound approach outperformed its luminescent counterpart, and ultrasound signals from engineered bacteria provided a high level of spatial resolution and reached deep areas that could not be monitored by a luminescence-based approach. Using ultrasound, the authors detected bacteria coating the surface of the colon and present at cell concentrations similar to those used in therapeutic treatments.

In vivo imaging systems that enable real-time monitoring of tumour-infiltrating luminescent bacteria can effectively monitor bacterium-associated tumours just below the skin in mice[9,10], but are of little use for monitoring more-internal anatomy. Bourdeau and colleagues' ultrasound approach provides good images of engineered strains of *S. enterica* Typhimurium that reside deep within an internal murine tumour (an ovarian adenocarcinoma) that developed from transplanted human ovarian-cancer cells.

This ultrasound technique might also be helpful for the validation and tuning of approaches that use engineered bacterial cells to target tumours. *In vivo* imaging is an important part of assessing these treatments in animal models, including determining the correct dosage and estimating treatment-response times. Even at this proof-of-concept level, there is enormous promise that this non-invasive method might be used to monitor the effect of a bacterium-based cancer therapy in an individual over time. This work might also offer a tool for the optimization of other therapies and diagnostics being developed in which a synthetic-biology approach is used to engineer cells to have biological pathways that are not normally present in a particular cell type[11].

Moreover, Bourdeau and colleagues' work might be complemented by another sound-based imaging technique, called photoacoustic imaging. In this approach, light or radio-frequency pulses trigger a thermal expansion of target tissues that generates acoustic waves[12]. Integrating photoacoustic imaging with the authors' method could allow the precise location of bacteria to be determined alongside detailed information of the surrounding tissue *in vivo*.

Other extensions and applications of the work by Bourdeau and colleagues can be envisaged. For example, engineered groups of bacteria[13,14] might be designed to produce an ultrasound signal in response to specific ranges of physiological and environmental conditions in the gut. And bacterial cells engineered to respond if they interact with gut cells might help to trace the gut's functional biogeography. The ability to selectively control the expression of the acoustic response genes could be helpful in designing experiments to monitor how newly introduced bacteria colonize the gut or to observe the destruction of bacterial pathogens over space and time during therapy.

Perhaps this new technique could also be used to study systems beyond the body, such as the microbial ecosystems in healthy or damaged soil habitats. The soil can have a rich microbial community, and the spatial ecology of soil microbes is not fully understood[15]. Charles Darwin's image of a "tangled bank" of complex organismal interactions is relevant to both the ecological networks in the soil and the complexity of the cellular interactions in the gut. Flexible investigation tools are needed to understand these types of ecology, and future studies building on the work of Bourdeau and colleagues to report precise, acoustic-based imaging of the spatial dynamics of cells might be a crucial step forward. ■

Ricard Solé *and* **Nuria Conde-Pueyo**
are at ICREA-Pompeu Fabra University, 08003 Barcelona, Spain. **R.S.** *is also at the Santa Fe Institute, Santa Fe, New Mexico, USA.*
e-mails: ricard.sole@upf.edu; nuria.conde@upf.edu

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CANCER

Escape from senescence boosts tumour growth

Some chemotherapies block cancer growth by driving tumour cells into a state of cell-division arrest termed senescence. It emerges that such cells have a boosted capacity to drive tumour growth if they exit senescence. SEE LETTER P.96

JAN PAUL MEDEMA

If cells encounter certain types of stress, they can enter a state of cell-division arrest termed senescence[1], which is usually thought to be irreversible. Senescence protects organisms from potentially dangerous cellular proliferation, for example by preventing cell division after severe DNA damage. Many anti-cancer therapies cause cancer-cell senescence, which is considered to be a positive outcome of such treatment. However, Milanovic *et al.*[2] reveal on page 96 the unexpected twist that chemotherapy-induced senescence might generate tumour cells that have an enhanced potential to drive tumour growth if they exit senescence.

Senescence induction has been studied intensively for decades. The phenomenon was first described in fibroblast cells grown *in vitro*, and entry into the senescent state in this context was considered to be a hallmark of cellular ageing[3]. Subsequent research has revealed that the induction of senescence is a cellular response that occurs during both physiological and pathological processes[1].

The protein p53 is one of the key proteins that can act as a cellular sensor and drive a cell to enter senescence. It responds to DNA damage, and its action can cause permanent cell-cycle arrest by activating the proteins $p16^{INK4a}$ and p21. A senescent state can also be promoted by addition of methyl groups to specific amino-acid residues on histone