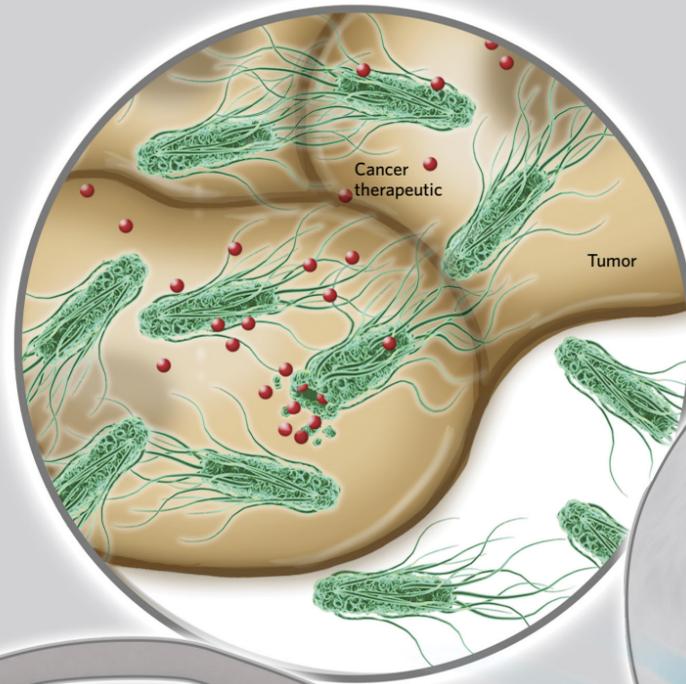


BUILDING BACTERIA TO FIGHT CANCER

Synthetic biologists are applying new strategies in genetic engineering to encode traits and smart circuits in bacteria for more effective in vivo monitoring and drug delivery. At the same time, engineers are developing instruments for external control and guidance of bacteria with the aim of enhancing their ability to find and access tumors. Here are a few examples.

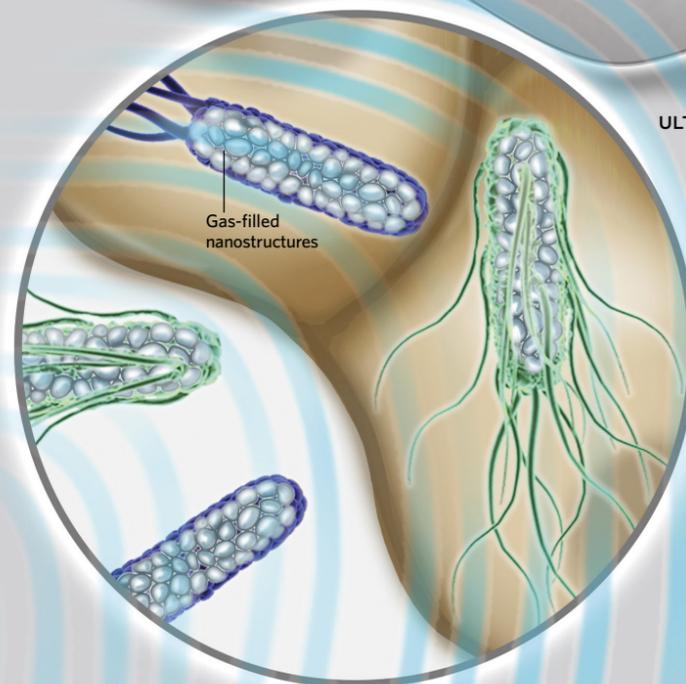
BACTERIAL BOMBS

Jeff Hasty of the University of California, San Diego, in collaboration with Sangeeta Bhatia of MIT (and T.D. in Bhatia's lab), engineered an attenuated *Salmonella enterica* bacterial strain to synchronously release cancer therapeutics when the population reaches a critical density, allowing periodic drug delivery in mouse tumors (*Nature*, 536:81-85, 2016). The effect is based on quorum lysis, meaning when a critical bacteria cell density is sensed by the population, they lyse and release the drug, while surviving bacteria keep proliferating until the critical threshold is reached again to repeat the cycle.



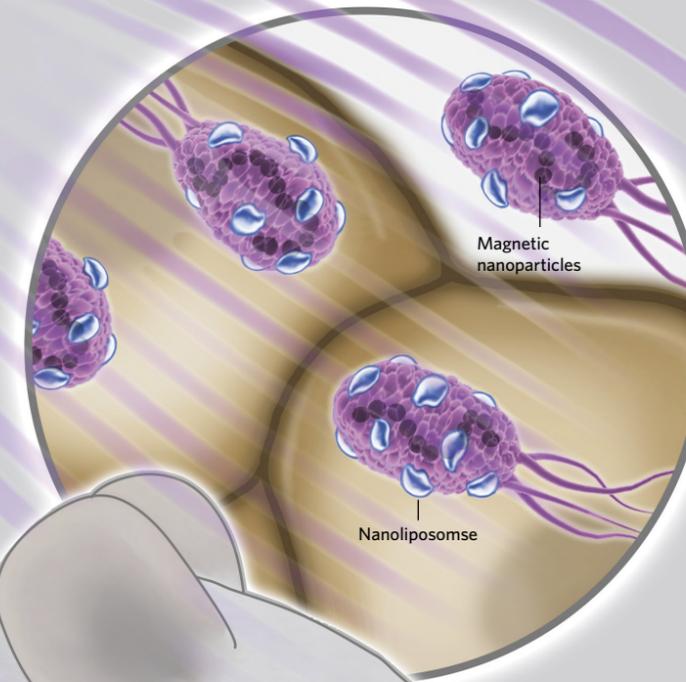
ENCODED NANOSTRUCTURES FOR IMAGING

Mikhail Shapiro of the University of California, Berkeley, and colleagues encoded gas-filled nanostructures in microorganisms, including bacteria and archaea (*Nat Nanotechnol*, 9:311-16, 2014). These structures, when produced by the microbes, serve as contrast agents for ultrasound imaging, allowing researchers to visualize where they go in the body—critical for cancer diagnostics as well as to monitor treatment status by allowing researchers to visualize bacterial accumulation in tumors over time. The group recently demonstrated multiplexing of this approach by encoding a distinct reporter in each of two bacteria, *E. coli* and *Salmonella*, to localize and distinguish the microbe in the guts and tumors of mice (*Nature*, 553:86-90, 2018).



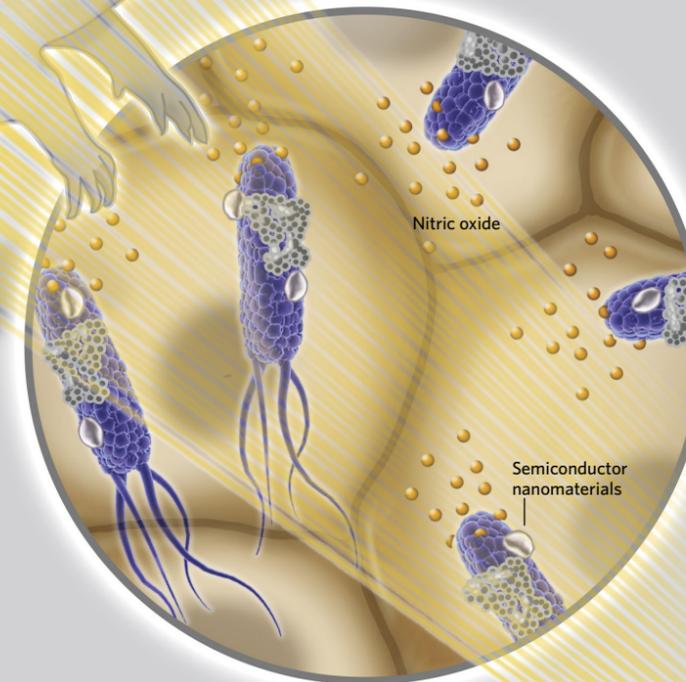
MAGNETICALLY ASSISTED NAVIGATION

Sylvain Martel of Polytechnique Montréal and colleagues attached drug-containing nanoliposomes onto a magnetotactic bacterial strain called MC-1 that was injected in close proximity to tumors in mice. These bacteria naturally biomineralize magnetic nanoparticles inside their membranes, allowing the researchers to use magnetic fields to guide the bacteria to—and into—tumors (*Nat Nanotechnol*, 11:941-47, 2016), where they can deliver therapeutics or serve as imaging contrast agents.



SHINING LIGHT ON TUMORS

Di-Wei Zheng and colleagues at Wuhan University in China used light to enhance the metabolic activities of *E. coli* by attaching to the bacteria's surfaces semiconductor nanomaterials that under light irradiation produce photoelectrons. These triggered a reaction with the bacteria's endogenous nitrate molecules, increasing the formation and secretion of a cytotoxic form of nitric oxide by 37-fold. In a mouse model, the treatment led to an 80 percent reduction in tumor growth (*Nat Commun*, 9:1680, 2018).



ULTRASOUND

LIGHT

Mesa Schumacher