

● BIOTECHNOLOGY

Vaginal monocultures

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Maintaining a healthy balance of vaginal bacteria can significantly improve a woman's defences against a host of invading pathogens, including common urinary tract infections and sexually transmitted diseases, and even HIV. It may also cut numbers of pre-term births among pregnant women, say researchers.

'The vaginal microbiota are totally different from the types of microbiota we usually talk about, for example, in the gut,' says Katherine T. Moortgat, CEO of California biotech Osel. 'Where the indicator of gut health is microbial diversity, in the vagina, a healthy microbiota is dominated by a single genus, *Lactobacillus*, with just a handful of common species.'

Scientists at Osel hope to capitalise on this knowledge by developing a 'live biotherapeutic' to target a common disruption of the vaginal microbiome called bacterial vaginosis, which affects nearly a third of women aged 15-44. Women with the condition are at much greater risk for sexually transmitted infections, and have higher rates of pre-term birth when pregnant. Around 10% of US babies are born pre-term.

Currently, the only approved drugs for bacterial vaginosis are antibiotics, but around 58% of women will see a recurrence of the problem after therapy. 'Antibiotics affect not only the pathogenic bacteria, but also the beneficial bacteria in the microbiome, often leading to further imbalance and dysbiosis,' says Moortgat. 'The aim is to prevent the recurrence of bacterial vaginosis so women don't have to take continued rounds of antibiotics.'

In May 2016, Osel announced the start of a Phase 2b trial aimed at deploying its biotherapeutic, *LACTIN-V*, which contains the beneficial bacterium *Lactobacillus crispatus*, to prevent the recurrence of bacterial vaginosis after antibiotic therapy. Conducted at four US centres, the study will enrol over 200 women to



assess the efficacy of *LACTIN-V* against placebo, and compare colonisation of the beneficial bacterium during the period of dosing.

The therapeutic is based on a single strain of *Lactobacillus crispatus*, formulated as a powder and delivered via a tampon-like applicator over a period of two weeks during the trial. *Lactobacillus crispatus* is special because it produces both lactic acid, which helps to lower vaginal pH to around 4, and hydrogen peroxide (H_2O_2) – which further 'antagonises' pathogenic bacteria seeking to gain entry, Moortgat explains.

The same *LACTIN-V* biotherapeutic is currently being evaluated in another Phase 2b trial for urinary tract infections, which nine out of 10 times are caused by *E. coli* infection. Meanwhile, the company is also developing an engineered *Lactobacillus* strain to express antibodies against the HIV-1 virus.

A recent study by South African and North American researchers, presented at the International AIDS 2016 Conference, found that an overgrowth of certain bacteria in the vagina was associated with both higher transmission of HIV and reduced efficacy of an anti-HIV drug – and highlighted the importance of a healthy vaginal microbiome in preventing the transmission of HIV.