This gross mixture has big benefits for the study of bacteria

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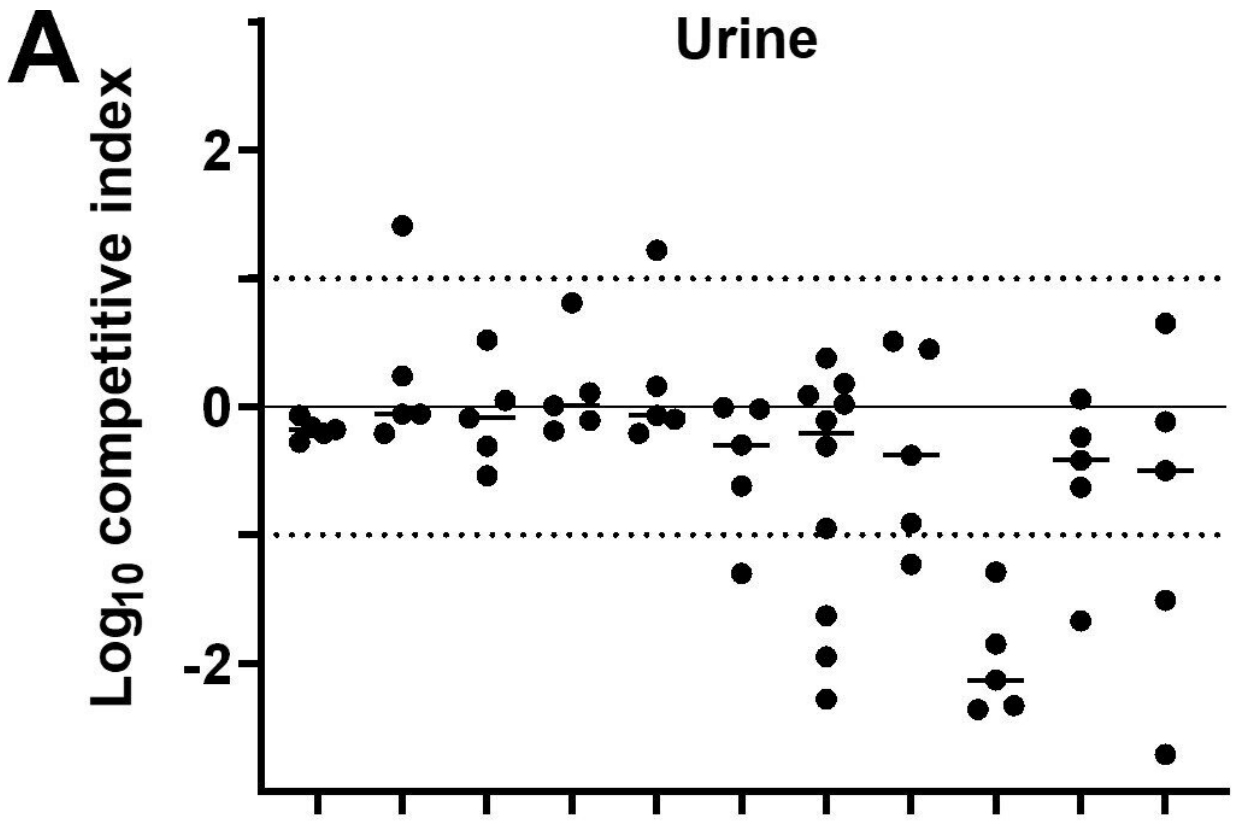

Determining the bottleneck of infection for *P. mirabilis* during UTI. (**A–C**) CBA/J mice were transurethrally inoculated with 10^7 CFU. The inoculum contained different ratios of wild-type HI4320 and marked mutant *spa47* (kan^R) that was previously determined to have no fitness defect (23). The measured ratios are indicated on the *x*-axis. At 24 h post-inoculation, (**A**) urine, (**B**) bladder, and (**C**) kidneys were harvested. Each sample was subjected to differential plating to enumerate the ratio of wild type to *spa47* in the organ. A competitive index (CI) was calculated and is plotted on the *y*-axis. Each dot

represents a single mouse (n = 5–10); bars indicate the median. A log CI of 0 indicates that the wild type and mutant were recovered in the same ratio as were introduced in the inoculum. Dotted lines at ±1 indicate the acceptable maximum variation for this experiment. Credit: *Infection and Immunity* (2023). DOI: 10.1128/iai.00355-23

Animal models are a necessary research tool for understanding how diseases develop and how therapies work in biological systems and can be credited for breakthroughs ranging from effective antibiotics to the COVID-19 vaccines.

The responsible and judicious use of animal models is prioritized by research institutions around the world, and a unique research protocol developed by Melanie Pearson, Ph.D., of the Department of Microbiology & Immunology, and her team at the University of Michigan Medical School is garnering widespread interest among microbiologists.

In a recent paper in the journal *Infection and Immunity*, her group describes a product called organ agar that could be deployed to more efficiently screen bacteria that cause urinary tract infections.

Agar is a gelatinous product made of seaweed routinely used in laboratories to grow colonies of bacteria in petri dishes.

Pearson discovered that creating a mixture composed of the agar plus human urine and the organ her team wanted to study, specifically the bladder and kidneys, enabled their team to screen more than 1,700 mutants of the UTI-causing bacteria *Proteus mirabilis* using a quarter of the mice typically required.

Pearson explains that in a classic mouse study of a urinary tract infection, mutated bacteria—bacteria that are missing individual genes— are introduced into an animal's bladder, and then the dominant strains as are tested to determine what bacterial genes are important for infection. Knowing this could enable researchers to target specific variants for drug development, for example.

The use of organ agar has multiple potential benefits, explains Pearson.

For one, it can help microbiologists get around what is known as the bottleneck problem.

In a living system, only a certain number of mutants are able to gain a foothold, with the rest lost at random.

When Pearson tried the screening method using organ agar, her team found that the dominant bacteria reproduced those that were dominant in a live animal.

What's more, bacteria that did not do well on organ agar also did not do well in a live animal.

Furthermore, organ agar could enable researchers without access to animal models to create physiologically relevant models of infection or colonization and allow for more efficient screening of bacterial and other microorganism candidates for further study.

More information: Melanie M. Pearson et al, Organ agar serves as physiologically relevant alternative for in vivo bacterial colonization, *Infection and Immunity* (2023). DOI: 10.1128/iai.00355-23

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