Combining oral vaccination and niche competition to fight antimicrobial resistance gene reservoirs

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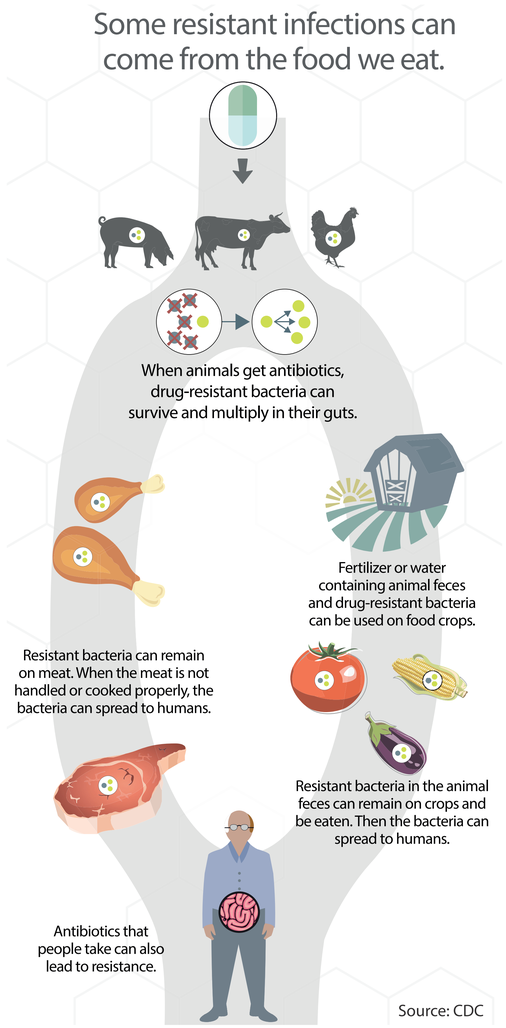
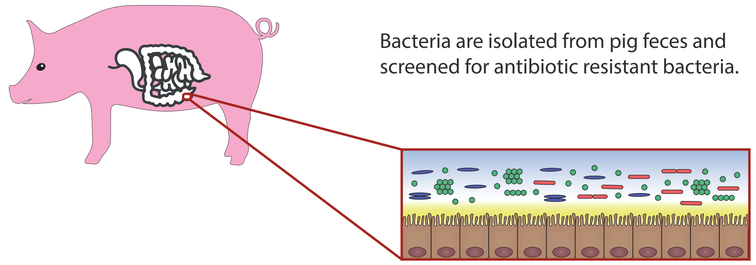
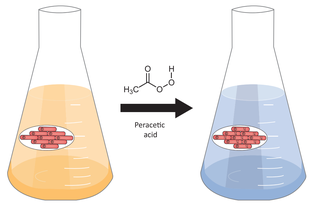
Antibiotic resistance emergence and spread



Eliminate antimicrobial resistance gene reservoirs

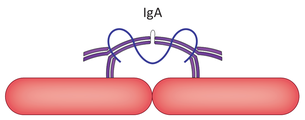


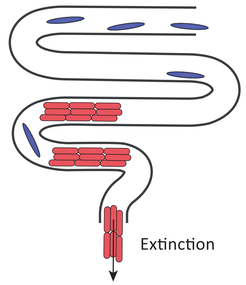
Bacteria are isolated from pig feces and screened for antibiotic resistant bacteria.



The isolated bacteria are used to produce an inactivated bacterial vaccine.

Oral administration of this vaccine induces IgA secretion into the intestinal lumen. These specific antibodies bind to the bacteria and lead to "enchained growth".

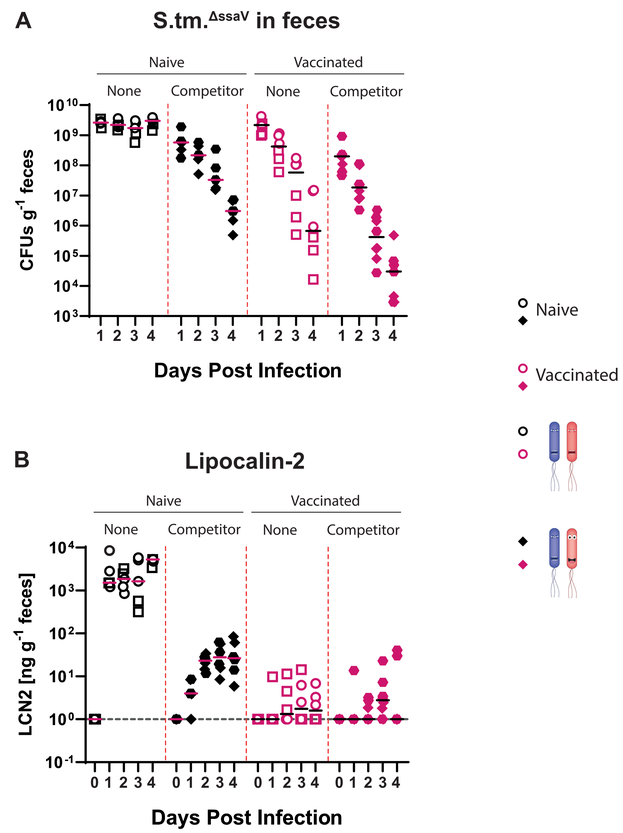




Enchained bacteria are cleared from the gut by the intestinal flow. This will eventually lead to extinction while planctonic bacteria are only partially lost. Elimination will be further supported by the introdution of a harmless bacterium that competes with the targeted one for the same intestinal niche.

Moor, ... Slack. High-avidity IgA protects the intestine by enchaining growing bacteria. Nature (2017).
Moor, ... Slack). Peracetic Acid Treatment Generates Potent Inactivated Oral Vaccines from a Broad Range of Culturable Bacterial Species. Front Immunol (2016).

Vaccination and niche competition have a combined effect on pathogen elimination and intestinal inflammation



C57BL/6 mice were vaccinated four times with 10^{10}-10^{11} peracetic acid (PA) killed bacteria (pink symbols) or mock-vaccinated (black symbols) in weekly intervals. One week after the final bosst, mice were infected with attenuated S.tm. only (open symbols) or S.tm. and an avirulent, non-cross-reactive competitor (filled symbols).

A Colony forming units (CFUs) of S.tm. ΔssaV were determined by selective plating of feces. Vaccination and introduction of a niche competitor alone leads to a marked decrease in pathogenic S.tm. and this loss is even more pronounced when both treatments are combined.

B Lipocalin-2 levels in feces were measured by ELISA. Oral vaccination as well as niche competition both greatly inhibit intestinal inflammation.