Bacteriocin production augments niche competition by enterococci in the mammalian gastrointestinal tract

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Enterococcus faecalis is both a common commensal of the human gastrointestinal tract and a leading cause of hospital-acquired infections.

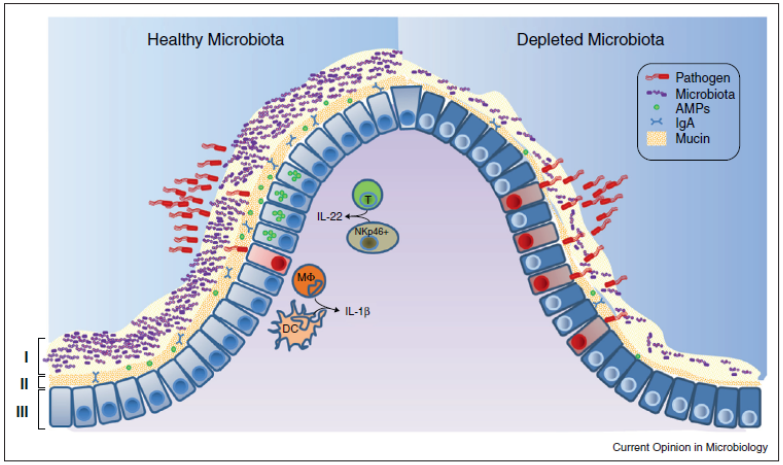
Systemic infections with multidrug-resistant enterococci occur subsequent to gastrointestinal colonization.
Preventing col- onization by multidrug-resistant *E. faecalis* could therefore be a valuable approach towards limiting infection.

However, little is known about the mechanisms *E. faecalis* uses to colonize and com-pete for stable gastrointestinal niches.

Pheromone-responsive conjugative plasmids encoding bacteriocins are common among enterococcal strains and could modulate niche competition among enterococci or between enterococci and the intestinal microbiota. We developed a model of colonization of the mouse gut with *E. faecalis*, without disrupting the microbiota, to evaluate the role of the conjugative plasmid pPD1 expressing bacteriocin 21 in enterococcal colonization.

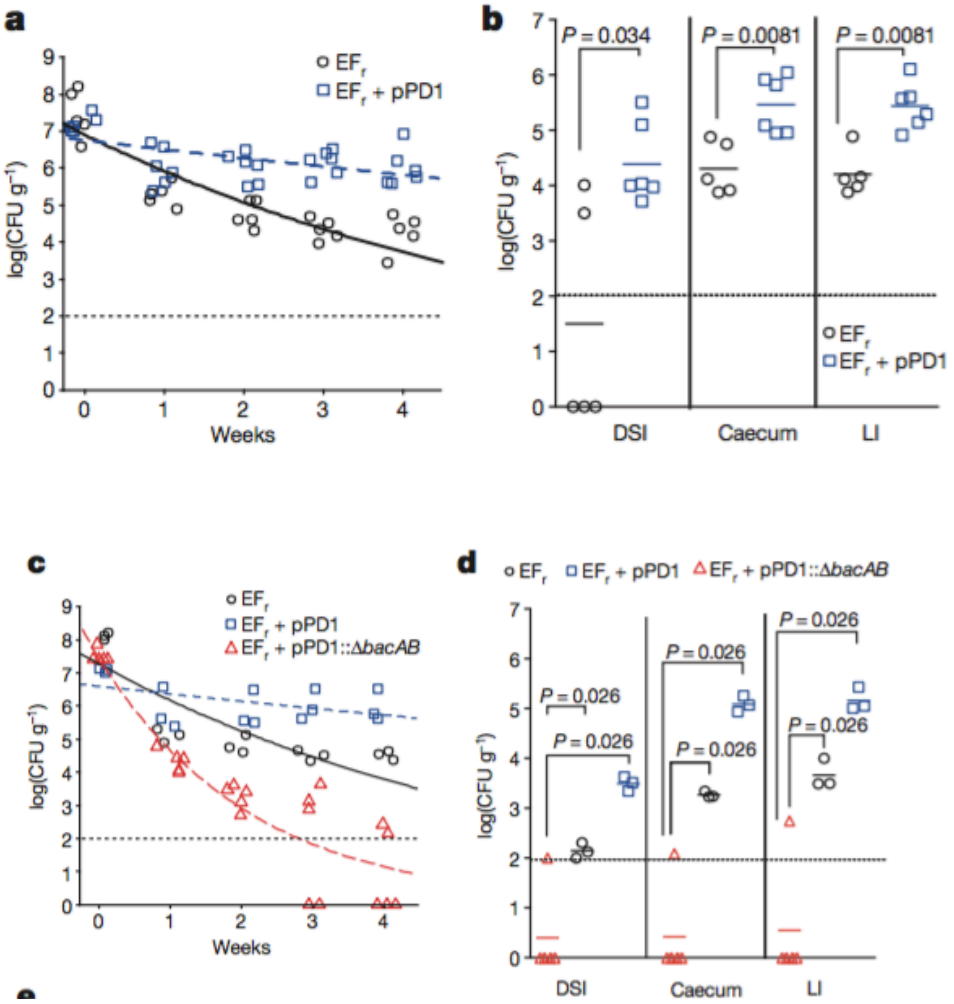
Here we show that *E. faecalis* harbouring pPD1 replaces indigenous enterococci and outcompetes E. faecalis lacking pPD1.

Furthermore, in the intestine, pPD1 is transferred to other *E. faecalis* strains by conjugation, enhancing their survival..



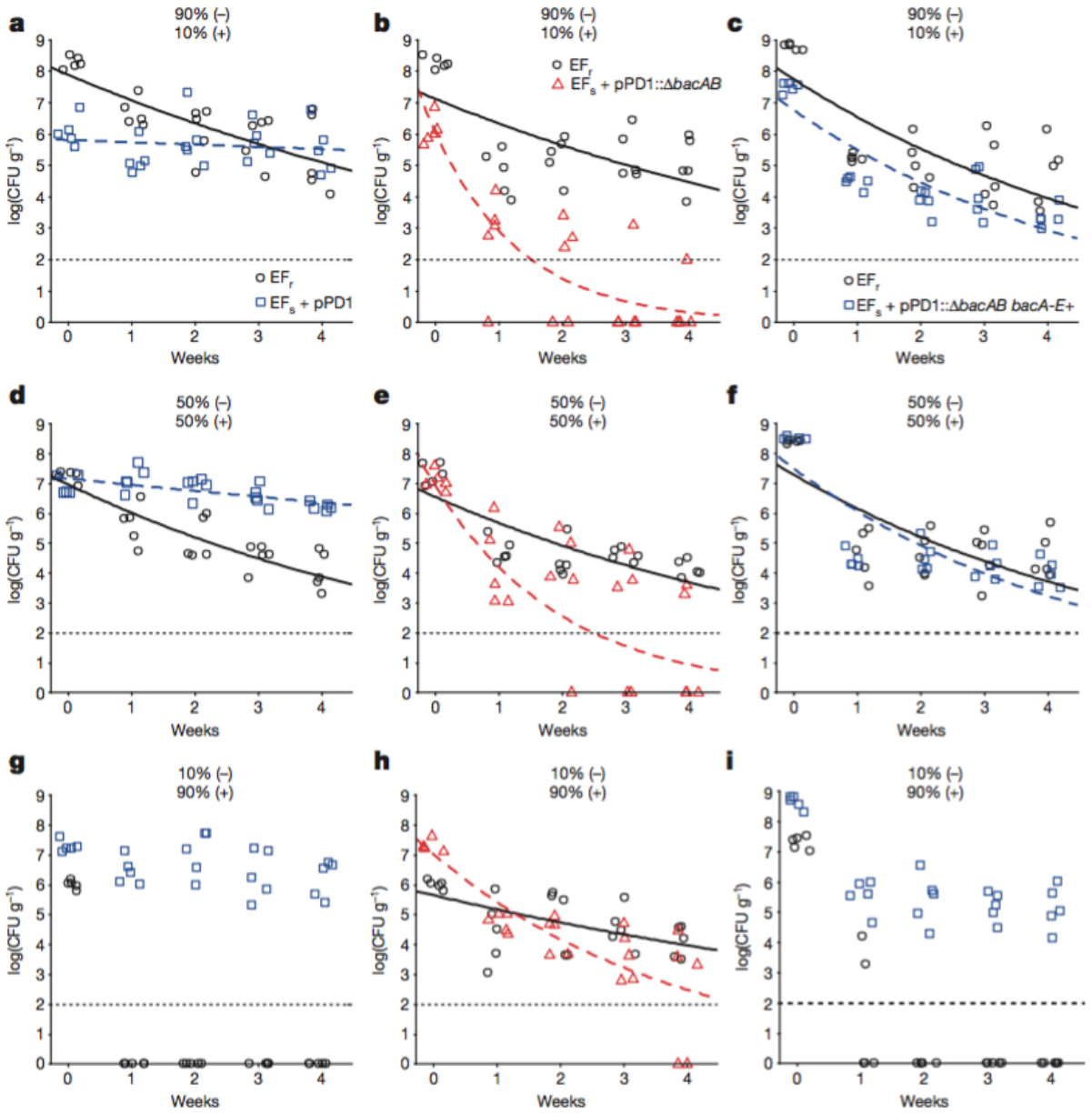
Colonization with an *E. faecalis* strain carrying a conjugation-defective pPD1 mutant subsequently resulted in clearance of vancomycin-resistant enterococci, without plasmid transfer.

Therefore, bacteriocin expression by commensal bacteria can influence niche competition in the gastrointestinal tract, and bacteriocins, delivered by commensals that occupy a precise intestinal bacterial niche, may be an effective therapeutic approach to specifically eliminate intestinal colonization by multidrug-resistant bacteria, without profound disruption of the indigenous microbiota



pPD1 enhances E. faecalis competition for an intestinal niche.

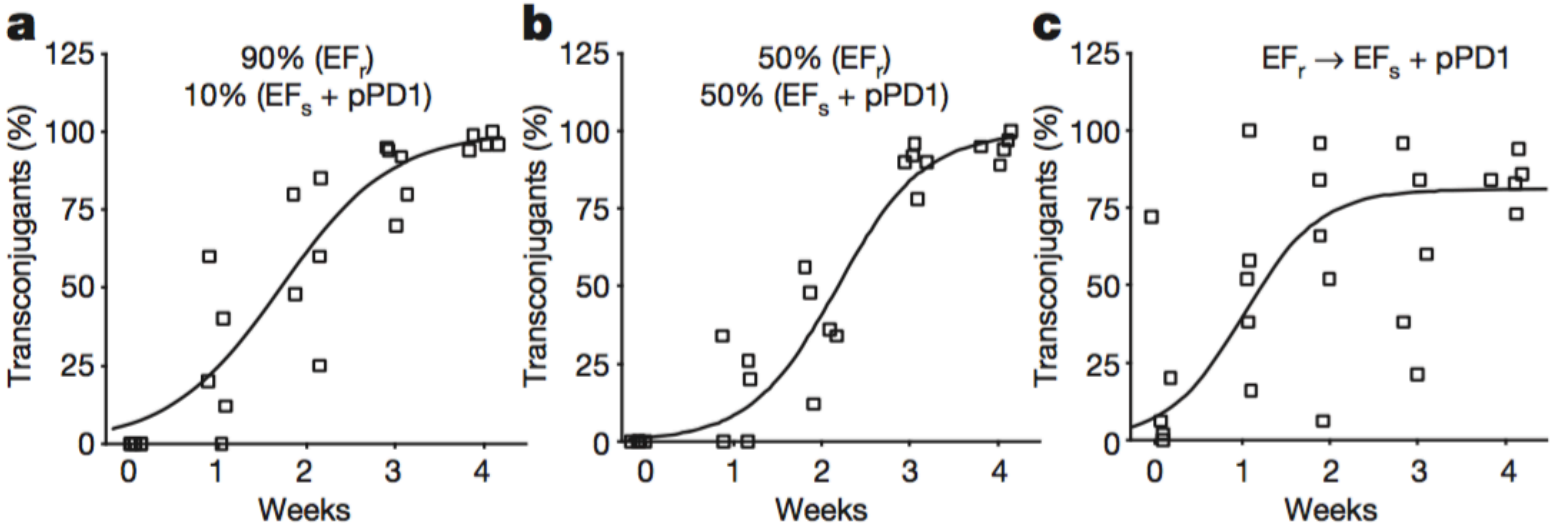
Mice were colonized by Efr or EFr 1 pPD1, which were enumerated weekly from faeces (a) and at week 4 from each segment of the gastrointestinal tract (b) (distal small intestine (DSI), caecum and large intestine (LI)). c, d, Mice were colonized with EFr 1 pPD1::DbacAB, Ef or EFr 1 pPD1. Faecal abundance of *E. faecalis* was determined weekly (c) and in the gastrointestinal tract at week 4 (d).



plasmid-carrying spectinomycin-resistant E. faecalis (EFs 1 pPD1)

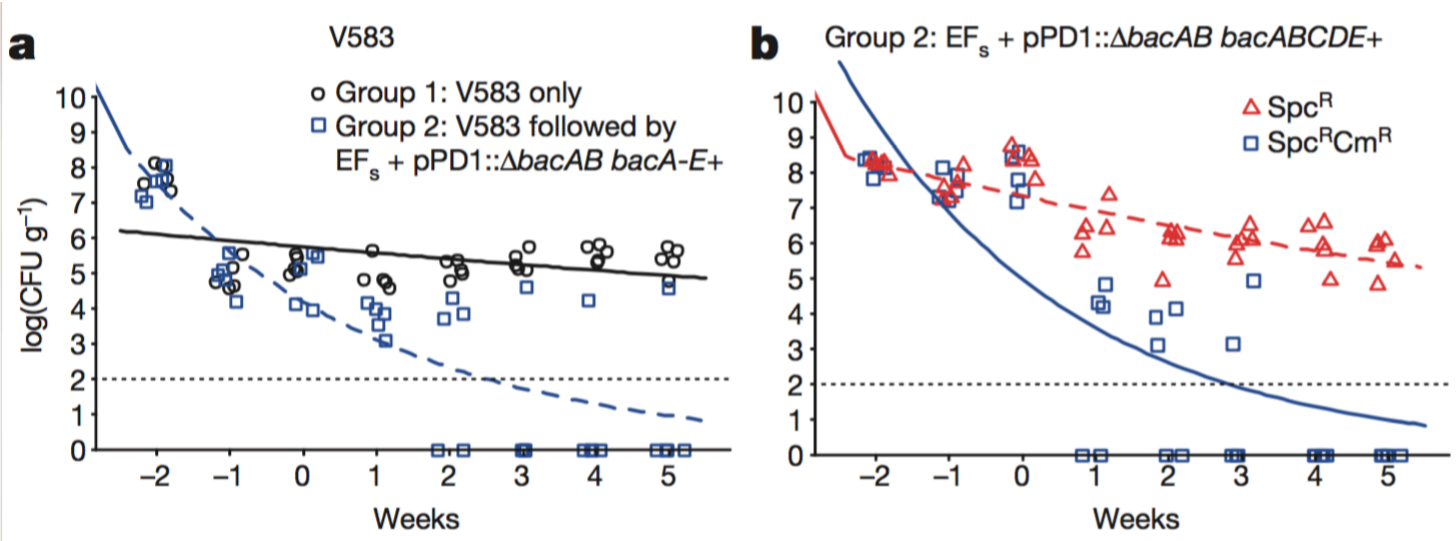
Bacteriocin provides a competitive survival advantage to *E. faecalis* in the gastrointestinaltract.

Mice were given mixtures of EFr (–) and EFs 1 pPD1 (+) (a, d, g), EFr and EFs 1 pPD1::DbacAB (+) (b, e, h) or EFr and EFs 1 pPD1::DbacAB bacA-E 1 (+) (c, f, i) in drinking water at the indicated ratios. Faecal shedding was determined weekly. Each symbol represents an individual animal. Lines are fitted using an exponential decay model.



pPD1 is transferred via conjugation within the mouse gastrointestinal tract

a,b,Mice were colonized with mixtures of EFr and EFs 1 pPD1 in drinking water at the indicated ratios. Faecal EFr colonies (100 per animal) were screened weekly for pPD1. c, Mice were stably colonized with EFr and then challenged with EFs 1 pPD1. Faecal EFr colonies (50 per animal) were screened weekly for pPD1. In a–c, each symbol represents the percentage of faecal transconjugants in an individual animal. The fitted logistic curve is overlain. The results in a–c are from one experiment each



Bacteriocin reduces V583r colonization (vancomycin-resistant strain)

Mice were colonized with V583r. V583r was removed from the drinking water of both groups two weeks before sampling (week –2). Group 1 received sterile water, whereas group 2 received EFs 1 pPD1::DbacAB bacA-E1 in their drinking water for two additional weeks, followed by sterile water at week 0. Faecal levels of V583r (a) and EFs 1 pPD1::DbacAB bacA-E1 (b) were enumerated weekly. The retention of complementation plasmid pAM401A::bacA-E1 by

EFs 1 pPD1::DbacAB bacA-E1 was determined weekly (b). Lines are fitted using an exponential decay model and the rate of decay is significantly different between the two groups in both a (P , 0.0001) and b (P , 0.0001). Each symbol represents an individual animal and data are representative of three biologically independent experiments. The black dotted lines indicate the limit of detection at 100 CFU per g faeces. SpcR, spectinomycin resistant; SpcRCmR, spectinomycin resistant, chloramphenicol resistant.