Supplementary Information

Clostridium sporogenes uses reductive Stickland metabolism in the gut to generate ATP and produce circulating metabolites

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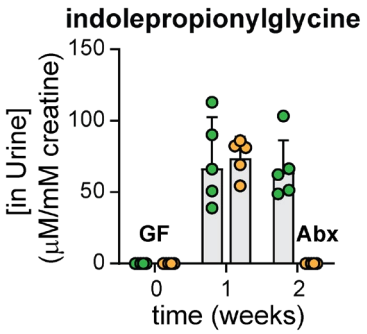
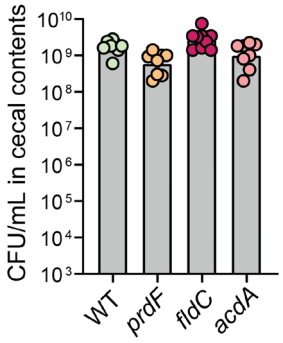
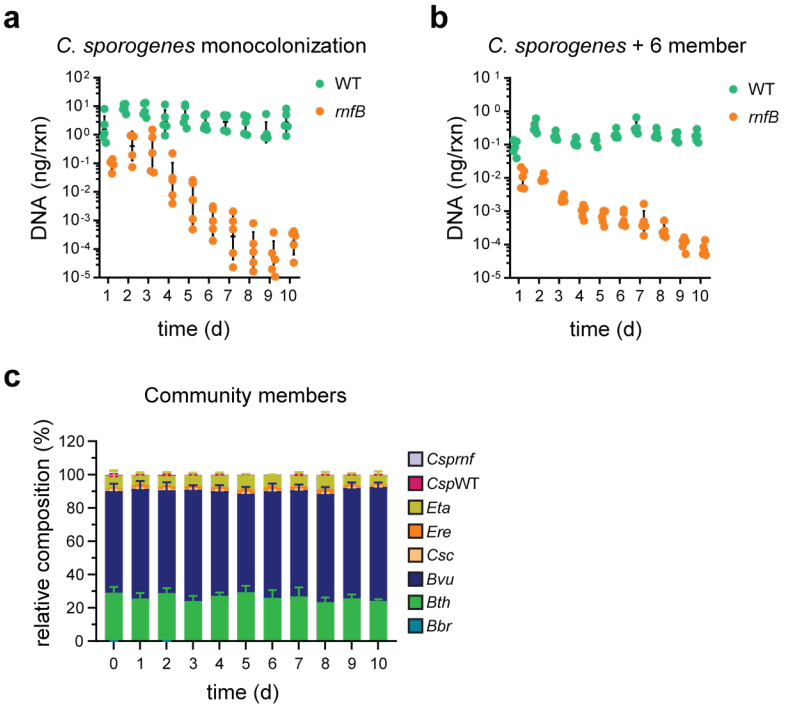
Supplementary Figures



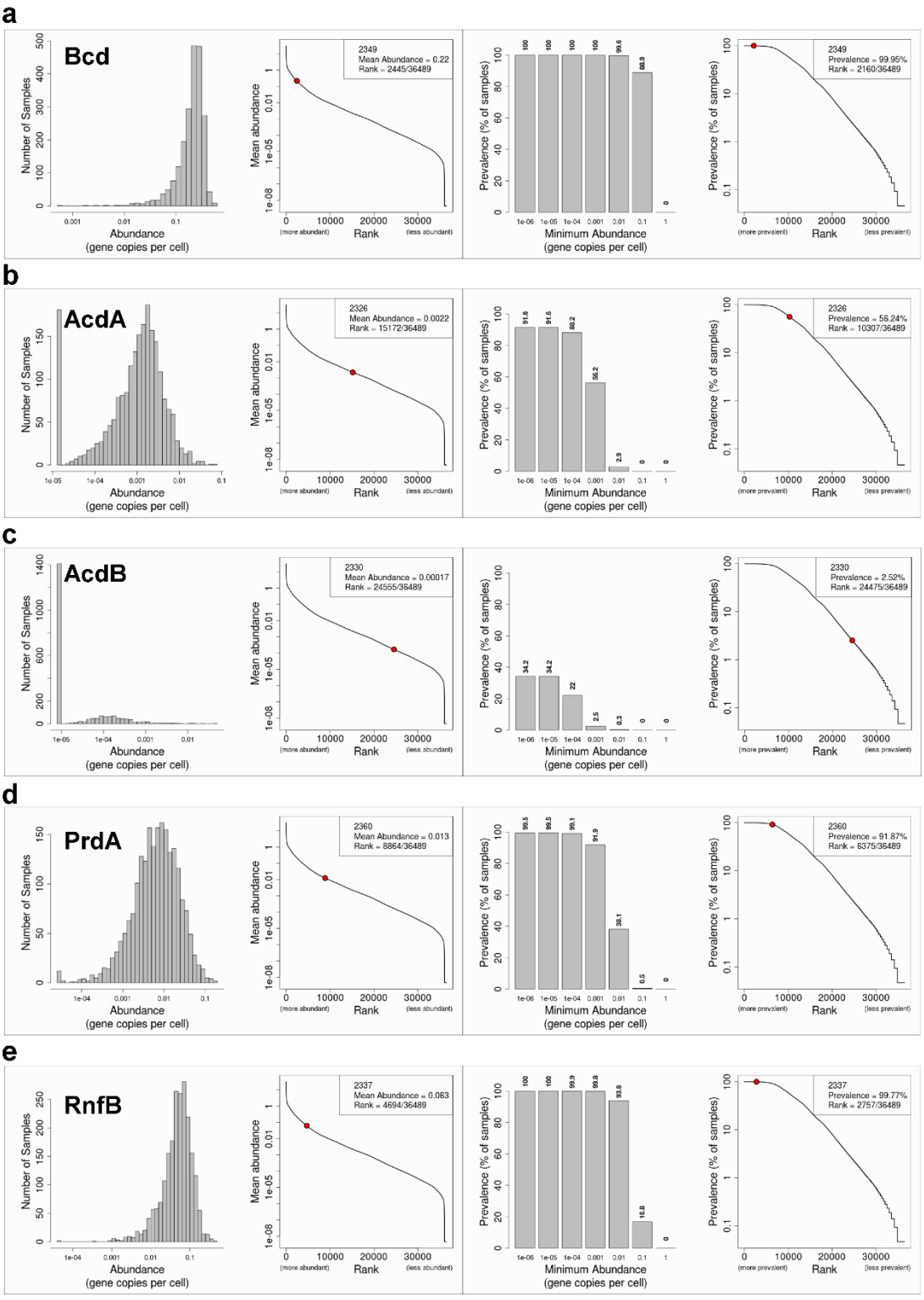
Supplementary Figure 1. Indolepropionylglycine (IPGly) is the excreted form of indolepropionate in urine of mice mono-colonized with *C. sporogenes*.
Indolepropionylglycine was quantified in urine of mice described in **Fig. 3b** using LC-MS and normalized to urine creatinine levels. GF, germ-free; Abx, antibiotic treated. Means and standard deviations for urine IPGly normalized to creatinine are shown for n = 5 mice. Female mice (*Mus musculus* (Tac:SW)), aged 10-12 weeks were used for the experiments.



Supplementary Figure 2. The *prdF, fldC, and acdA* mutants colonize the gastrointestinal tract of mice to similar levels as the wild-type strain. Cecal contents from mice monocolonized with either wild-type *C. sporogenes* or its *prdF*, *fldC*, or *acdA* mutants were collected after two weeks of colonization and dilution-plated on RCM agar plates and colony forming units (CFU) were counted. Data are plotted as means +/- standard deviations from n = 8 mice per group (WT, *prdF*, *acdA*) or n = 9 mice per group (*fldC*). Male mice (*Mus musculus* (Tac:SW)), aged 8-11 weeks were used for the experiments.



Supplementary Figure 3. Levels of wild-type and *rnfB* mutant *C. sporogenes* in gnotobiotic competition experiments and stability of defined community members over time. A) Germ-free mice were colonized by oral gavage a 1:1 mixture of wild-type (WT) or *rnfB* mutant *C. sporogenes* and feces were collected daily for 10 days. Genomic DNA was purified and wild-type and *rnfB* mutant *C. sporogenes* were quantified by Q-PCR. Plots show the amount of wild-type or *rnfB* mutant DNA per PCR reaction. B-C) Germ-free mice were colonized by a defined microbial consortium consisting of 6 bacteria (*Edwardsiella tarda* ATCC 23685 (Eta), *Eubacterium rectale* ATCC 33656 (Ere), *Clostridium scindens* ATCC 35704 (Csc), *Bacteroides vulgatus* ATCC 8482 (Bvu), *Bacteroides thetaiotaomicron* VPI-5482 (Bth), and *Bifidobacterium breve* UCC2003 (Bbr)). One week later, mice were administered by oral gavage a 1:1 mixture of wild-type or *rnfB* mutant *C. sporogenes* and feces were collected daily for 10 days and genomic DNA was purified. In B) wild-type and *rnfB* mutant *C. sporogenes* were quantified by Q-PCR and plots show the amount of wild-type or *rnfB* mutant DNA per PCR reaction. For C), taxa plots were generated using Q-PCR with organism specific primers for each community member over time. For A-C, data are plotted as means +/- standard deviations from n = 5 mice per group. Male mice (*Mus musculus* (Tac:SW)), aged 8-11 weeks were used for the experiments.



Supplementary Figure 4. Abundance and prevalence of electron transfer proteins within human fecal metagenomic datasets. *C. kluyveri* Bcd (EDK32509.1), *C. sporogenes* AcdA (EDU39257.1), AcdB (EDU36591.1), PrdA (EDU36353.1), or RnfB

(EDU37753.1) were used as a query to search ~2,000 human microbiome datasets using the metaquery tool (http://metaquery.docpollard.org/). On the left, plots show the relative abundance of the query genes and on the right, plots show the prevalence of the query genes. On the left, red dots represent the mean abundance of the protein in metagenomes and corresponding rank of all proteins in the metaquery database. On the right, red dots indicate the prevalence of the protein among metagenomes and corresponding rank of all proteins in the metaquery database.