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Abstract Title:

Early-life gut microbiome modulation reduces the abundance of antibiotic resistant bacteria.

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Abstract Description:

Introduction: The rapid emergence of antibiotic-resistant (AR) pathogens is a global threat. Recent studies have shown that antibiotic resistance genes (ARGs) can be acquired in early life and may have long-term sequelae. Limiting the spread of AR without triggering the development of additional resistance mechanisms is of great clinical value. Here, we used shotgun metagenomics to characterize the effect of Bifidobacterium longum subsp. infantis EVC001 modulation of the microbiome on the abundance of ARGs in breastfed infants.

Methods: Healthy, breastfed infants were fed B. infantis EVC001 for three weeks starting at day 7 postnatal. Stool samples were collected at day 21 postnatal and processed for shotgun metagenomics. Selected AR bacterial species were isolated, sequenced and tested for minimal inhibitory concentrations to clinically relevant antibiotics.

Results: The EVC001-fed group showed a 129% increase in abundance of Bifidobacterium and a 90% decrease in ARGs compared to healthy breastfed controls ($P < 0.0001$). ARGs that differed significantly between groups were predicted to confer resistance to beta lactams, fluoroquinolones or multiple drug classes, and the majority belonged to Escherichia, Clostridium and Staphylococcus. Minimal inhibitory concentration assays confirmed resistance phenotypes among isolates with these genes. Notably, we found extended-spectrum beta lactamases among healthy, vaginally delivered breastfed infants who had never been exposed to antibiotics.

Conclusions: Colonization of breastfed infants by a single strain of B. longum subsp. infantis had profound impacts on the fecal metagenome, including a 9-fold reduction in ARGs. This highlights the importance of developing novel approaches to limit the spread of these genes among clinically relevant bacteria. Future studies are needed to determine whether colonization

with B. infantis EVC001 decreases the incidence of antibiotic resistant infections in breastfed infants.