Researchers compare the gut viromes of Malawian children with severe acute malnutrition

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A small child in Mumbai, with a shaved head, eating bread with her hand. Credit: Wen-Yan King/Wikipedia

(Medical Xpress)—Malnutrition is a leading cause of child mortality, and evidence is accumulating that it is not solely attributable to food insecurity. Maternal behaviors, environmental factors, and a host of complex developmental variables can contribute to the onset of severe acute malnutrition (SAM). Recently, an international group of researchers conducted a study of the gut DNA viromes of twins in Malawi that were discordant for severe acute malnutrition in order to define a familial risk for childhood malnutrition and to provide a viral dimension to the body of knowledge about the gut microbiome. They have reported their findings in the *Proceedings of the National Academy of Science*.

The bacterial population of the human gut microbiota goes through postnatal developmental stages that researchers have characterized in pediatric studies. During the first two to three years of life, the microbiome in healthy infants develops from an immature state to a recognizable adult stage. In severe acute malnutrition, normal postnatal maturation of the microbiota is disrupted. Children with SAM in Malawi and Bangladesh have gut microbiota that appear to have the characteristics of those of much younger individuals.

Significantly, this immaturity is unaffected by the current peanut-based ready-to-use therapeutic food (RUTF) interventions, even when treated children reach normal weight. Such therapy has dramatically reduced mortality, but fails to ameliorate long-term health problems associated with childhood malnutrition, and the development of the gut microbiome may be a contributing factor.

In their study, the researchers found that discordance for malnutrition among 317 twin pairs from five rural Malawian villages was surprisingly high during the first three years of life. They compared the gut viromes of these twins with those of twins concordant for healthy status in order to characterize normal versus postnatal acquisition of the microbiota's

viral component.

Previous studies have yielded models of age-discriminatory bacterial strains that serve as a signature of normal developmental biology; the time-dependent changes in the gut microbiota are similar between unrelated individuals living in different geographic areas, which suggests a set of developmental rules that have not yet been established.

The current study adds to this body of knowledge by contributing a developmental viral component. The researchers quantified gut virome abundances as a function of individual, twin-pair, age, health, and family variables and yielded a set of age-discriminatory phage and eukaryotic gut viruses.

Rather than providing a direct therapeutic approach to malnutrition, the study seeks to enlarge the existing picture of the microbiomes of malnourished and healthy people. For instance, by establishing a baseline for microbiome health, it may someday be possible to transplant healthy gut microbes into malnourished individuals receiving RUTF therapy in order to improve their long-term health.

However, the authors observe that "viral-bacterial dynamics in vivo are complex; the correlations between phage and bacterial strain abundances are not always obvious and involve negative correlations shifted in time as a result of a predator-prey dynamic, whereas prophages have linear positive correlations. As a consequence, answering this question promises to be challenging."

More information: "Gut DNA viromes of Malawian twins discordant for severe acute malnutrition." *PNAS* 2015 ; published ahead of print September 8, 2015, DOI: 10.1073/pnas.1514285112

Abstract

The bacterial component of the human gut microbiota undergoes a definable program of postnatal development. Evidence is accumulating that this program is disrupted in children with severe acute malnutrition (SAM) and that their persistent gut microbiota immaturity, which is not durably repaired with current ready-to-use therapeutic food (RUTF) interventions, is causally related to disease pathogenesis. To further characterize gut microbial community development in healthy versus malnourished infants/children, we performed a time-series metagenomic study of DNA isolated from virus-like particles (VLPs) recovered from fecal samples collected during the first 30 mo of postnatal life from eight pairs of mono- and dizygotic Malawian twins concordant for healthy growth and 12 twin pairs discordant for SAM. Both members of discordant pairs were sampled just before, during, and after treatment with a peanut-based RUTF. Using Random Forests and a dataset of 17,676 viral contigs assembled from shotgun sequencing reads of VLP DNAs, we identified viruses that distinguish different stages in the assembly of the gut microbiota in the concordant healthy twin pairs. This developmental program is impaired in both members of SAM discordant pairs and not repaired with RUTF. Phage plus members of the Anelloviridae and Circoviridae families of eukaryotic viruses discriminate discordant from concordant healthy pairs. These results disclose that apparently healthy cotwins in discordant pairs have viromes associated with, although not necessarily mediators, of SAM; as such, they provide a human model for delineating normal versus perturbed postnatal acquisition and retention of the gut microbiota's viral component in populations at risk for malnutrition.