Breastfeeding influences the neonatal virome

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The first viruses to colonize the infant gut are shown to arise from bacteria, with human-cell viruses colonizing the gut later, at around four months of age. Exclusive and partial breastfeeding were associated with fewer human viruses in the gut of infants compared with formula-feeding alone.

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Competing interests
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The problem

Although the human gut contains bacteria soon after birth, infant meconium exhibits few if any 'virus-like particles' (VLPs). However, viruses soon start to colonize the gut, reaching a level of 10^9 per gram of stool by one month after birth. This level persists in the gut throughout life. Importantly, some of these viruses can go on to cause gastrointestinal disorders. Little is known about how the viruses come to colonize the gut, and understanding this will help researchers to determine the effects on longer-term health, and to protect against diseases such as viral gastroenteritis.

The solution

To investigate the origin of VLPs in the infant gut, we isolated and sequenced (using shotgun metagenomic sequencing) the nucleic-acid content of VLPs from stools collected from 20 infants at birth and at one and four months later. Infants were born to self-identified African American mothers from an urban US setting. VLPs were undetectable in most of the samples collected at birth. By 1 month of age, the counts reached an average of 1.6×10^9 per gram of stool, and they remained at around this level at 4 months of age.

We also analysed the full gut microbiome of these same infants, and found that bacteria rapidly colonized the gut after birth, with bacterial DNA predominating over human DNA in samples from 1-month- and 4-month-old infants. Targeted microbiological analyses revealed that the gut virome grows in a stepwise fashion, with a first wave of colonization arising from 'pioneer bacteria' containing viral sequences integrated in their genomes (Fig. 1). The first wave of virus production in infant stools could be mapped to the induction of prophages, including those associated with *Escherichia coli*, *Enterococcus* and *Klebsiella* bacteria. By four months, a second wave of virus colonization had occurred, and was found to consist of human-cell viruses known to be pathogenic in infants, including *Adenoviridae, Anelloviridae, Caliciviridae and Picornaviridae*.

In the original cohort, breastfeeding — either exclusively or together with formula — was associated with fewer human viruses in the stools compared with formula-feeding alone. This correlation was reproduced in two validation cohorts: 125 infants from the United States and 100 from Botswana.

Future directions

These data clarify the origin of the human gut virome and suggest that breastfeeding could protect against many classes of pathogenic virus. The metagenomic methods used in this study and the resulting data will be useful for assessing the effect of the virome on health outcomes later in life, and for gauging the efficacy of antiviral strategies in infants. Of particular interest, mixed feeding of breast milk with formula also seemed to protect against viral infection, providing encouragement for mothers to continue breastfeeding even if it is not done exclusively. Future studies are needed to investigate the effects of viral colonization in early life on long-term health outcomes, and to clarify the interactions between the antiviral components in breast milk and the human virome. The human gut virome is discussed further in related content[1–6].

EXPERT OPINION

"This work supports the idea that the early virome (that is, the genetic material of viruses at month one) arises mainly from 'prophages' introduced by pioneer bacteria. The proportion of viruses that grow on human cells then increases over time. The authors report a negative correlation between breastfeeding and the abundance of viruses in human cells, suggesting that full or partial breastfeeding could offer protection against viral infections during one of life's most vulnerable stages." **Editorial team, *Nature*.**

FIGURE

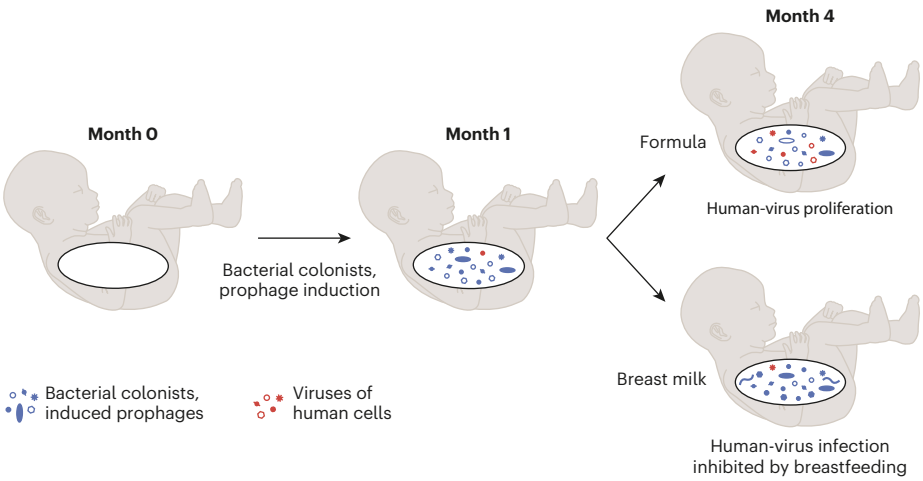

Figure 1 | Microbial colonization of the infant gut. Pioneering microbes, complete with integrated bacterial viruses, colonize the neonatal gut by 1 month of age. At 4 months of age, the infection of the infant gut by potentially harmful human viruses can be reduced through diets supplemented with breast milk. Figure adapted from Fig. 3 of full paper.

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