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## **FUT2 SECRETOR STATUS AND DIARRHEAL ILLNESS - ROLE OF MATERNAL GENOTYPE AND BREASTFEEDING**

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### **Background:**

About 20% of individuals have an inactive fucosyltransferase-2 (*FUT2*) gene and cannot secrete Lewis blood group antigens into their body fluids or mucosal surfaces. Non-secretors are intrinsically resistant to certain viruses that exploit *FUT2* antigens to infect host cells and cause diarrhea. Maternal secretor status affects whether breastmilk contains *FUT2*-dependent oligosaccharides, which may influence infant gut microbiota and viral pathogenicity.

### **Objective:**

We assessed the independent and combined impact of maternal and infant secretor status and breastfeeding on diarrhea during early life.

### **Methods:**

We determined *FUT2* secretor status using single nucleotide polymorphism (rs601338) data from mothers and children from the UK Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort (N=5347 dyads). Diarrheal episodes during infancy were reported by caregivers. Associations and effect modification were assessed using logistic regression.

### **Results:**

Overall, 25% of infants and mothers were *FUT2* non-secretors, 32% of infants were breastfed for at least 6 months, and 27% experienced diarrhea during this period. As expected, infant non-secretor status (OR 0.87, 95%CI 0.77-0.99) and breastfeeding (OR 0.42, 95%CI 0.37-0.47) were independently protective against diarrhea. A potential interaction was detected between breastfeeding and maternal secretor status, suggesting that breastmilk from non-secretor mothers may be more protective (OR 0.68, 95%CI 0.53-0.86) than breastmilk from secretor mothers (OR 0.86, 95%CI 0.75-0.99) (p for interaction=0.09).

### **Conclusion:**

Our results confirm that infant non-secretor status and breastfeeding are protective against diarrhea and provide new evidence that maternal secretor status modifies the effect of breastfeeding. Further investigation is needed to confirm and understand why non-secretor milk may offer greater protection against diarrhea. This research could have important implications for the treatment and provision of donor breastmilk and the development of breast milk substitutes for infants who cannot be breastfed.