Diarrhoea

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Congenital diarrhoea and enteropathy genetics

Congenital diarrhoea and enteropathy (CODE) disorders are rare and primarily affect the intestinal epithelium in infancy, leading to substantial morbidity and mortality. In a new multicentre study published in *The New England Journal of Medicine*, investigators in Canada and the USA characterized the genetic profile of CODE disorders via next-generation sequencing and identified known and novel pathogenic variants.

The researchers analysed the exomes or genomes of 139 infants (including 10 sibling pairs) with a clinical diagnosis of congenital diarrhoea. Next-generation sequencing data revealed variants in 24 known monogenic CODE genes, such as *EPCAM* and *SLC9A3*, including a novel variant in *NEUROG3*. Three CODE candidate genes, *GRWD1*, *MYO1A* and *MON1A*, were then functionally characterized in cell-based assays and zebrafish models. The researchers further classified those three genes through proximity-dependent biotin identification, showing that variants dysregulated intestinal pathways and protein function, such as goblet cell dysfunction, microvilli mislocalization and endosomal sorting.

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