SUPPLEMENTARY FIGURE LEGENDS

Figure S1: TTC7A mutations in MIA-CID patients

Electropherograms of TTC7A mutations identified in MIA-CID patients A9, B3, C3, D3, E3 and F3. Sequencing of cDNA from A1 and A2 (the mother and father of A9) highlighted heterozygous deletions of exons 2 and 3 and of exon 2, respectively. The serine substitution (S569L) in patient D3 inherited from her mother occurred in a residue that has been well conserved over evolution. Sequencing of cDNA obtained from her father D2 (after cloning of the lower band) highlighted an heterozygous 4 bp deletion in exon 11 associated with exon 12 deletion. For F3, sequencing of cDNA obtained from his father (F2) highlighted an heterozygous deletion of exon 12.

Figure S2: Efficient epithelial outgrowth from patient-derived intestinal biopsies

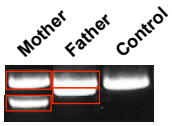
A. Ileum biopsy from a severely affected region. The magnified image shows the only epithelial villus that could be found in this specimen (black arrow). Scale bars: 1 mm. **B.** Time course of organoid growth after seeding (from the patient biopsy shown in A). Red arrows show epithelial structures and blue arrows show non-epithelial tissues that do not expand. Scale bars: 0.1 mm. **C.** Organoids ten days after seeding with a duodenal biopsy from another patient. Overview images (left) show efficient epithelial outgrowth and detailed images (right) show representative examples of organoids with disturbed epithelial morphology. Scale bars: 0.1 mm.

Supplementary videos 1 and 2

Time lapse imaging of patient (MUT) and control (WT) organoids. Bright field microscopical images were acquired in 30 min intervals 2 days after seeding and during a total period of 2

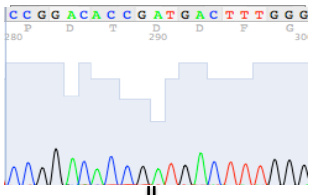
days (time points are shown as hours:min:seconds). Control organoids are single layered and undergo a continuous budding process. Patient cultures are characterized by the formation of multiple vacuoles and undergo cycles of swelling and collapsing. Both were cultured in the presence of Y-27632.

PATIENT A9

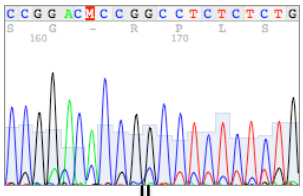


Mother A1

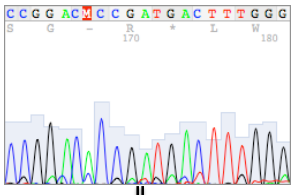
Upper band

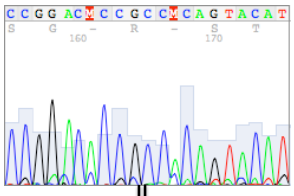


Lower band



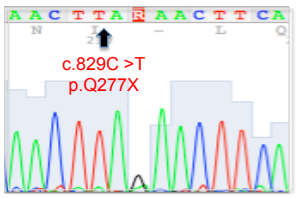
Father A2





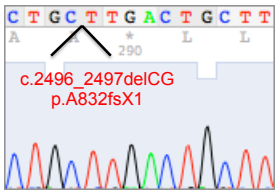
PATIENT B3

Exon 6



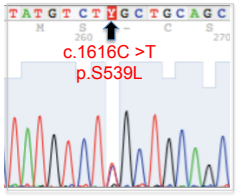
PATIENT C3

Exon 20



PATIENT D3

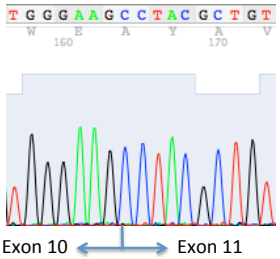
Exon 14



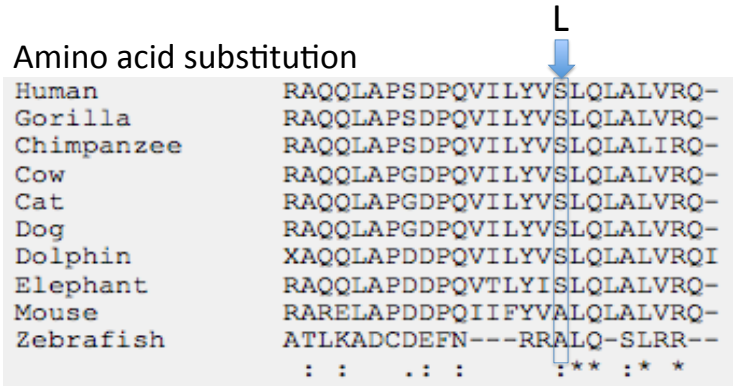
D2 Control

Father D2

Exon 10 – 11

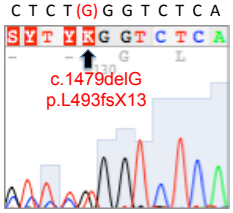


Amino acid substitution

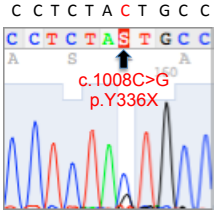


PATIENT E3

Exon 12

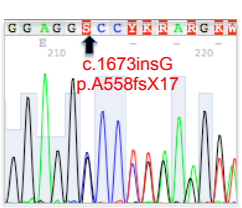


Exon 8



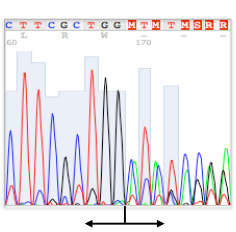
PATIENT F3

Exon 15



Father F2

Exon 11



Exons 12+13

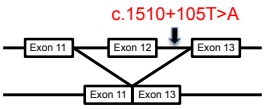
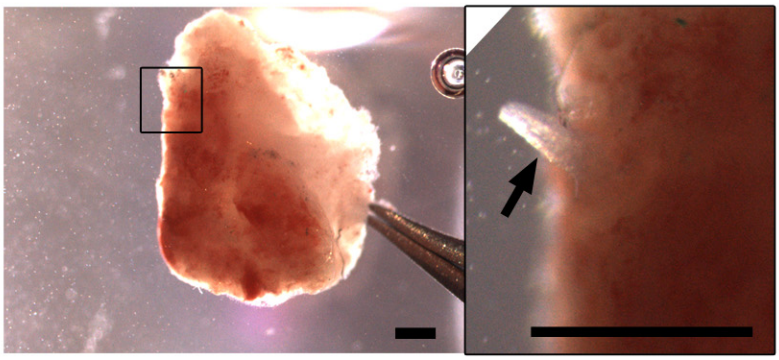
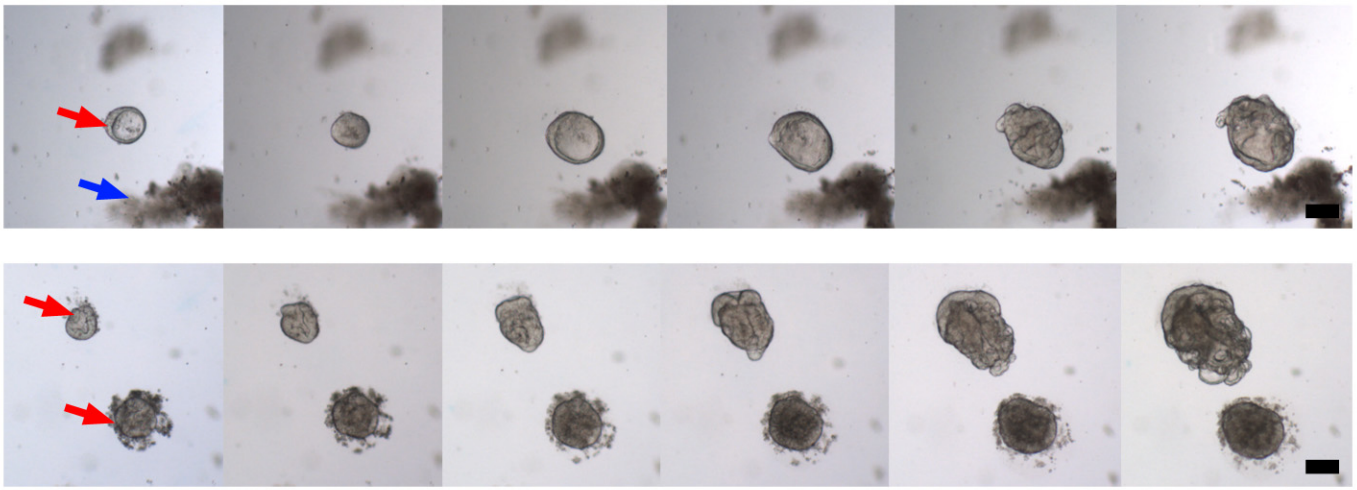
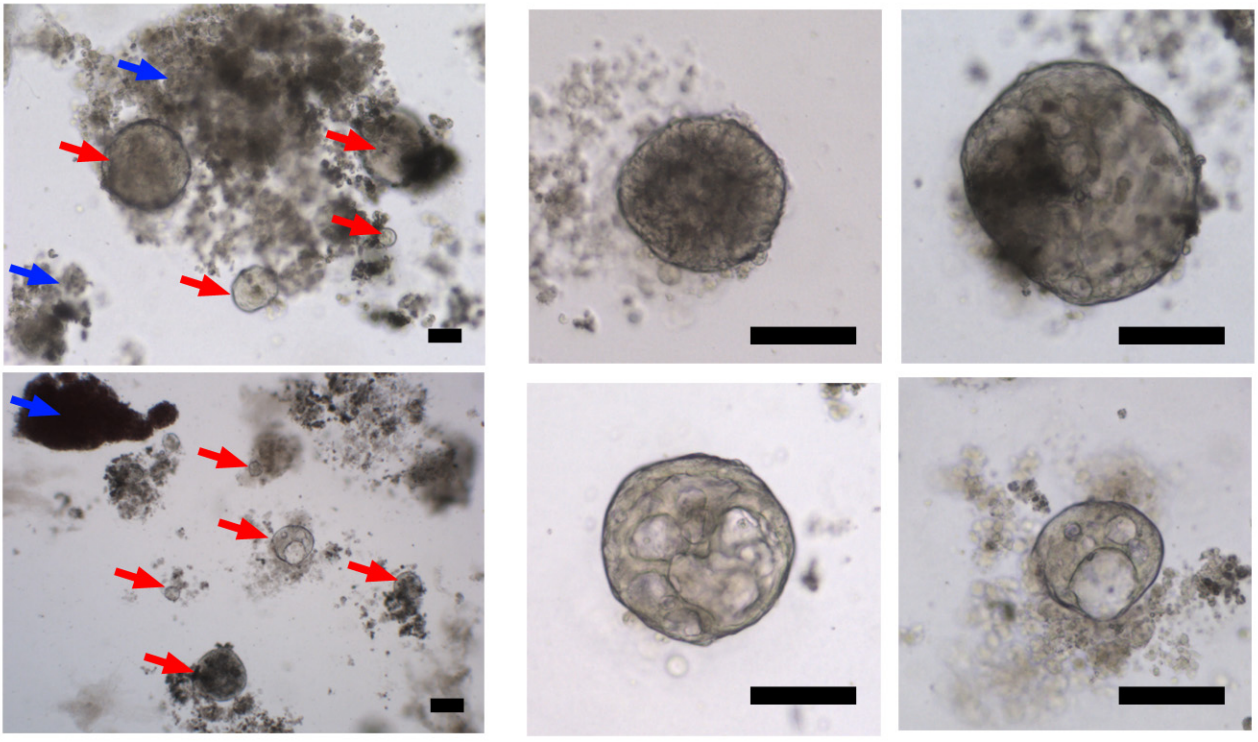


Fig. S2

A patient biopsy



B day 2 day 3 day 4 day 5 day 6 day 7



C day 10