

LETTER

First known case of paediatric inflammatory bowel disease in a western lowland gorilla may be linked to a familial mutation in the *MEFV* gene

We read with interest the recent work by Schwerd *et al*¹ showing yet another example of human monogenic diseases that can present with IBD-like intestinal inflammation. Among the genes and diseases related to these often early onset monogenic IBD cases in humans is also the *MEFV* gene encoding for pyrin. The DNA sequence of gorillas shows >98% identity to the human genome.² However, so far, there are only individual case descriptions of severe colitis due to infections^{3–6} and, to our knowledge, no cases of IBD have been reported in gorillas so far.

We here report two closely related female western lowland gorillas living in captivity and showing partly overlapping GI symptoms, following the relocation into new groups in different zoos. The first case Enea (figure 1A) shows the typical clinical signs of a chronic IBD, most likely Crohn's disease (CD). After a psychological stress situation,

the relocation to a new zoo involving minor dietary adaptations, the gorilla suffered from diarrhoea over a period of several months and showed signs of increased inflammation with a clear increase in C reactive protein (476 mg/L) and calprotectin (1128 mg/kg), while pathogenic germs were excluded in the stool examination. A colonoscopy showed multiple segmental inflammatory lesions with superficial ulcerous and aphthous fibrin-covered lesions (figure 1B). The biopsies revealed clear inflammatory infiltrations with a highly diffuse UC. The endoscopic image showed discontinuous segmental colitis with fissural ulcerations and erosions, comparable to CD, although epithelioid cell granulomas were not detectable in histology (figure 1C). Enea showed a clear response to high-dose steroid therapy. However, due to problems with the acceptance of oral medication, reliable administration was not possible. Four weeks later the patient suffered a relapse. Subcutaneously administered tumour necrosis factor-alpha antibody (400 mg certolizumab) showed no improvement in the gorilla's overall condition and she completely refused fluid and food intake and therefore had to be euthanised a week later. Due to the mourning process in the gorilla group, the autopsy could only be performed 48 hours after death. Autolytic

destruction made histological processing impossible. There was no evidence of serositis. Multifocal confluent ulcerations of the mucosa and submucosa were found in the colon area, whereby single giant cells were described histologically next to the necrosis.

The second case Habibu showed similar symptoms after transfer to another zoo, including diarrhoea and emesis. Inflammatory changes were also detectable in the laboratory, but symptoms were not as pronounced as in Enea. In addition, she had a bite injury on her foot with osteomyelitis, which could partially overlay the detectable inflammatory changes. After extensive antibiotic therapy, the wound healed and the gorilla was better off with an accompanying hypercaloric diet, as can also be successfully performed in human juvenile CD, her weight increased and the diarrhoea stopped.

The two patients share the same father (N'gola) and part of the maternal lineage (figure 1D), so a genetic involvement in disease development was deemed possible. Using human exome enrichment and sequencing we discovered a homozygous missense variant in *MEFV* (c.C505A;p.L169M) shared by the patients, for which the healthy father is heterozygous. The variant shows a minor allele frequency of 0.0006% in humans, with no known homozygotes and is located in exon 2, which, together with exon 10, is a mutational hotspot in humans.⁷ Defects in *MEFV* cause Familial Mediterranean Fever in humans and have been shown to be involved in early onset IBD,^{8,9} leading us to the conclusion that the detected variant is a likely candidate for IBD involvement, pointing to a shared genetic basis for paediatric IBD across different species.

Britt-Sabina Petersen,¹ Bernd Bokemeyer,^{2,3} Christian Wenker,⁴ Stefan Hoby,⁵ Katrin Baumgartner,⁶ Hermann Will,⁶ Marc P Hoepfner,¹ Stefan Schreiber,^{1,3} Ingo Mecklenburg,⁷ Andre Franke¹

¹Institute of Clinical Molecular Biology, Christian-Albrechts-Universität zu Kiel, Kiel, Germany

²Gastroenterology Practice, Minden, Germany

³Department of Internal Medicine, University Medical Center Schleswig-Holstein Campus, Kiel, Germany

⁴Zoo Basel, Basel, Switzerland

⁵Tierpark Bern, Bern, Switzerland

⁶Tiergarten Nürnberg, Nuremberg, Germany

⁷Department of Internal Medicine, Klinikum Landsberg am Lech, Landsberg am Lech, Germany

Correspondence to Andre Franke, Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel, 24118 Kiel, Germany; a.franke@mucosa.de

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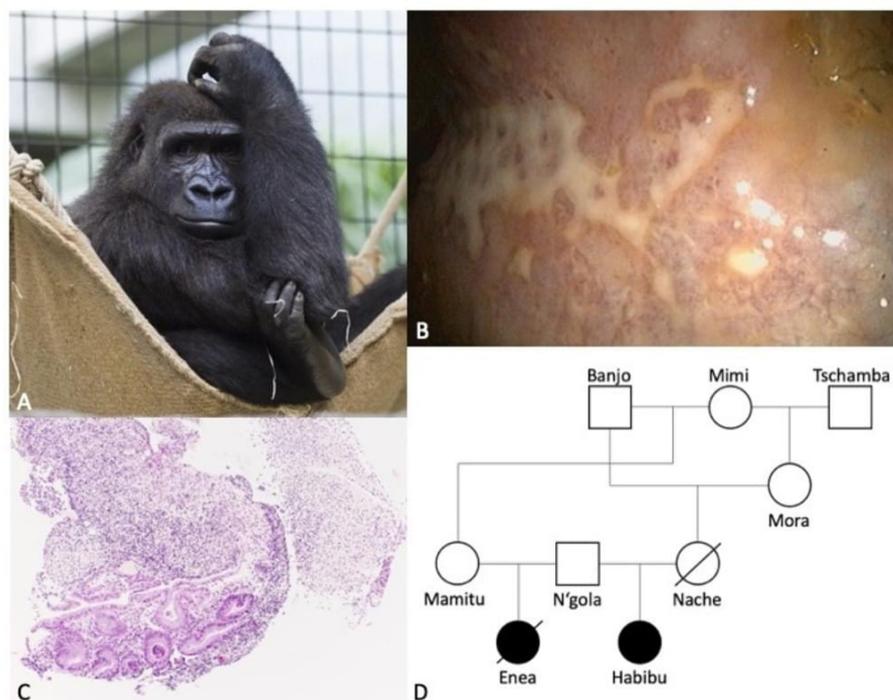


Figure 1 (A) Patient 1, Enea, aged 7 years, a western lowland gorilla (date of birth 1 January 2006 in Zurich, Switzerland). (B) Colonoscopy of patient 1 showing segmental colitis with fissural ulcers. (C) Ulcerated colon mucosa with evidence of disrupted and distorted glands, corresponding to an aphthoid ulcer (H&E staining, 10x). (D) Pedigree showing relationship of the two patients.

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