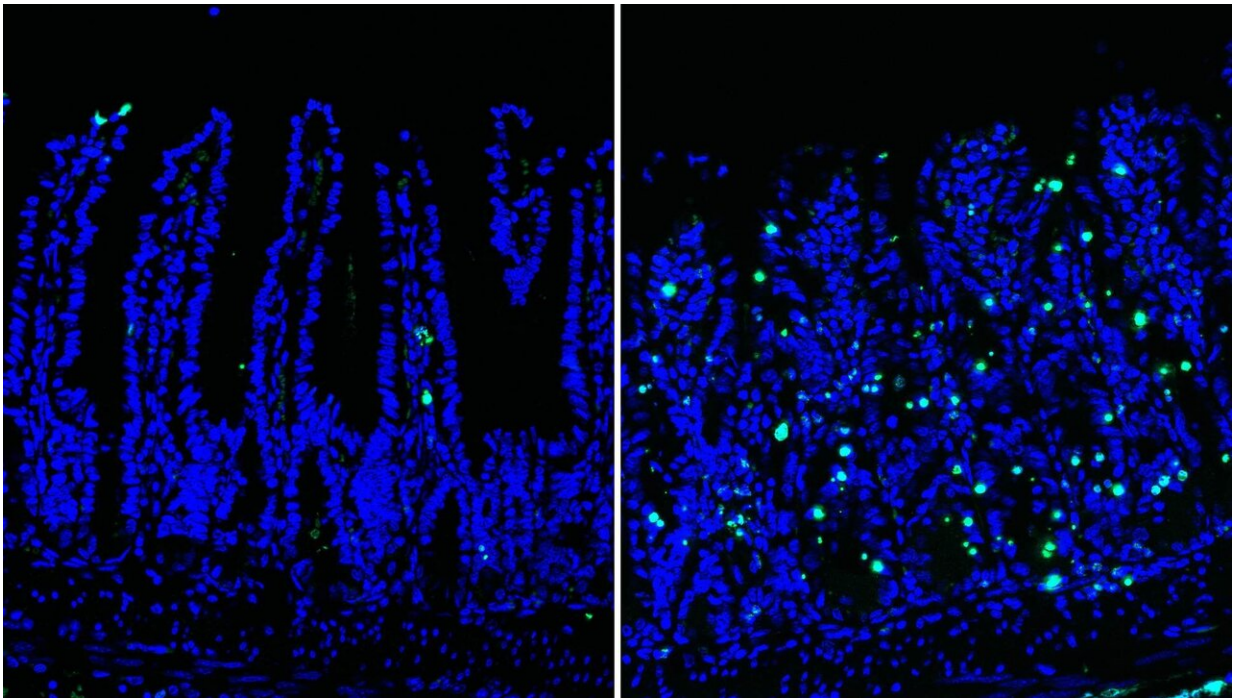


Intestinal health: Research team identifies enzyme essential for stem cell survival

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Healthy (right) vs diseased (left) bowel: Extensive DNA damage (green) within the intestinal epithelium leads to inflammatory cell death and disrupts intestinal homeostasis. Credit: CRTD

The intestinal epithelium is the inner layer of the intestinal wall, which separates host tissue from the intestinal microbiota. This layer of cells plays a crucial role in water, electrolyte and nutrient absorption, while limiting the entry of bacteria, viruses, fungi, toxins and antigens into host

tissue to ensure intestinal homeostasis. The diverse functions carried out by the intestinal epithelium are supported by multiple specialised intestinal epithelial cells, which are replaced every three to five days from a pool of intestinal stem cells. This makes the intestinal epithelium one of the most rapidly renewing tissues in adult mammals.

Which pathways govern intestinal epithelial differentiation under constitutive conditions? Epithelial differentiation is largely controlled by the tissue-specific activity of transcription factors. Access to DNA is provided by accessible chromatin (euchromatin), while compacted heterochromatin limits access of transcription factors to DNA. Researchers at the TU Dresden Center for Regenerative Therapies (CRTD) have now investigated the significance of the regulation of heterochromatin formation in the [intestinal epithelium](#) and published their findings in the renowned international scientific journal *Gut*.

In their study, Prof. Sebastian Zeißig's team demonstrated the essential role of the SETDB1 protein involved in heterochromatin formation during [intestinal epithelial cells](#) differentiation, and its importance in preventing inflammation. The scientists observed in mice the consequences of the enzyme loss in the intestinal stem cells: Endogenous retroviruses, which represent a relevant part of the human genome, accumulate within a few days, which leads to DNA damage, inflammatory cell death, and loss of intestinal epithelial stem cells as well as of differentiated epithelial cells. This limits the absorption of fluid and nutrients, causes intestinal inflammation and inevitably leads to death within a few days.

"Our study reveals a fundamental importance of SETDB1 and heterochromatin formation in the maintenance of epithelial genome stability and the control of intestinal homeostasis," explains Prof Sebastian Zeißig, CRTD research group leader and physician at the Medical Clinic I of the University Hospital Carl Gustav Carus Dresden.

"It remains to be seen whether mutations in this gene can also contribute to intestinal inflammation in humans, for example, in inflammatory bowel diseases."

More information: Lea Južnić et al. SETDB1 is required for intestinal epithelial differentiation and the prevention of intestinal inflammation, *Gut* (2020). [DOI: 10.1136/gutjnl-2020-321339](https://doi.org/10.1136/gutjnl-2020-321339)

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