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Co-authored article published in Nature Immunology: Transcriptomic analysis of intestine following administration of a transglutaminase 2 inhibitor to prevent gluten-induced intestinal damage in celiac disease

We are excited to share novel research results on celiac disease (CeD) co-authored by scientists from Zedira. A consortium of European researchers led by Keijo Viiri (Tampere University) published an article in *Nature Immunology* providing new insight on the molecular mechanisms underlying the efficacy of ZED1227. The first-in-class tissue transglutaminase inhibitor ZED1227 [1] was already successfully evaluated in a phase 2a gluten challenge study in patients with celiac disease [2]. Now, the authors report transcriptomic analysis of patient derived duodenal biopsies to detail the pathways of TG2 inhibition to attenuate gluten-induced morphological deterioration.

The paper indicates that epithelial *"interferon signaling was one of the most significantly affected pathways in the gluten challenge study"*. The 100 mg dose of ZED1227 entirely blocked the gluten-induced transcriptomic changes supporting former histomorphometry findings [2]. Based on the data, the authors concluded that *"transcriptomic findings strongly support the results of the clinical trial with ZED1227, which demonstrated that the inhibition of TG2 activity can efficiently and specifically prevent gluten-induced mucosal damage."* Further, the authors emphasized *"halting the adaptive immunity pathway in CeD pathogenesis is sufficient to prevent gluten-induced mucosal damage, as we did not detect any molecular traces of mucosal damage remaining after ZED1227 treatment"*. The data from the first transcriptome-level analysis of biopsies from patients receiving the blocker ZED1227 clearly contribute to our understanding of efficacy of pharmaceutical transglutaminase inhibitors.

We sincerely thank the participating patients and the dedicated researchers of the ZED1227 ([TAK-227](#)) clinical trials who contributed to this study. Your unwavering commitment and enthusiasm drive us forward in our mission to make a meaningful impact on patients' lives and advance transglutaminase research in academia and industry.

Here you find the open-access article and author affiliations:

<https://www.nature.com/articles/s41590-024-01867-0>

[1] [Buechold et al., Cells 2022, 11\(10\), 1667](#)

[2] [Schuppan et al., N Engl J Med 2021; 385:35-45](#)

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We are continuously expanding our product portfolio to meet the evolving needs of researchers in the field of transglutaminase R&D. Should you have any questions or queries about our products, please do not hesitate to contact us at contact@zedira.com

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