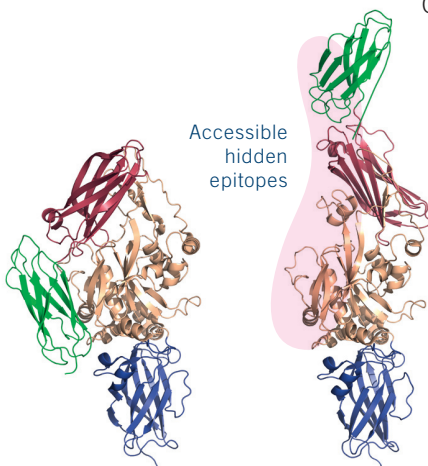


Open tTG™

→ The second generation antigen in celiac disease diagnostics Improving diagnostic sensitivity and specificity

Since its discovery as the auto antigen in celiac disease by Dieterich and Schuppan in 1996 tissue transglutaminase has become the major serological marker in celiac disease. By the exploitation of latest knowledge on the pathophysiology Zedira developed the second generation antigen: **Open tTG™**

Tissue transglutaminase is the key player in celiac disease – on the one hand as **antigen** but even more important as the **enzyme** catalyzing the essential step triggering the chronic inflammation: the deamidation of gliadin-peptides in the intestinal mucosa.



Crystallization of tissue transglutaminase revealed a fascinating property of tissue transglutaminase: the more ball shaped enzyme opens like a pocketknife upon substrate binding. In consequence hidden and most relevant epitopes become accessible.

Combining small molecule drug development with cutting edge recombinant biotechnology Zedira scientists created **Open tTG™**.

Whereas the closed form (left) of tissue transglutaminase is generally present in healthy tissue, the open form (right) is more prominent during inflammation. Very likely the open conformation displays the immunodominant molecule in the intestinal mucosa responsible for the induction and maintenance of inflammation in celiac disease.

The production of tissue transglutaminase modified with an active site specific irreversible inhibitor allows the stabilization in the unique open conformation, yielding **Open tTG™** – the tissue transglutaminase conformation present in celiac disease.

ELISA based examinations using **Open tTG™** as antigen revealed improved sensitivity and specificity in comparison to standard tTG as antigen.

Example: 25 celiac disease patient's sera with low titers have been analysed with standard tTG-ELISA versus **Open tTG™**-ELISA.

The cut off is 3 U/ml and the grey area is up to 5 U/ml. In the standard tTG-ELISA 8 sera are **equivocal** but turned **clearly positive** when measured with **Open tTG™**-ELISA. In general a much higher signal intensity is generated further improving reliability.

