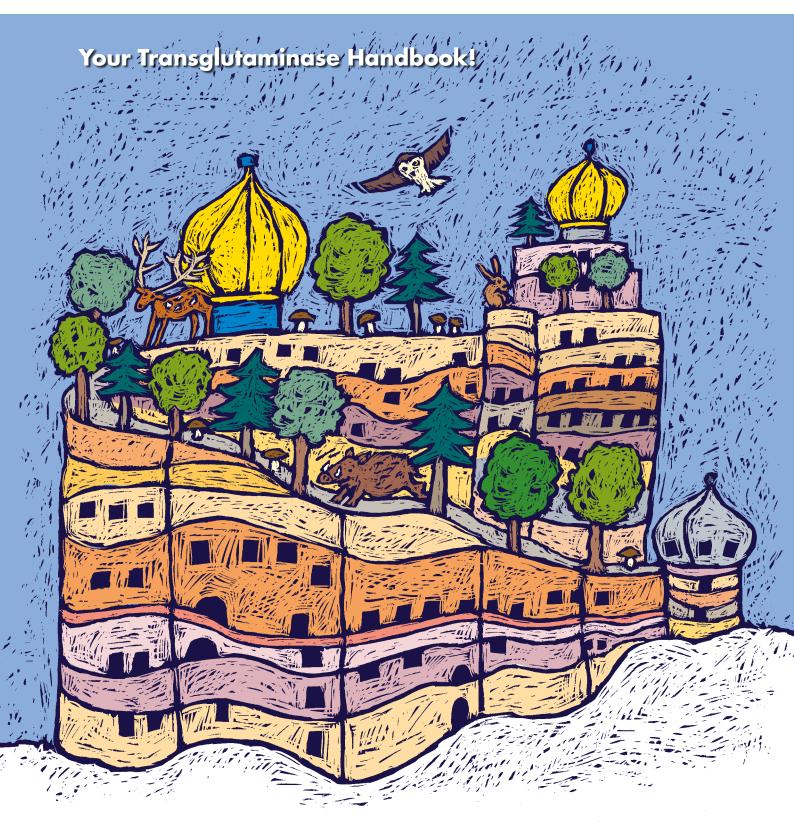
Transglutaminase

Specialty Reagents





- Transglutaminases
- Microbial Transglutaminase
- Protein Labeling
- Assays & Substrates
- Inhibitors

- Antibodies & Microarrays
- Proteases
- Cereal Proteins
- Blood Coagulation
- Celiac Disease Products



20232024

Editorial

Dear Valued Customers, Dear Friends,

The 2023 edition of the "Transglutaminase Specialty Reagents" catalogue is the first issue available only as an electronic version. This reflects changing user behavior that prefers digital product information and ordering systems. Moreover, retiring the printed catalogue saves natural resources and contributes to sustainability.

Zedira is located in Darmstadt in the middle of Germany and Europe, which was reflected by the cover series of prominent buildings in Darmstadt in the 2012 to 2022 catalogues.

With the electronic version of our catalogue, we introduce a new series of Darmstadt-related cover designs. In this edition, the illustrator and graphic designer Nicola Koch infuses humor and a subtle sense of whimsy into her piece, "Waldspirale". Nicola transformed the building's rooftops into a lush forest, complete with its inhabitants, encapsulating the essence of the project. Stay tuned for future covers.

"The Decade of Transglutaminase Ahead" was our enthusiastic header of the 2022 catalogue edition. The time seems right for a first critical assessment of what has happened in the past year and a half.

Our small molecule compound ZED1227 [Buechold et al., 2022], the first clinically tested transglutaminase blocker which validated tissue transglutaminase (TG2) as a therapeutic target in celiac disease [Schuppan, Mäki et al., 2021], was licensed to Takeda Pharmaceuticals in October 2022. By joining forces with our European licensee Dr. Falk Pharma for clinical development, a phase 2b study has been initiated. Furthermore, GSK dropped its celiac program on the TG2 blocker GSK3915393 acquired from Sitari in early 2023 after a pipeline review and reprioritization process, leaving our compound ZED1227 the only clinical stage drug candidate in the TG2 inhibitor field.

Is TG2 a target in non-alcoholic fatty liver disease (NAFLD)? This question is going to be answered by Dr. Falk Pharma's phase 2a clinical trial using our TG2 inhibitor ZED1227 in patients with NAFLD, which began in March 2022.

Generally, TG2 is considered a therapeutic target in several fibrotic disorders. Therefore, scientists at Zedira developed a novel class of TG2 inhibitors to address indications like Idiopathic Pulmonary Fibrosis (IPF), NAFLD, and Diabetic Nephropathy. Most exciting is ZED3269, our clinical candidate optimized for potency, selectivity, and oral bioavailability.

Zampilimab, an antibody binding to the active conformation of human TG2, was tested by UCB Pharma in a Phase 1/2 study in adult kidney transplant recipients with chronic allograft injury. The study ended prematurely due to recruitment challenges. The monoclonal antibody was licensed in late 2021 to the Chiesi group, which started a clinical trial (NCT05513950) in Idiopathic Pulmonary Fibrosis (IPF) patients in January 2023. Results are expected in May 2024.

In summary, we see an ongoing and dynamic interest in TG2 as a therapeutic target - and are curious to see what will come next.

What is new in our "Transglutaminase Specialty Reagents" portfolio:

You, our esteemed customers, told us that you need reliable and isoenzyme-specific transglutaminase activity assays. Therefore, we initiated the development of a transglutaminase assay platform. The first novel assay launched addresses TG2. The new isopeptidase assay kits F014 and F016 are unprecedented products to precisely determine even low TG2 concentrations in complex matrices like tissues.

In February 2023, we launched Andracon™, our high-quality recombinant microbial transglutaminase in its novel formulation. The production is backed by a scaled process so that we can fulfill our customers growing demands. Andracon™ is the first choice in enzymatic Antibody Drug Conjugate (ADC) manufacturing as well as for tissue remodeling approaches.

Last but not least, Zedira supports efforts to reestablish an interdisciplinary meeting for the transglutaminase community to connect researchers from all fields where transglutaminases are involved (15th International Research Conference on Transglutaminases in Human Disease Processes, 19.-23.05.2024, in Bertinoro, Italy).



Sincerely yours,
Ralf and Martin, on behalf of the entire Zedira team



Zedira is certified according to

DIN EN ISO 9001:2015

according to ISO 9001:2015, the globally recognized standard that ensures the company's products and services consistently meet customer requirements through effective quality management.

Since obtaining this certification, the entire Zedira team has successfully maintained ISO compliance in all surveillance and recertification audits without any nonconformities, affirming their commitment to excellence in biotechnology research, development, production, and distribution. This achievement demonstrates Zedira's dedication to continuous improvement and customer satisfaction.

Since 2019, Zedira' quality management system is certified

SEFÖRDERT VOM









Zedi - Zedira's transglutaminase mascot

In honor of Heinrich Waelsch, Nirmal Sarkar and Donald Clarke who discovered transglutaminase in extracts from guinea pig liver in 1957, we chose the guinea pig as our mascot. Zedi's mission is to inform you of novel products and activities in the transglutaminase research field.

In the catalogue Zedi highlights the most important products we recommend to scientists working with transglutaminases.

Stay informed about Zedira's new products as well as general activities like conferences in the fields of transglutaminase, celiac disease, thrombosis, and haemostasis:

- Visit our homepage www.zedira.com
- Register for the Transglutaminase Newsletter (send an e-mail to contact@zedira.com)

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The content of this catalogue is subject to change without notice. Prices apply according to our website. To view the latest product developments, prices, and availability please visit our homepage: www.zedira.com.

For any questions, please contact us via e-mail: contact@zedira.com.

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Transglutaminases

Background information

The history of the enzyme class of transglutaminases started more than 60 years ago, when the term transglutaminase (TG) was introduced in the scientific literature by Heinrich Waelsch and co-workers.

Today, we know TGs are a family of nine different isoenzymes in the human body. Although TGs have one basic common

feature – the formation of high molecular weight aggregates by covalent protein cross-linking – they fulfill a multitude of other catalytic and physiological functions.

The sketch below gives you a rough overview of the TG family members and their implications in physiology, diseases, and diagnostics – as it is known today.

Deficiencies

TG1: lammellar ichthyosis
 TG3: uncombable hair syndrome
 TG5: acral peeling skin syndrome
 FXIII: bleeding, impaired wound healing, abortions

Diagnostic markers

TG2-autoantibodies
TG3-autoantibodies
TG6-autoantibodies
Factor XIII-activity

Functions

cross-linking protein modification signaling (G-protein) structural protein

Location

intracellular, extracellular intranuclear plasma

Cell biology

differentiation
cell adhesion
apoptosis
cell-cell interaction
cell-matrix interaction
phagocytosis
vascularisation
wound healing
inflammation
receptor mediated endocytosis

Skin

cornified envelope formation trans-epidermal water loss barrier function

Autoimmune diseases celiac disease

celiac disease dermatitis herpetiformis gluten ataxia

Neurodegeneration

Alzheimer's disease Chorea huntington Parkinson's disease

Eyes

cataract formation

Skin diseases

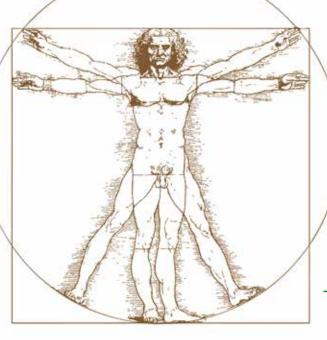
acne, psoriasis

Fibrosis

scarring scleroderma lung fibrosis liver fibrosis and cirrhosis diabetic nephropathy

Cancer

drug resistance carcinogenesis vascularisation



The transglutaminase family

TG1: keratinocyte transglutaminase TG2: tissue transglutaminase TG3: epidermal transglutaminase TG4: prostate transglutaminase TG5: transglutaminase 5 TG6: neuronal transglutaminase TG7: transglutaminase 7 FXIII: blood coagulation factor XIII B4.2: inactive structural protein

Coagulation

fibrin cross-linking decoration with antifibrinolytics clot stability half-life and composition

ECM

stabilisation attachment and spreading of cells profibrotic factor

Products

Transglutaminase 1

Synonyms: Keratinocyte transglutaminase, TG1, TGase 1, TG_K

 Art. No.
 Name
 Unit
 Price

 T009
 Human keratinocyte transglutaminase
 150 μg
 400 €

(TG1, recombinantly produced in **E. coli**)

Reference: Hauser et al., Int. J. Mol. Sci. 2022, 23:4475; Chrobok et al., PLoS One. 2018, 13:e0196433; Plank et al., J Invest

Dermatol. 2018, pii: S0022-202X(18)32817-3; Fischer et al., J. Invest. Dermatol. 2013, 133:1170-7; Fukui et al., FEBS J. 2013, 280:1420-9; Schaertl et al., J. Biomol. Screen. 2010, 15:478-87; Yamane et al., FEBS J. 2010,

277:3564-74

T035 Human keratinocyte transglutaminase 150 μg 400 €

(TG1, recombinantly produced in insect cells)

Reference: Tatsukawa et al., 2022, PREPRINT, doi 10.21203/rs.3.rs-1603071/v1;

Transglutaminase 2

Synonym: Tissue Transglutaminase, TG2, TGase 2, TG_C , tissue type protein-glutamine- γ -glutamyltransferase

In the table below, you find an overview of human TG2 variants available. Please have a look on the following pages for more detailed product descriptions.

Do you need any other TG2 variants?

Just contact us for customized production: contact@zedira.com

	Human TG2 variants available									
Source		Wild type	•	Mutants			Open tTG™			
E. coli	T002	T106		T018	T167	T168	T169	T1 <i>7</i> 3		
Insect cells	T022		T067						T051	T148
HEK cells	T034									
Description	wild type (WT)	biotinylated WT	endotoxin free WT	Cys277Ser mutant	Beta-barrel 1+2 domain deletion-mutant	Cys230Ala mutant	Arg580Ala mutant	Arg116Cys mutant	Open tTG™	biotinylated Open tTG™

Need individual domains of human TG2? Please contact us!

Transglutaminases

Human Transglutaminase 2



Art. No.	Name	Unit	Price
T002	Human tissue transglutaminase	250 µg	400 €
	(hTG2, recombinantly produced in E. coli)	1 mg	1200 €
Reference:	Alshintari et al., Mediterr J Pharm Pharm Sci. 2023, 63-68; Chrobok et al., PLoS G	One. 2018, 13	:e0196433;
	Hietikko et al., Acta Derm Venereol. 2018, 98:366-72; Sánchez-Lara et al., Vet Pathol.	2015, 52:513-	23; de Jager
	et al., J. Neurochem. 2015, 34:1116-28; Fukui et al., FEBS J. 2013, 280:1420-9; Van	den Akker et al	., PLoS ONE
	2011, 6:e23067; Schaertl et al., J. Biomol. Screen. 2010, 15:478-87; Byrne et al., Clir	. Immunol. 201	0, 136:426-
	31; Yamane et al., FEBS J. 2010, 277:3564-74; Perez Alea et al., Anal. Biochem. 200	9, 389:150-6	
T018	Inactive human tissue transglutaminase	250 µg	400 €
	(hTG2, Cys277Ser-mutant, recombinantly produced in <i>E. coli</i>)	1 mg	1200 €
Reference:	Shinde et al., J. Mol. Cell Cardiol. 2018, 117:36-48; Van den Akker et al., PLoS ONE	2011, 6:e230d	57
T022	Human tissue transglutaminase	250 µg	400 €
	(hTG2, recombinantly produced in insect cells)	1 mg	1200 €
Reference:	Heerwig et al., Int. J. Mol. Sci. 2023, 24, 1650; Hauser et al., Int. J. Mol. Sci. 2022,	23:4475; Tatsu	ıkawa et al.,
	2022, PREPRINT, doi 10.21203/rs.3.rs-1603071/v1; Lexhaller et al., Nutrients. 2019	P, 11:2263; Eng	gstrom et al.,
	Sci. Rep. 2017, 7:77; Hardes et al., Anal. Biochem. 2012, 428:73-80;		
T034	Human tissue transglutaminase	100 µg	400 €
	(hTG2, recombinantly produced in human embryonic kidney cells)		
T051	Open tTG™	250 µg	550 €
	(inhibited human tissue transglutaminase, stabilized in its open conformation,	1 mg	1650 €
	recombinantly produced in insect cells)		
Reference:	Lortat-Jacob et al., J. Biol. Chem. 2012, 25:18005-17; Lindfors et al., J. Clin. Immunol.	2011, 31:436	-42;
	Pallav et al., Dig. Liver Dis. 2012, 44:375-8		
T067	Human tissue transglutaminase, endotoxin free	250 µg	450 €
	(hTG2, recombinantly produced in insect cells)	1 mg	1350 €
T106	Biotinylated human tissue transglutaminase	100 µg	400 €
	(biotinylated hTG2, recombinantly produced in E. coli)	250 µg	800 €
T148	Biotinylated human Open tTG™	50 µg	400 €
	(biotinylated inhibited human tissue transglutaminase (T051),	250 µg	1600 €

stabilized in its open conformation, recombinantly produced in insect cells)



Art. No.	Name	Unit	Price
T167	Short human tissue transglutaminase, aa 1-465	250 µg	400 €
	(hTG2, Barrel 1 and 2 deletion-mutant, recombinantly produced in <i>E. coli</i>)		
Reference:	Stamnaes et al., PLOS ONE 2015, 10:e0134922		
T168	Human tissue transglutaminase, C230A mutant	250 µg	400 €
	(hTG2, Cys230Ala-mutant, recombinantly produced in <i>E. coli</i>)	1 mg	1200 €
Reference:	Stamnaes et al., JBC 2010, 285:25402-9		
T169	Human tissue transglutaminase, R580A mutant	250 µg	400 €
	(hTG2, Arg580Ala-mutant, recombinantly produced in <i>E. coli</i>)	1 mg	1200 €
Reference:	Liu et al., PNAS 2002, 99:2743-7		
T173	Human tissue transglutaminase, R116C mutant	1 mg	1200 €
	(hTG2, Arg116Cys-mutant , recombinantly produced in E. coli)		

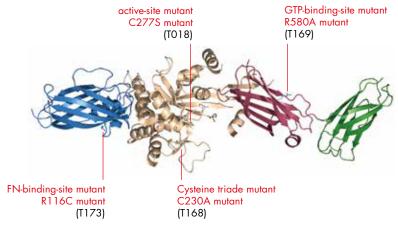


Figure: "Open" conformation structure of TG2. Available mutants are indicated.

Need individual domains of human TG2? Please contact us!

Transglutaminases

Animal Transglutaminase 2



Art. No.	Name	Unit	Price
T039	Guinea pig liver transglutaminase	10 U	410 €
	(gpTG2, recombinantly produced in E. coli)		
Reference:	Alshintari et al., Mediterr J Pharm Pharm Sci. 2023, 63- 68; Hauser et a	I., Amino Acids. 2017,	49:567-83
	Wodtke et al., Chembiochem. 2016, 17:1263-81		
T038	Rat tissue transglutaminase	250 µg	400 €
	(rTG2, recombinantly produced in E. coli)	1 mg	1200 €
Reference:	Sánchez-Lara et al., Vet Pathol. 2015, 52:513-23		
T040	Mouse tissue transglutaminase	250 µg	400 €
	(mTG2, recombinantly produced in E. coli)	1 mg	1200 €
Reference:	Chrobok et al., PLoS One. 2018, 13:e0196433; Shinde et al., J. Mol. Cell C	ardiol. 2018, 117:36-48	;
	Schaertl et al., J. Biomol. Screen. 2010, 15:478-87; Schulze-Krebs et al., Bra	in Res. 2016, 1631:22-3	3
T156	Biotinylated mouse tissue transglutaminase	250 µg	550 €
	(Biotin-mouse TG2, recombinantly produced in <i>E. coli</i>)	1 mg	1650 €
T150	Biotinylated mouse open TG2	50 µg	400 €
	(Product derived from T102, recombinantly produced in <i>E. coli</i>)	250 µg	1600 €
T072	Dog tissue transglutaminase	250 µg	400 €
	(cITG2, recombinantly produced in insect cells)	1 mg	1200 €
T108	Cynomolgus tissue transglutaminase	250 µg	550 €
	(mfTG2, recombinantly produced in human embryonic kidney cells)		
T159	Pig tissue transglutaminase	250 µg	400 €
	(sTG2, recombinantly produced in E. coli)	1 mg	1200 €
T184	Cat tissue transglutaminase	200 µg	400 €
	(fcTG2, recombinantly produced in E. coli)		
Transglutan	iinase 3		
Synonym:	Epidermal transglutaminase, TG3, TGase 3, epidermal protein-glutamine-γ-glut	amyltransferase, TG _E	
Art. No.	Name	Unit	Price
T013	Human epidermal transalutaminase. Dispase activated	200 µg	550 €



Art. No.	Name	Unit	Price
T013	Human epidermal transglutaminase, Dispase activated	200 µg	550 €
	(TG3a, recombinantly produced in insect cells)		
- (2017 60.701027	
Reference:	Hauser et al., Int. J. Mol. Sci. 2022, 23:4475; Akbar et al., J. Med. Chem.	2017, 00.7910-27	
Reference:	Hauser et al., Int. J. Mol. Sci. 2022, 23:4475; Akbar et al., J. Med. Chem.	2017, 00.7910-27	
Reference:	Hauser et al., Int. J. Mol. Sci. 2022, 23:44/5; Akbar et al., J. Med. Chem. Human epidermal transglutaminase	200 µg	400 €
		,	400 €

Transglutaminase 4

Synonym: Prostate Transglutaminase, TG4, TGase 4

 Art. No.
 Name
 Unit
 Price

 T042
 Human prostate transglutaminase
 100 μg
 400 €

(TG4, recombinantly produced in **E. coli**)

Reference: Csobán-Szabó et al., Int. J. Mol. Sci. 2021, 22:12448;

Csobán-Szabó et al., bioRxiv 2021, DOI 10.1101/2021.09.01.458359

Transglutaminase 5

Synonym: TG5, TGase 5, TG_x

 Art. No.
 Name
 Unit
 Price

 T086
 Human transglutaminase 5
 100 μg
 400 €

(inactive TG5 inclusion body preparation, recombinantly produced in *E. coli*)

Transglutaminase 6

Synonym: Neuronal Transglutaminase, TG_y, TG6, TGase 6



Art. No.	Name	Unit	Price
T021	Human neuronal transglutaminase	250 µg	500 €
	(TG6, recombinantly produced in insect cells)	1 mg	1500 €
Reference:	Hauser et al., Int. J. Mol. Sci. 2022, 23:4475; Fukui et al., FEBS J. 2013	, 280:1420-9; Schaertl et a	l., J. Biomol.
	Screen. 2010, 1 <i>5</i> :4 <i>7</i> 8-8 <i>7</i>		
T064	Inhibited human neuronal transglutaminase	250 µg	685 €

Need individual domains of human TG6? Please contact us!

(inhibited TG6, recombinantly produced in insect cells)

Transglutaminase 7

Synonym: TG7, TGase 7

Art. No.	Name	Unit	Price
TO11	Human transglutaminase 7	250 µg	400 €
	(TG7, recombinantly produced in E. coli)		
Reference:	Kuramoto at al., Arch: Biochem Biophys. 2013, 537138-43; Fukui et al., FEBS J. 20	13, 280:1420-9	

Transglutaminases

Factor XIII

Synonym: Coagulation factor XIII, FXIII, F13, Fibrin stabilizing factor, FSF, Laki-Lorand factor

Human Factor XIII-A

rien.	

numan raci	or Alli-A ₂		
Art. No.	Name	Unit	Price
T027	Human blood coagulation Factor XIII-A₂	200 µg	400 €
	(hFXIII, A subunit, recombinantly produced in insect cells)		
Reference:	Gates et al., Molecules 2023, 28:1634; Li et al., Res. Pract. Thromb. Haemost.	2022, 6:e12766; Bö	hm et al,. J.
	Med. Chem. 2014, 57:10355-65; Nikolajsen et al., J. Biol. Chem. 2014, 289:	6526-34; Heil et al., T	hromb. Res.
	2013, 131:e214-e22; Schaertl et al., J. Biomol. Screen. 2010, 15:478-87		
T063	Human blood coagulation Factor XIII-A ₂ , Val34Leu-mutant	200 µg	400 €
	(hFXIIIVal34Leu, A subunit, recombinantly produced in insect cells)		
Reference:	Heil et al., Thromb. Res. 2013, 131:e214-e22		
T070	Human Factor XIII a, Thrombin activated	200 µg	550 €
	(hFXIIIa, recombinantly produced in insect cells)		
Reference:	Hauser et al., Int. J. Mol. Sci. 2022, 23:4475; Chrobok et al., PLoS One. 201	8, 13:e0196433; Akl	oar et al., J.
	Med. Chem. 2017, 60:7910-27; de Jager et al., Neuropathol. Appl. Neurobio	l. 2016, 42:255-72; H	lamedani et



al., Chem. Commun. 2015, 51:1135-39; Böhm et al,. J. Med. Chem. 2014, 57:10355-65 T092 450 € Human blood coagulation Factor XIII-A, 100 µg (hFXIII, A subunit, recombinantly produced in human embryonic kidney cells) T197 Coagulation factor XIII, recombinant human Factor XIII-A, 100 E 725 € 250 E (Recombinant fibrin stabilizing factor, HSA formulation, 1450 € recombinantly produced in **insect cells**) $1\ E$ is defined as the Factor XIII activity of $1\ mL$ citrated plasma from healthy human donors Note:

Need individual domains of human Factor XIII? Please contact us!

Human Factor XIII-B

Art. No.	Name	Unit	Price
T050	Human blood coagulation Factor XIII B subunit	00 µg	400 €
	(hFXIII-B, F13B, recombinantly produced in insect cells)		
Reference:	Li et al., Res. Pract. Thromb. Haemost. 2022, 6:e12766; Böhm et al., J. Med. Chem.	2014, 57	7:10355-65;
	Heil et al., Thromb. Res. 2013, 131:e214-e22; Katona et al., Blood. 2014, 123:1757-63		

Human Factor XIII activation peptide (AP-FXIII)

Art. No.	Name	Unit	Price
A125	Human Factor XIII activation peptide	10 mg	475 €
	(Ac-SETSRTAFGGRRAVPPNNSNAAEDDLPTVELQGVVPR-OH, AP-FXIII)		
Reference:	Dodt et al., Br. J. Haematol. 2015, 172:452-60		
T187	Factor XIII activation peptide, recombinant	500 µg	400 €
	(recombinantly produced in E. coli , fused to carrier protein)		
Animal Factor	or XIII-A $_2$		
Reference:	Heil et al., Thromb. Res. 2013, 131:e214–e22		
Art. No.	Name	Unit	Price
T061	Mouse blood coagulation Factor XIII-A ₂	200 µg	400 €
	(mFXIII, A subunit, recombinantly produced in insect cells)		
T062	Dog blood coagulation Factor XIII-A ₂	200 µg	400 €
	(clFXIII, A subunit, recombinantly produced in insect cells)		
T065	Rat blood coagulation Factor XIII-A ₂	200 µg	400 €
	(rFXIII, A subunit, recombinantly produced in insect cells)		
T066	Pig blood coagulation Factor XIII-A ₂	200 µg	400 €
	(sFXIII, A subunit, recombinantly produced in insect cells)		
T161	Cynomolgus blood coagulation Factor XIII-A ₂	200 µg	400 €
	(Macaca fascicularis FXIIIA, mfFXIIIA, recombinantly produced in insect cells)		

Transglutaminases

Spotlight - First structure of Factor XIII in an active conformation

Thrombotic events are a major cause of morbidity and mortality, particularly in industrialized countries. Accordingly, a remarkable effort has been undertaken to develop drugs targeting coagulation factors or platelet activation to prevent thromboembolic events. However, current anticoagulants are associated with adverse bleeding events.

For decades, factor XIIIa (FXIIIa) has been considered a suitable target for anticoagulation treatment in at-risk patients due to its unique mode of action. Direct-acting FXIIIa blockers would not impair thrombin level or platelet activity, however, the lack of structural information about FXIIIa's active conformation as well as about the architecture of the active site prevented any rational design of selective inhibitors until now.

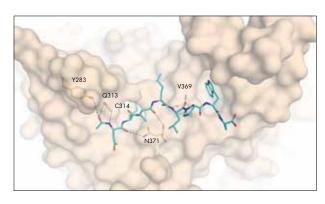
In cooperation with the group of Prof. Gerhard Klebe in Marburg, Zedira scientists reported the first crystal structure of FXIIIa° in complex with an irreversible peptide inhibitor. This novel structure exposes the active site along with concomitant rearrangements, which allowed the elucidation of the mechanism of plasma transglutaminase. But most importantly, the structure solved at 1.98 Å provides the blueprint for rational drug design.

Reference:

Structure of Active Coagulation Factor XIII Triggered by Calcium Binding: Basis for the Design of Next-Generation Anticoagulants

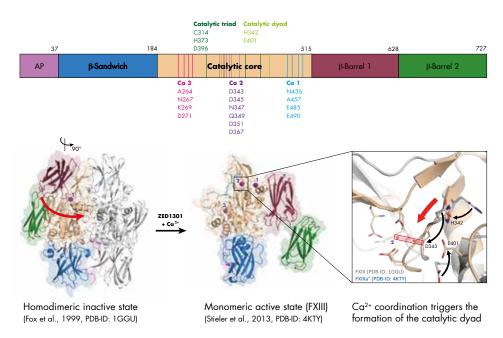
Martin Stieler, Johannes Weber, Martin Hils, Peter Kolb, Andreas Heine,
Christian Büchold, Ralf Pasternack, Gerhard Klebe

Angewandte Chemie Intl. Ed. 2013, 52:11930.



Binding Mode of ZED1301 in the Active Site of FXIIIa°.

The inhibitor ZED1301 (purple) binds covalently to Cys314 of the catalytic center. The crystal structure reveals that the peptidic lead compound interacts via several H-bonds with FXIII.



Structure of Active Coagulation Factor XIII

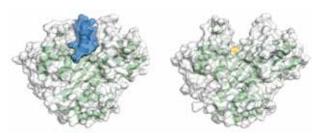
In the inactive state, recombinant FXIII exists as a dimer. Upon binding of the irreversible blocker ZED1301 (A108) and three calcium ions per subunit, FXIII dissociates and the ß-barrel 1 and ß-barrel 2 domains undergo a remarkable shift exposing the active site (upper left). The crystal structure of FXIII in its active conformation provides detailed information on an atomic level regarding the role of calcium in the activation process. Calcium coordination affects the shape of the active site of FXIII and triggers the formation of the catalytic dyad (H342, E401).

Microbial Transglutaminase

MTG - A unique tool for site specific antibody conjugation - and beyond

Microbial transglutaminase (MTG synonymous with BTG for bacterial transglutaminase) is a Ca²⁺-independent transglutaminase originally isolated from *Streptomyces mobaraensis* [1, 2]. Under the brand Andracon™, MTG is available as a high-quality recombinant enzyme (T250; T300).

MTG is a crosslinking enzyme that, as with all transglutaminases, catalyzes the formation of covalent bonds between the glutamine and lysine side chains of proteins. The active site cysteine of MTG nucleophilically attacks the γ -carbon in glutamine forming an acyl-enzyme complex. This reactive complex is resolved by a reaction with the ϵ -amine group of the protein-bound lysine, resulting in a covalently crosslinked protein. Importantly, instead of protein-bound lysine, small-molecule primary amine derivatives (e.g., biotin, fluorescent dyes, or cytotoxins) are also accepted as co-substrates. Some examples are shown in the "protein labeling" section on page 18.



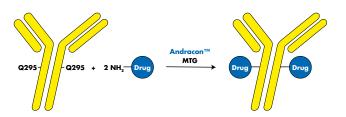
Microbial Transglutaminase crystal structures. Left: Pro-Transglutaminase (PDB-ID: 31U0) [3]. The propeptide is shown in blue. Right: active Transglutaminase (PDB-ID: 11U4) [4]. Active site cysteine is marked in yellow.

MTG is Ca^{2+} -independent, in contrast to eukaryotic transglutaminases. It is active over a broad pH range from pH 4 to pH 9 and stable up to $50^{\circ}C$.

Based on its stability and Ca²⁺-independence, in the past decades, MTG has been broadly used in the food industry for the improvement of food products like pasta, baked goods, sausage, and yogurt.

While MTG accepts a broad range of primary amines, it is selective for the protein-bound glutamine substrate depending on the latter's structural environment. This feature opened a novel application option for MTG in the pharmaceutical field. A current trend in oncology and even beyond is the development of drugs based on antibody-drug conjugates (ADCs). Such innovative biomolecules enable the targeted delivery of cytotoxic payloads to cancer cells.

Enzymatic conjugation using MTG is a state-of-the-art method for the production of site specific conjugated and homogenous ADCs (Figure 2) with a defined drug-to-antibody ratio (DAR) [5 - 10].



Antibodies can be conjugated homogenously and site specifically with payloads at Q295 using MTG. Alternatively, MTG-substrate sequence tags introduced by genetic modification into the antibodies can be used for conjugation.

Andracon™

Zedira developed a highly purified and comprehensively characterized MTG branded **Andracon™**. Andracon™ is the product of choice for ADC conjugation. Zedira's general philosophy is to meet the increasing requirements of our customers, both in quantity and regulatory aspects. For example, Andracon™ products T250 and T300 are now also characterized for impurity thresholds of host cell protein (HCP) and host cell DNA, endotoxin, and microbial burden.

Zedira offers the whole toolbox for working with MTG:

MTG product T255 contains a C-terminal His_c-Tag enabling easy removal of MTG from a reaction mixture. Activity assays, ELISAs for MTG detection, antibodies, inhibitors, and substrates are available as well.

Please have a look at the following pages and explore our broad MTG tools.

For more detailed information on MTG please look at our MTG handbook, available as a PDF or hard copy upon request.

References:

- [1] Ando et al., Agric. Biol. Chem. 1989, 53:2613-17
- [2] Pasternack et al., Eur. J. Biochem. 1998, 257:570-6
- [3] Yang et al., J Biol Chem. 2011, 286:7301-7
- [4] Kashiwagi et al. J Biol Chem. 2002, 277:44252-60
- [5] Jeger et al., Angew. Chem. Int. Ed. Engl. 2010, 49:9995-7
- [6] Dennler et al., Bioconjugate Chem. 2014, 25, 569-78
- [7] Strop, Bioconjugate Chem. 2014, 25, 5, 855-62
- [8] Dickgiesser et al., Enzyme-Med. Ligation Meth., 2019, S. 135-49.
- [9] Schneider et al., Analytical biochem. 2020, 595, 113615.
- [10] Anami & Tsuchikama; ADC: Methods and Protocols 2020, 71-82.

Microbial Transglutaminase

Andracon™ – your brand for high-quality microbial transglutaminase



Special features:

- Recombinantly produced in E. coli
- Ultra-pure and highly active
- Batch-to-batch consistent quality
- Scientific and technical support
- Available from 25 U vials up to bulk amounts
- License free
- Produced according to an SOP in an ISO9001:2015 certified environment
- Extensively characterized, e. g. for host cell protein, host cell DNA, and endotoxin-levels
- Customer audits for qualification according to ICH Q7 guidelines are possible

Reference:

Our MTG is well documented in the scientific literature.

Sitorasmi et al., F1000Research 2023, 12:48; Stricker et al., Int. J. Mol. Sci. 2022, 23, 2248; Kaempffe et al., J. Pharm. Sci. 2021, S0022-3549(21)00400-7; Früh et al., ACS Nano 2021, 15, 12161–70; Chowdari et al., J. Med. Chem. 2020, 63:13913-50; Stricker et al., J. Pediatr. Gastroenterol. Nutr. 2019, 68:e43-e50; Spycher et al., ChemBioChem 2017, 18:1923-7; Steffen et al., J. Biol. Chem. 2017, 292:15622-35; Dennler et al., Chembiochem. 2015, 16:861-7; Dennler et al., Bioconjugate Chem. 2014, 25, 569-78; Kaufmann et al., Food Addit. Contam. Part. A 2012, 29:1364-73; Jeger et al., Angew. Chem. Int. Ed. Engl. 2010, 49:9995-7; Gianfrani et al., Gastroenterology 2007, 133:780-9; Pfleiderer et al., Microbiol. Res. 2005, 160:265-71; Ando et al., Agric. Biol. Chem. 1989, 53:2613-17; Pasternack et al., Eur. J. Biochem. 1998, 257:570-6.

Art. No.	Name	Unit	Price
T250	Andracon™ – recombinant microbial transglutaminase	250 U	2140 €
	(HEPES-formulated, (frozen) liquid)	500 U	3750 €
		1000 U	7250 €
		Bulk	On Request
T300	Andracon™ – recombinant microbial transglutaminase	25 U	270 €
	(HEPES-formulated, lyophilized)	100 U	975 €
		250 U	2140 €
		10 x 25 U	2140 €
		500 U	3750 €
		20 x 25 U	3750 €

Products

Microbial Transglutaminase

Synonym: Bacterial transglutaminase, MTG, BTG

Art. No.	Name	Unit	Price
T255	Microbial transglutaminase with C-terminal His ₆ -Tag	25 U	400 €
	(MTG-His ₆ , recombinantly produced in E. coli ,	10 x 25 U	3150 €
	gene derived from Streptomyces mobargensis	20 x 25 U	5550 €

Microbial Pro-Transglutaminase

Art. No.	Name	Unit	Price
T016	Microbial (bacterial) Pro -transglutaminase	250 µg	300 €
	(Pro-MTG, recombinantly produced in E. coli , gene derived from Streptomyces mobaraensis)		
Reference:	Pasternack et al., Eur. J. Biochem. 1998, 257:570-6		

Inhibitor



Antibodies to Microbial Transglutaminase

Art. No.	Name	Unit	Price
A020	Polyclonal antibody to microbial protransglutaminase (pro-MTG)	500 µg	400 €
Immunogen:	Bacterial protransglutaminase (T016), raised in rabbit		
Format:	Purified IgG		
A051	Biotinylated polyclonal antibody to microbial transglutaminase (MTG)	50 µg	400 €
Format:	Purified via affinity chromatography on protein A, followed by biotin-labeling		
A143	Monoclonal antibody to microbial transglutaminase (clone XM67, IgG1)	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in mouse		
Format:	Purified IgG, recommended as capture antibody		
A144	Monoclonal antibody to microbial transglutaminase (clone XM68, IgG2a)	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in mouse		
Format:	Purified IgG, recommended as detection antibody		
A145	Polyclonal antibody to microbial transglutaminase	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in rabbit		
Format:	Purified IgG		
Note:	A145 replaces polyclonal antibody A019		

New

Microbial Transglutaminase

Activity Assay Kits for Microbial Transglutaminase

Asi Nis	NI	11.5	D.:
Art. No.	Name	Unit	Price
F015	ZediXcite Fluorogenic MTG-Assay Kit	1 Kit	600 €
	Isopeptidase-activity based MTG assay (313/418 nm)		
Application:	Fluorescent measurement of transglutaminase activity, optimized for MTG		
M001	MTG-ANITA-KIT	1 Kit	610 €
	(<u>A</u> mmonium- <u>Ni</u> cotinamidADPH-GLDH- <u>T</u> ransglutaminase- <u>A</u> ssay)		
Z 018	Z-Glutamyl-Hydroxamate-Glycine	100 mg	150 €
	This product replaces Art. No. G048		
Application:	Reference substance to determine the concentration of product formed by mi	crobial transglutaminase (M	NTG).
Z009	ZediXclusive Microbial Transglutaminase Assay Kit	1 Kit	390 €
Application:	Determination of microbial transglutaminase activity		
Reference:	Grossowicz et al., J. Biol. Chem. 1950, 187:111-25		
	See Spotlight next page!		

ELISA for MIC	robiai iransgiutaminase		
Art. No.	Name	Unit	Price
E021	ZediXclusive Microbial Transglutaminase (MTG) ELISA	1 Kit	425 €
Application:	ELISA for the detection of Microbial Transglutaminase (MTG) in food samples.		
	See Spotlight next page!		

Spotlight - Detection of MTG protein and activity in food and processing aids

Microbial transglutaminase is used as a processing aid in the food industry in order to improve the quality of sausage, pasta, bread, and yogurt.

Zedira provides the tools to determine MTG activity (Z009) and MTG protein (E021) in MTG raw materials, formulations, and food samples in easy-to-use kit formats.

In addition, the analysis of raw materials, formulations, and food samples for MTG activity and protein is also available on a fee for service basis. Please contact us for a quote.









Raw Materia

Formulation

Processed Food

Z009

Microbial Transglutaminase Assay Kit

Activity determination of high activity MTG-samples (raw material and formulations)

Lower Limit of Detection: 0.3~U/mL

15 μg/mL 15 ppm

3 x 11 cuvette assays, chromogenic (525 nm)

E021

Microbial Transglutaminase ELISA

Immuno-detection of MTG (native and denatured) in food samples

Lower Limit of Detection:

Native: 3 ng/L

3 ppb

Denatured: 60 ng/mL

60 ppb

96-well microtiter assays, chromogenic (450 nm)

Services for the determination of Microbial Transglutaminase (MTG)

Microbial Transglutaminase is widely used in food applications. At Zedira, we provide services for the determination and detection of MTG in your sample.

Please contact us for a quote! (+49 6151 66628 0 or send an e-mail to contact@zedira.com)

Service categories include, but are not limited to:

- Determination of MTG **activity** in food preparations
- Determination of MTG protein in food preparations
- Determination of gluten/gliadin content in food and food preparations

Protein Labeling

Spotlight - Microbial Transglutaminase Labeling

Chemical modification of proteins is widely used. However, there are several drawbacks and limitations like heterogeneous products and batch-to-batch variations. Transglutaminase and especially calcium-independent, highly purified microbial (bacterial) transglutaminase are smart tools for "site-specific target labeling", yielding homogenous products.

A protocol has been published by the group of Prof. Roger Schibli in Zürich: "Enzymatic antibody modification by bacterial transglutaminase"; Dennler P, Schibli R, Fischer E, Meth. in Mol. Bio. 2013, 1045, 205-215.

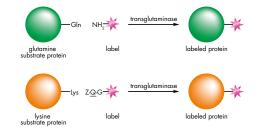
In conclusion, enzymatic labeling using transglutaminase is characterized by:

- Homogeneity
- Defined degree of labeling
- Defined label position(s)
- Minimized amounts of unlabeled protein
- Bioactivity equal to the unlabeled protein
- · High solubility in water

Requirements of the target protein

- Accessible lysine residues
- Or accessible glutamine residues
- If no lysine or glutamine residues are accessible, transglutaminase substrate sequence tags can be introduced recombinantly

Principle of TGase-catalyzed protein labeling



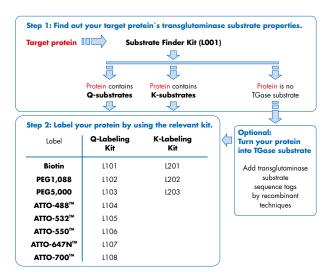
TGase Protein Labeling Kits

Our labeling kits exploit Microbial Transglutaminase catalytic activity to label proteins. Transglutaminase also accepts short glutamine-containing peptides and – as already mentioned – primary amines as substrates. Consequently, protein-bound glutamines can be labeled using primary amines, and protein-bound lysines can be labeled with short glutamine-containing peptides.

Primary amines as well as glutamine-containing peptides may carry a broad variety of labels like biotin, PEG, fluorescent dyes, etc.

Transglutaminase labeling requires substrate sequences on the target protein surface, which are generally not abundant on proteins. Therefore, in the first step, the target protein has to be analyzed for its transglutaminase substrate properties, which is performed using the Substrate Finder Kit.

The target protein is accessible to transglutaminase labeling if it contains either glutamine substrate sequence(s) or lysine substrate sequence(s) or both. If the target protein contains neither glutamine nor lysine substrate sequences, transglutaminase substrate tags may be introduced by recombinant techniques.



Currently, kits for Glutamine (Q)- or Lysine (K)-labeling with the following labels are available: Biotin, PEG1,088, PEG5,000, ATTO-488 $^{\text{TM}}$, ATTO-532 $^{\text{TM}}$, ATTO-550 $^{\text{TM}}$, ATTO-647N $^{\text{TM}}$, and ATTO-700 $^{\text{TM}}$.

Please contact us if additional labels are required.

Products

L202

L203

TGase Protein Labeling Kits

Name	Unit	ъ.
	Oilli	Price
Substrate Finder Kit	1 Kit	390 €
Determination of protein's MTG substrate properties		
eling Kits		
Name	Unit	Price
Biotin TGase Protein Q -Labeling Kit, sufficient for 5x 1 mg labeling reactions	1 Kit	550 €
PEG1,088 TGase Protein Q -Labeling Kit, sufficient for 5x 1 mg labeling reactions	1 Kit	550 €
PEG5,000 TGase Protein Q -Labeling Kit, sufficient for 5x 1 mg labeling reactions	1 Kit	550 €
ATTO-488™ TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction	1 Kit	610€
ATTO-532™ TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction	1 Kit	610€
ATTO-550™ TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction	1 Kit	610€
ATTO-647N™ TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction	1 Kit	610€
ATTO-700™ TGase Protein Q -Labeling Kit, sufficient for 1 mg labeling reaction	1 Kit	610 €
eling Kits		
Name	Unit	Price
Biotin TGase Protein K -Labeling Kit, sufficient for 5x 1 mg labeling reactions	1 Kit	550 €
	Determination of protein's MTG substrate properties Sling Kits Name Biotin TGase Protein Q-Labeling Kit, sufficient for 5x 1 mg labeling reactions PEG1,088 TGase Protein Q-Labeling Kit, sufficient for 5x 1 mg labeling reactions PEG5,000 TGase Protein Q-Labeling Kit, sufficient for 5x 1 mg labeling reactions ATTO-488 TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction ATTO-532 TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction ATTO-647N TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction ATTO-700 TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction ATTO-700 TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction ATTO-700 TM TGase Protein Q-Labeling Kit, sufficient for 1 mg labeling reaction	Determination of protein's MTG substrate properties Comparison of protein's MTG substrate properties

PEG1,088 TGase Protein **K**-Labeling Kit, sufficient for 5x 1 mg labeling reactions

PEG5,000 TGase Protein **K**-Labeling Kit, sufficient for 5x 1 mg labeling reactions

1 Kit

1 Kit

550 €

550 €

Protein Labeling

Amine-donors (Q-Labeling)

Suitable substrates for labeling of your target molecule with accessible glutamine residues (Q-Labeling).

For more details see Section: Assays & Substrates

Biotin Labels

Art. No.	Name	Unit	Price
B002	N-(Biotinyl)cadaverine	25 mg	1 <i>7</i> 5 €
		100 mg	475 €
Click-Chemist	ry Labels		
Art. No.	Name	Unit	Price
A152	3-Azidopropan-1-amine	100 mg	1 <i>7</i> 5 €
Application:	Amine donor substrate for transglutaminase, suitable for click chemistry		
A153	4-Azidobutan-1-amine	100 mg	175 €
Application:	Amine donor substrate for transglutaminase, suitable for click chemistry		
PEG Labels			
Art. No.	Name	Unit	Price
P010	(PEG1,088)amine, monodisperse	10 mg	200 €
Application:	Polyethylene glycol amine substrate of transglutaminase		
P011	(PEG5,000)amine, polydisperse	10 mg	200 €
Application:	Polyethylene glycol amine substrate of transglutaminase		
Fluorescent Lo	abels		
Art. No.	Name	Unit	Price
A106	(ATTO-488™)cadaverine	1 mg	275 €
A112	(ATTO-532™)cadaverine	1 mg	275 €
A113	(ATTO-550™)cadaverine	1 mg	275 €
A114	(ATTO-647N™)cadaverine	1 mg	325 €
A115	(ATTO-700™)cadaverine	1 mg	325 €
A169	(ATTO-542™)cadaverine	1 mg	350 €
D006	N-(Dansyl)cadaverine	100 mg	175 €
K004	"KxD", Boc-Lys-en-DNS	10 mg	275 €
R001	N-(Tetramethylrhodaminyl)cadaverine, N-(TAMRA)cadaverine	10 mg	200 €
Reference:	Dennler et al., Chembiochem. 2015, 16:861-7; Lee et. al., J. Biotechnol. 2013,		

Glutamine-donor peptides (K-Labeling)

Suitable substrates for labeling of your target molecule with accessible lysine residues (K-Labeling).

For more details see Section: Assays & Substrates

Biotin Labels

Art. No.	Name	Unit	Price
C091	Z-Gln-Gly-CAD-Biotin	25 mg	350 €
Reference:	Spidel et al., Bioconjugate Chem. 2017, 28:2471-84; Zindel et al., PLoS One 2016,	11:e0149145;	
	Pasternack et al., Anal. Biochem. 1997, 249:54-60		

Click-Chemistry Labels

Art. No.	Name	Unit	Price
C079	Z-Gln-Gly-PEG(3)-N ₃	25 mg	500 €
Application:	Glutamine donor substrate for transglutaminase, suitable for click chemistry	O NH2	$O \longrightarrow \int_{2} O \longrightarrow N_{3}$

PEG Labels

Art. No.	Name	Unit	Price
C092	Z-Gln-Gly-(PEG1,088), monodisperse	25 mg	500 €
Application:	Polyethylene glycol glutamine substrate of transglutaminase		
C093	Z-Gln-Gly-(PEG5,000), polydisperse	25 mg	500 €
Application:	Polyethylene glycol glutamine substrate of transglutaminase		

Fluorescent Labels

Art. No.	Name	Unif	Price
C002	Z-Gln-Gly-CAD-DNS	25 mg	175 €
		100 mg	400 €
C090	Z-Gln-Gly-CAD-TAMRA	25 mg	500 €
Reference:	Spycher et al., ChemBioChem 2017, 18:1923-7		

Assays & Substrates

Background information

Transglutaminases are defined as protein-glutamine: amine glutamyl transferases (EC 2.3.2.13). Based on a modified double-displacement mechanism tey catalyze an acyl transfer reaction between the γ -carboxamide group of a peptide-bound glutamine residue and the ϵ -amino group of a peptide-bound lysine. The active site consists of a catalytic triad (Cys, His, and Asp).

The formation of a γ -glutamyl thioester between the active site cysteine and the the γ -carboxamide of the glutamine results in the release of ammonia. This activated species subsequently reacts with nucleophilic primary amines, yielding either an isopeptide bond (pathway 1) or a (γ -glutamyl)amine bond (pathway 2). If no is amine available, the acyl-enzyme intermediate reacts with water yielding glutamic acid (pathway 3).

Reaction pathways of transglutaminase

Guideline for Assay Selection

The table below supports the selection of the appropriate assay in terms of assay principle, selectivity, sensitivity, and equipment.

		Flu	orogenic Ass	ays		Chromogenic Assays			
Kit	F001	F014	F016	F015	<u>T036</u>	<u> 2009</u>	<u>Z010</u>	M001	M003
Principle	lso-peptidase	Iso-peptidase	Iso-peptidase	Iso-peptidase	Trans- amidation	Trans- amidation	Trans- amidation	Trans- amidation with NH ₃ detection	Trans- amidation
Substrates	Abz-substrate peptide	Abz-substrate peptide	N-Me-Abz- substrate peptide	Abz-substrate peptide	Casein / Dansyl- cadaverine	Z-QG-OH / Hydroxyl- amine	Z-QQPF-OH / Hydroxyl- amine	β-Casein	Substrate protein / Biotinyl- cadaverine
Selectivity	Non-specific, optimized for FXIII. Suitable for TG2, TG1, TG3, TG6, TG7	Specific for TG2	Specific for TG2	Specific for MTG	Non-specific, suitable for TG2, FXIII, TG1, TG3, TG6, TG7, MTG	Specific for MTG	Specific for TG2	Developed for MTG, non-specific	Non-specific, suitable for TG2, FXIII, TG3
Sensitivity	2.5–40 nM (FXIII, 0.2-3 µg/ml)	1.25-10 nM (TG2, 0.1-0.8 µg/ml)	1.25-10 nM (TG2, 0.1-0.8 µg/ml)	2.5-80 nM (MTG, 1-3 µg/mL)	10-50 nM (TG2, 0.8-3.9 µg/mL)	11 nM (MTG, 0.43 µg/ml)	6 nM (TG2, 0.43 µg/ml)	tbd	3.9 pM (TG2, 300 pg/mL)
Absorption [nm]						525	525	340	450 / 620
Excitation [nm]	313–330	313–330	360	313–330	330				
Emission [nm]	418	418	460	418	500				

Spotlight - ZediXcite: NEW Fluorogenic Isopeptidase Assay Kits

Transglutaminases are primarily recognized for their crosslinking activity; however, they can also cleave isopeptide bonds. This unique feature provides easy-to-handle, robust, and precise fluorogenic assays to measure transglutaminase isoenzymes. These assays are suitable for drug discovery programs and quality assurance protocols.

Transglutaminases cleave the carboxamide bond and thereby release the dark quencher (2,4-dinitrophenyl, DNP), which is attached to a cadaverine spacer. The increase in fluorescence results from the unquenched fluorophore attached to the N-terminus.

Recently, Zedira developed three novel modified peptides. These peptides serve as the cornerstone for our Zedi*Xcite* fluorogenic isopeptidase assay kits: **F014**, **F016** (both for TG2, covering different wavelengths, please refer to page 22 for details), and **F015** (MTG, microbial transglutaminase) in addition to our well-established FXIII-Assay Kit **F001**.

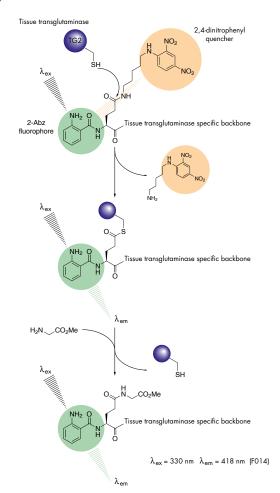
The ready-to-use assay kits **F001**, **F014**, **F016**, and **F015** are characterized by their performance and sensitivity. The kinetic data for the optimized substrate peptides are reported in the following table.

	FXIIIa	hTG2	hTG2	MTG
Assay	F001	F014	F016	F015
$K_{_{m}}$ [μ M]	10.5	5.7	5.5	43.7
k_{cat} [s ⁻¹]	0.14	0.01	0.03	0.02

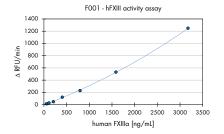
Furthermore, the non-specific fluorogenic substrate A101 (included in F001) is not only suitable for FXIII measurement but also for the determination of TG1, TG2, TG3, and TG6.

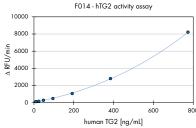
The kinetic data for these transglutaminase isoenzymes are displayed in the following table.

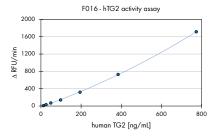
A101	FXIIIa	hTG1	hTG2	hTG3	hTG6	hTG7
K _m [μM]	10.5	77	8.6	13.4	55.9	10.6
k_{cat} [s ⁻¹]	0.137	0.006	0.002	0.035	0.006	0.003



The assay principle for F014 is exemplarily illustrated above: Transglutaminase catalyzes the cleavage of a carboxamide bond in the side chain of a specific peptidic backbone. The release of the dark quencher is followed by the incorporation of glycine methyl ester. After the dark quencher is released, the fluorescence of the fluorophore increases. This assay is designed to continuously monitor TG activity.







Performance of Zedi*Xcite* activity assay kits F001 (also contains thrombin), F014, and F016: Plots of the increase in fluorescence emission dependent on the respective transglutaminase concentration as measured in triplicate on a microplate reader.

New

Assays & Substrates

Assays

Isopeptidase-Fluorogenic Assays



Art. No.	Name	Unit	Price
A101	FXIII-Assay Substance, Abz-NE(CAD-DNP)EQVSPLTLLK-OH	10 mg	575 4
Application:	Fluorescent measurement of transglutaminase activity, also suitable for TG1, TG2, TG3	, and TG6	
Reference:	Please find selected literature on our website www.zedira.com		
F001	ZediXcite 330/418 Fluorogenic FXIII-Assay Kit	1 Kit	600
	Isopeptidase-activity based FXIII assay (330/418 nm)		
	Ready to use, contains FXIII-Assay Substance (A101) and thrombin		
Application:	Fluorescent measurement of transglutaminase activity, optimized for FXIII		
Reference:	Durda et al., Transfus Apher Sci. 2018, 57:700-4; Sossdorf et al., Crit. Care. 2009, 13	3:R208;	
	Oertel et al., Anal. Biochem. 2007, 367:152-8		
F014	ZediXcite 330/418 Fluorogenic TG2-Assay Kit	1 Kit	600
	Isopeptidase-activity based TG2 assay (330/418 nm)		
Application:	Fluorescent measurement of transglutaminase activity, optimized for TG2		
F015	ZediXcite 330/418 Fluorogenic MTG-Assay Kit	1 Kit	600
	Isopeptidase-activity based MTG assay (330/418 nm)		
Application:	Fluorescent measurement of transglutaminase activity, optimized for MTG		
F016	ZediXcite 360/460 Fluorogenic TG2-Assay Kit	1 Kit	650
	Isopeptidase-activity based TG2 assay (360/460 nm)		
Application:	Fluorescent measurement of transglutaminase activity, optimized for TG2		
A168	Abz-Peptide-Calibrator	10 mg	475
Application:	Calibrator for fluorescent Abz-substrates. Applicable for quantification of fluorescence	release	
A171	N-Me-Abz-Peptide-Calibrator	10 mg	525
Application:	Calibrator for fluorescent N-Me-Abz-substrates. Applicable for quantification of fluoresc	cence release	
Transglutami	nase Fluorogenic Activity Assay		
Art. No.	Name	Unit	Pric
T036	Transglutaminase Assay Kit ("DCC"), fluorescent, Casein, Dansylcadaverine	1 Kit	300
- (Lorand et al., Anal. Biochem. 1971, 44:221-31		
Reference:			
	uno Assay (EIA)		
Enzyme Imm	uno Assay (EIA) Name	Unit	Pric
Enzyme Imm Art. No.	Name		
Enzyme Imm Art. No. E018	Name Zedi <i>Xclusive</i> Tissue Transglutaminase EIA	Unit 1 Kit	
Enzyme Imm Art. No. E018 Application:	Name		Pric 550
Enzyme Imm Art. No. E018 Application: Reference:	Name ZediXclusive Tissue Transglutaminase EIA Determination of TG2 protein quantity in biological fluids		

Photometric Activity Assays

Art. No.	Name	Unit	Price
M001	MTG-ANITA-KIT	1 Kit	610 €
	$(\underline{A}$ mmonium- \underline{Ni} cotinamidADPH-GLDH- \underline{I} ransglutaminase- \underline{A} ssay)		
Reference:	Steffen et al., J. Biol. Chem. 2017, 292:15622-35		
M003	Tissue Transglutaminase Pico-Assay Kit	1 Kit	425 €
Application:	Determination of tissue transglutaminase activity		
Reference:	Furini et al., J. Am. Soc. Nephrol. 2018, 29:880-905		
T114	Blood Coagulation Factor XIII-Microassay Kit, colorimetric	1 Kit	470 €
Application:	Colorimetric measurement of transglutaminase activity, optimized for blood coagu	ulation factor XIII (FXIII)	
Z009	ZediXclusive Microbial Transglutaminase Assay Kit	1 Kit	390 €
Reference:	Grossowicz et al., J. Biol. Chem. 1950, 187:111-25		
Z 010	ZediXclusive Tissue Transglutaminase Assay Kit	1 Kit	450 €
	(Chromogenic activity assay optimized for tissue transglutaminase, also suitable	e for epidermal transgli	utaminase)

Spotlight - Tissue Transglutaminase Assay Kit Z010 (chromogenic)

Lexhaller et al., Nutrients. 2019, 11:2263

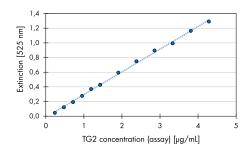
TG2 is present in various tissues and involved in a plentitude of physiological as well as pathological processes. The enzyme catalyzes the acyl transfer reaction between the γ -carboxamide group of peptide-bound glutamine residues and a variety of primary amines, particularly the ϵ -amino group of lysine (Lorand L. et al., 1962). The assay **Z010** enables the measurement of TG2 activity according to the chromogenic hydroxamate detection principle (Grossowicz, N. et al., 1950).

The ZediXclusive Tissue Transglutaminase Assay Kit **Z010** uses Z-QQPF as the amine acceptor substrate and hydroxylamine as the amine donor. In the presence of tissue transglutaminase, hydroxylamine is incorporated into Z-QQPF to form Z-glutamylhydroxamate-QPF, which develops a colored complex with iron (III) that is detectable at 525 nm.

Assay characteristics:

Reference:

- Easy to use chromogenic endpoint assay
- Optimized for tissue transglutaminase (TG2)
- Results within 30 min





Assays & Substrates

Z-QQPL-OH

Substrates

Glutamine-donor peptides

	• •		
Art. No.	Name	Unit	Price
A105	NQEQVSPLTLLK , alpha ₂ -Antiplasmin peptide (1-12)	25 mg	500 €
Synonym:	Asn-Gln-Glu-Gln-Val-Ser-Pro-Leu-Thr-Leu-Leu-Lys-OH dihydrochloride		
Application:	Factor XIII glutamine donor substrate) H P Y H P	LH P
References:	Kárpáti et al., Clin. Chem. 2000, 46:1946-55;		AN COH
	Pénzes et al., J. Thromb. Haemost. 2009, 7:627-33;	1 1	NH ₂ *HCI
	Reed et al., Circulation 1999, 99:299-304		
B001	Biotinyl-Thr-Val- <u>Gln</u> -Gln-Glu-Leu-OH	5 mg	175 €
Synonym:	Biotinyl-L-Threoninyl-L-Valinyl-L-Glutaminyl-L-Glutaminyl-L-Glutamyl-L-Leucin; A25-peptide	25 mg	525 €
Application:	Biotinylated glutamine donor substrate for tissue transglutaminase	O _⋛ NH ₂	О₩ОН
Reference:	Zindel et al., PLoS One 2016, 11, e0149145;		
	Recktenwald et al., J. Biol. Chem. 2016, 291:13580-90;		H. A. A. OH
	Chou et al., J. Biol. Chem. 2011, 286:27825-35;	H₂N .	* o
	Tseng et al. J., Cell. Biochem. 2009, 107:899-907;		
	Trigwell et al., Anal.Biochem. 2004, 330:164-6; Esposito et al., Protein Sci. 2003, 12:	1290-7;	
	Esposito et al., Am. J. Gastroenterol. 2003, 98:1813-20; Ruoppolo et al., Prot. Sci. 20	03, 12:1290-7;	
	Orrù et al., J. Biol. Chem. 2003, 278:31766-73; Groenen et al., J. Biol. Chem. 1994,	269:831-3;	
Z004	Z- <u>Gln</u> -Gln-Pro-Leυ-OH	25 mg	325 €



Synonym: Application:

C001	Z- <u>Gln</u> -Gly-OH	1 g	100 €
Synonym:	Z-Glutaminylglycin; Benzyloxycarbonyl-L-Glutaminyl-Glycin		ONH ₂
Application:	Glutamine donor substrate for microbial transglutaminase and gpTG2		L L OH
Reference:	Pasternack et al., Eur. J. Biochem. 1998, 257:570-6;		н ö
	Grossowicz et al., J. Biol. Chem. 1950, 187:111-25		

C002	Z- <u>Gin</u> -Gly-CAD- <mark>DNS</mark>	25 mg	1 <i>7</i> 5 €
Synonym:	1-N-(Benzyloxocarbonyl-L-Glutaminyl-Glycinyl)-5-N-(5´-N´,N´-	100 mg	400 €
	dimethylamino-1'-naphtalenesulfonly)-diaminopentane	O→NH ₂	
Application:	Fluorescent glutamine donor substrate for microbial transglutaminase		
Reference:	Jeitner et al., Anal. Biochem. 2001, 292:198-206;	Н 0 н	н
	Pasternack et al., Anal. Biochem. 1997, 249:54-60		

References: Hartley et al., J. Biol. Chem. 2008, 283:16790-800; Zhang et al., Life Sci. 1997, 60:2323-32;

 $(\text{H-DAEFRHDSGYEVHH}\underline{\textbf{QK}} \texttt{LVFFAEDVGSN}\underline{\textbf{K}} \texttt{GAIIGLMVGGVVIA-OH})$

Jarrett et al., Biochemistry 1993, 32:4693-7

Glutamine donor substrate for tissue transglutaminase

"Hitomi"-peptides

Transglutaminase-isoenzyme specific glutamine donor substrates identified by Kiyotaka Hitomi et al. at Nagoya University, Japan.

Art. No.	Name	Unit	Price
B007	Keratinocyte transglutaminase (TG1)-substrate-peptide K5	10 mg	350 €
Sequence:	Biotinyl-YEQHKLPSSWPF		
Reference:	Freedman et al., J. Invest. Dermatol.2021, 141:874-882.e6; Schulze-Krebs et al.,	Brain Res. 2016, 1	631:22-33;
	Itoh et al., J. Histochem. Cytochem. 2013, 61:793-801; Sugimura et al., J. Biol. G	Chem. 2006, 281:	7699-706;
	Sugimura et al., FEBS J. 2008, 275:5667-77; Yamane et al., FEBS J. 2010, 277:35	564-74	
B008	Tissue transglutaminase (TG2)-substrate-peptide T26	10 mg	350 €
Sequence:	Biotinyl-HQSYVDPWMLDH		
Reference:	Schulze-Krebs et al., Brain Res. 2016, 1631:22-33; van der Wildt et al., Nucl. Med	l. Biol. 2016, 43, 2	32-242;
	de Jager et al., J. Neurochem. 2015, 134:1116-28; Itoh et al., J. Histochem. Cytoc	hem. 2013, 61:793	3-801;
	Sugimura et al., J. Biol. Chem. 2006, 281:17699-706; Sugimura et al., FEBS J. 20	08, 275:5667-77;	
	Yamane et al., FEBS J. 2010, 277:3564-74		
B009	Epidermal transglutaminase (TG3)-substrate-peptide E51	10 mg	350 €
Sequence:	Biotinyl-PPPYSFYQSRWV		
Reference:	Schulze-Krebs et al., Brain Res. 2016, 1631:22-33; Sugimura et al., J. Biol. Chem.	2006, 281:1 <i>7</i> 699-	706;
	Sugimura et al., FEBS J. 2008, 275:5667-77; Yamane et al., FEBS J. 2010, 277:35	564-74	
B010	Blood coagulation FXIII-substrate-peptide F11KA	10 mg	350 €
Sequence:	Biotinyl-DQMMLPWPAVAL		
Reference:	Sugimura et al., J. Biol. Chem. 2006, 281:17699-706; Sugimura et al., FEBS J. 20	08, 275:5667-77;	
	Yamane et al., FEBS J. 2010, 277:3564-74		
B013	Neuronal transglutaminase (TG6)-substrate peptide Y25	10 mg	350 €
Sequence:	Biotinyl-DDWDAMDEQIWF		
Reference:	Fukui et al., FEBS J. 2013, 280:1420-9		
B014	Transglutaminase 7 (TG7)-substrate peptide Z3S	10 mg	350 €
Sequence:	Biotinyl-YSLQLPVWNDWA		
Reference:	Kuramoto et al., Arch: Biochem Biophys. 2013, 537:138-43		
B017	Microbial Transglutaminase (MTG)-substrate peptide M48	10 mg	350 €
Sequence:	Biotinyl-WALQRPHYSYPD		
Reference:	Sugimura et al., FEBS J. 2008, 275:5667-77		
A132	Microbial Transglutaminase (MTG)-substrate peptide Ac-M48	10 mg	350 €
Sequence:	Ac-WALQRPHYSYPD		

Spycher et al., ChemBioChem 2017, 18:1923-7; Sugimura et al., FEBS J. 2008, 275:5667-77

Reference:

Assays & Substrates

Amine-donors

Allille-dollors			
Art. No.	Name	Unit	Price
A106	(ATTO-488™)cadaverine	1 mg	275 €
Application:	Fluorescent amine donor substrate for transglutaminases		
Reference:	Dennler et al., Chembiochem. 2015, 16:861-7	H ₂ N SO ₃ SO ₃ H	NH H
A109	B-Amyloid peptide 1-42 (Aß 1-42)	1 mg	275 €
	(H-DAEFRHDSGYEVHH QK LVFFAEDVGSN K GAIIGLMVGGVVIA-OH)		
Reference:	Hartley et al., J. Biol. Chem. 2008, 283:16790-800; Zhang et al., Life Sci. 199	97, 60:2323-32;	
	Jarrett et al., Biochemistry 1993, 32:4693-7		
A112	(ATTO-532™)cadaverine	1 mg	275 €
Application:	Fluorescent amine donor substrate for transglutaminases		}
		H. 0 SO ₃ SO ₃ H	N NF
A113	(ATTO-550™)cadaverine	1 mg	275 €
Application:	Fluorescent amine donor substrate for transglutaminases		
A114	(ATTO-647N™)cadaverine	1 mg	325 €
Application:	Fluorescent amine donor substrate for transglutaminases		
A115	(ATTO-700™)cadaverine	1 mg	325 €
Application:	Fluorescent amine donor substrate for transglutaminases		
A169	(ATTO-542™)cadaverine	1 mg	350 €
Application:	Fluorescent amine donor substrate for transglutaminases		
B002	N-(Biotinyl)cadaverine	25 mg	175 €
Synonym:	N-(Biotinamido)-1,5-diaminopentane hydrochloride	100 mg	475 €
Application:	Biotinylated amine donor substrate for transglutaminases	s. 🖍 🔿 🗒 🚉	^ ^
Reference:	Csobán-Szabó et al., Int. J. Mol. Sci. 2021, 22:12448	NH NH	NH ₂ *HC
	Spycher et al., ChemBioChem 2017, 18:1923-7;	HNYNH	
	Steffen et al., J. Biol. Chem. 2017, 292:15622-35; Király et al., Amino Acids 2	016, 48:31-40; Reckten	wald et al.
	J. Biol. Chem. 2016, 291:13580-90; Dennler et al., Chembio-chem. 2015, 16	5:861-7; Wang et al., C	ell Death &
	Dis. 2013, 4:e808; Wang et al., PLoS Pathog. 2010, 6:e1000763; Ruoppolo	et al., Prot. Sci. 2003,	12:1290-7
	Lee et al., Clin. Chem. 1988, 34:906-10		
D002	N-(2,4-Dinitrophenyl)cadaverine	100 mg	175 €
Synonym:	N-{2,4-Dinitrophenyl}-1,5-diaminopentane hydrochloride	O ₂ N , NO ₂	2
Application:	Fluorescence quenching amine donor substrate for transglutaminases,	N N	NH ₂ *HC

used as co-substrate of transglutaminase activity assay together with Dansyl- ϵ -Aminohexanoyl-Gln-Gln-lle-Val-OH (D001)

Lorand et al., Proc. Natl. Acad. Sci. USA 1992, 89:11161-63

Murthy et al., Exp. Eye Res. 1998, 67:273-81; Parameswaran et al., J. Biol. Chem. 1997, 272:10311-17;

Reference:

Art. No.	Name	Unit	Price
D006	N-(Dansyl)cadaverine, DNS-CAD	100 mg	175 €
Application:	Fluorescent amine donor substrate for transglutaminases	♠ 9.8)
Reference:	Spycher et al., ChemBioChem 2017, 18:1923-7;	N S	N NH ₂
	Murthy et al., J. Biol. Chem. 1994, 269, 22907-11	v	
K004	"KxD", Boc-Lys-en-DNS	10 mg	275 €
Application:	Fluorescent amine donor substrate for transglutaminases		NH ₂
Reference:	Schaertl et al., J. Biomol. Screen. 2010, 15:478-87;		
	Case et al., Biochemistry 2007, 46:1106-15	Boc	N SO ₂
R001	N-(Tetramethylrhodaminyl)cadaverine	10 mg	200 €
Synonym:	5-(and 6)-((N-(5-aminopentyl)amine)carbonyl)tetramethylrhodamine hydrochloride	`N-	
Application:	Fluorescent amine donor substrate for transglutaminases	، ا	
Reference:	Dennler et al., Chembiochem. 2015, 16:861-7;		V V NH₂*HCI
	Lee et. al., J. Biotechnol. 2013, 168:324-30;	, - "	

Kasprzak et al., Biochemistry 1988, 27:4512-22

Protein Substrates

Art. No.	Name	Unit	Price
F004	Fibrinogen, purified from human plasma	50 mg	125 €
Synonym:	Factor I		
F006	FITC-labeled Fibrinogen (product derived from F004)	5 mg	225 €
Reference:	Mutch et al., J. Thromb. Haemost. 2010, 8:2017-24		
1001	Involucrine, human, recombinantly produced in <i>E. coli</i>	500 µg	400 €
Synonym:	hIVL		
Application:	Recombinant human involucrin may be used as transglutaminase substrate.		
P004	PT-Gluten	1 mg	250 €
Definition:	PT-Gluten is based on a wheat gluten preparation which has been	10 mg	1200 €
	proteolyzed by pepsin (porcine) and trypsin (porcine).		
Application:	PT-Gluten may be used in biochemical approaches, e.g. as substrate for transgluta	minases or	
	as antigen for gliadin antibodies.		
Reference:	Elli et al., Hum. Immunol. 2012, 73:992-7		

Inhibitors

Background information

Transglutaminases are involved in a multitude of physiological processes. One way to explore these processes is to use specific inhibitors. Rationally designed synthetic, small molecule inhibitors such as **Z006** ("Z-DON"; Z-DON-Val-Pro-Leu-OMe) or T101 will be of immeasurable help to scientists wishing to decipher the enigmatic roles of individual transglutaminases.

In the following section, Zedira's range of transglutaminase inhibitors is introduced with a special focus on their respective mechanisms of action.

"DON" compounds (6-diazo-5-oxo-L-norleucine containing peptides)

These potent molecules are side-chain modified peptides. The electrophilic "DON" group replaces the substrate glutamine. The active site cysteinyl residue attacks the carbonyl group (1). The subsequent reaction leads to the release of nitrogen (2) and the concomitant irreversible alkylation at the active site of the transglutaminases (3).

Zedira developed molecules frequently cited in scientific literature.

- "Z-DON" (Z006; Z-DON-Val-Pro-Leu-OMe) is a very potent and specific blocker of tissue transglutaminase (IC₅₀ about 0.02 μM, Z011 as control available) and is membrane permeable (see table page 32).
- "Boc-DON" (B003; Boc-DON-Gln-lle-Val-OMe) is a
 potent and specific blocker of tissue transglutaminase
 (IC_{so} about 0.3 µM) and is not membrane permeable (see table
 on page 32).

2-[(2-oxopropyl)thio]imidazolium derivatives

This class of non-peptidyl, active-site directed molecules was developed by Merck Sharp & Dohme in the 1990s. The active site cysteinyl residue attacks the carbonyl group (1) similar to the glutamine residue. However, the subsequent reaction leads to the release of the complementary thione (2) and the acetonylation of the cysteine (3) (Freund et al., Biochemistry 1994, 33:10109-19).

Although the molecules were developed to block coagulation factor XIIIa, the compounds inhibit tissue transglutaminase as well (Barsigan et al., J. Biol. Chem. 1991, Val 266:22501-9).

One candidate out of the series has been evaluated in animal models (e.g., Shebuski et al., Blood 1990, 75:1455-9). Please notice that the authors reported a plasma half-life of only 5 to 10 minutes.

Zedira offers three derivatives of the thioimidazolium scaffold.

- T101 (L-682.777) is a good blocker of tissue transglutaminase and coagulation factor XIIIa. Both enzymes are inhibited with an IC₅₀ of about 0.25 µM.
- D004 (L-683.685) is a good cell permeable blocker of tissue transglutaminase and coagulation factor XIIIa. Both enzymes are blocked with an IC₅₀ of about 0.35 μM.
- **D003** is a weak blocker of tissue transglutaminase with an IC_{50} of about 1.0 μ M.

Naturally occurring inhibitors

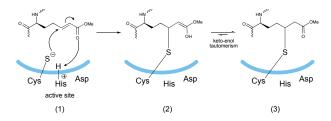
The FXIIIa-blocker **Tridegin** (T087) is a 66 amino acid polypeptide present in the saliva of the giant Amazon leech *Haementeria ghilianii*. Recent data revealed that the glutamine residue at position 52 of tridegin seems to react / bind to the active site of factor XIIIa (Böhm et al., ChemMedChem 2012, 7:326-333). Finney et al. (Biochem. J. 1997, 324:797-805) reported an IC $_{50}$ of about 10 nM for factor XIIIa, whereas Sicker (PhD thesis, 2008) measured an IC $_{50}$ of 2.5 μ M for the recombinant protein.

Using recombinant Tridegin (T087), we determined the IC $_{50}$ values against FXIIIa of 0.4 μ M (T036) and 1.8 μ M (F001) depending on the assay used (Product No. indicated in brackets). Human TG2 is not inhibited by recombinant Tridegin at concentrations up to 10 μ M.

Further, some microorganism-derived unspecific "factor XIII-blockers" with IC_{50} values in the micromolar range have been described, e.g., the antifungal antibiotic cerulenin (Tymiak et al., J. Antibiot. 1993, 46:204-6).

Michael acceptor (MA) inhibitors

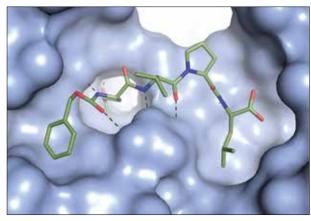
Zedira designed blockers bearing a Michael acceptor warhead. The electrophilic α , β -unsaturated carbonyl compounds are attacked by the active site cysteine residue (1) to form an irreversible complex (2,3).



The peptidic lead compound **ZED754** (Z013) was co-crystallized with tissue transglutaminase (PDB ID: 3S3P). The scaffold was subsequently optimized using medicinal chemistry.

Our clinical candidate ZED1227 is the first TG inhibitor in clinical trials (see Section: Services and Partnering for more information).

Compound **ZED1301** (A108) is a potent, selective factor XIII inhibitor.



Crystal structure of inhibited tissue transglutaminase.

The inhibitor Z006 (shown in light green) is covalently bound to the active site Cys277 (blue surface), which is located at the bottom of the catalytic tunnel. It mimics the peptide substrate. The main part of the inhibitor fits onto the protein surface, forming several hydrogen bonds and stabilizing the open conformation (PDB ID: 3S3J).

Inhibitors

Which transglutaminase inhibitor should I use in my experiments?

Although this is a commonly asked question, the answer is not always straight forward. Of course, inhibitor choice strongly depends on the respective experimental set-up and the target. Follow the guidelines below for finding the most suitable blocker for your task.

Please notice that all the following inhibitors should be considered as "tool compounds" but not "drugs".

Your target is tissue transglutaminase (tTG, TG2)?

We offer two potent inhibitors showing selectivity against other members of the transglutaminase family. Actually, the molecules Z-DON-Val-Pro-Leu-OMe (Z006; "Z-DON") and Boc-DON-Gln-lle-Val-OMe (B003; "Boc-DON") represent some of the most frequently cited inhibitors in the scientific literature.

Independent studies published by Schaertl et al. (2010) summarize the features of both compounds. They are very complementary to each other, since one is cell-permeable (Z006; "Z-DON"), while the other (B003; "Boc-DON") is not.

Characterization of irreversible peptidic inhibitors "Z-DON" and "Boc-DON" in transamidation assays.

Inhibitor	IC _{so} in μM					*Cytotox		
	hTG2	hTG1	hTG3	hTG6	FXIIIa	mTG2	cellular TG2	(hW)
Z006; "Z-DON"	0.02	7.3	0.2	0.15	67	0.07	40	146
B003; "Boc-DON"	0.3	1.1	20	0.98	24	0.6	_	_

Data taken from Schaertl et al., J. Biomol. Screen. 2010, 15:478-87. *Determined by "ATPlite" method with HEK cells.

Pan-transglutaminase blockers – forget about cyst(e)amine!

In case you would like to block "every" transglutaminase in your sample, we recommend using the well-known "Merck Sharp & Dohme" (MSD)-compounds.

Again, we offer a pair of complementary compounds, T101 and cell-permeable D004. They block any transglutaminase at concentrations between 1 - 10 μ M. However, it is not clear whether other proteins/enzymes (so-called "off-targets") are also influenced.

One point of emphasis: the MSD compounds are clearly better than cyst(e)amine, putrescine, or iodoacetamide!

Some papers describe the usage of cyst(e)amine, putrescine, or even iodoacetamide as "transglutaminase-inhibitors". From the perspective of a medicinal chemist, these "pseudo-substrate inhibitors" or "harsh chemicals" are not preferred since they are generally nonspecific (Schaertl et al., J Biomol Screen. 2010, 15:478-87). The topic of cystamine/cysteamine with respect to in vivo studies is discussed by Jeitner et al. (Bioscience Reports 2018, 38:BSR20180691).

Your target is Factor XIII?

ZED1301 (product number A108) is a potent molecule with unique properties. This peptidic blocker was used to solve the first crystal structure of FXIIIa in the active conformation (Stieler et al., Angew. Chem. Int. Ed. Engl. 2013, 52(45):11930-4). The IC₅₀ value is about 100 nM and the molecule shows selectivity (25-fold) over TG2.

Need a blocker for MTG?

Simply use C102 – our MTG inhibitor having an IC_{50} value of 125 μ M!

As you may have learned from the previous pages, Zedira has a broad portfolio of inhibitors to address even the most sophisticated tasks. Please do not hesitate to contact us for technical and scientific support.

Products

"DON" compounds

Art. No. Unit Price **B003** 400 € Boc-DON-Gin-Ile-Val-OMe, "Boc-DON" 10 mg

Product Name: tert.-Butyloxycarbonyl-(6-Diazo-5-oxonorleucinyl)-L-

Glutaminyl-L-Isoleucinyl-L-Valinmethylester

Boc-DON Synonym:

Application: Irreversible inhibitor of tissue transglutaminase; $IC_{50} \sim 0.3 \mu M$

Reference: Shinde et al., J. Mol. Cell Cardiol. 2018, 117:36-48; Basso et al., J. Neurosci. 2012, 9:6561-9

Verhaar et al., Neurochem. Int. 2011, 58:785-93; Schaertl et al., J. Biomol. Screen. 2010, 15:478-87;

McConoughey et al., EMBO Mol. Med. 2010, 2:1-22; Zeugolis et al., J. Biomed. Mater. Res. A. 2010, 15:1310-

20; Kristen et al., Circ. Res. 2008, 102:529-37; Mádi et al., Anal. Biochem. 2005, 343:256-62

Z006 Z-DON-Val-Pro-Leu-OMe, "Z-DON" 425 €

Product Name: Benzyloxycarbonyl-(6-Diazo-5-oxonorleucinyl)-L-Valinyl-L-Prolinyl-L-Leucinmethylester

Z-DON Synonym:

Application: Irreversible inhibitor of TG2 and TG6

TG2: $IC_{50} \sim 0.02 \, \mu M$; Cell permeable at 40 μM

TG6: IC₅₀ ~ 0.15 µM

As biochemical control see Z011 below!

Reference: Freedman et al., J. Invest. Dermatol.2021, 141:874-882.e6; Chrobok et al., PLoS One. 2018, 13:e0196433; Katt

> et al., Oncotarget. 2018, 9:34379-97; Algarni et al., Biochem. Pharmacol. 2017, 128:55-73; Wilhelmus et al., Sci. Rep. 2016, 6, 20569; de Jager et al., Neuropathol. Appl. Neurobiol. 2016, 42:255-72; Wilhelmus et al., Sci. Rep. 2016, 6:20569; van der Wildt et al., Nucl. Med. Biol. 2016, 43:232-42; Recktenwald et al., J. Biol. Chem. 2016, 291:13580-90; de Jager et al., J. Neurochem. 2015, 134:1116-28; Fischer et al., J. Invest. Dermatol. 2013, 133:1170-7; Hsieh et. al., PLoS One. 2013, 8:e81516; Wang et al., Cell Death & Dis. 2013, 4:e808; Johnson et. al., Am. J. Physiol. Heart Circ. Physiol. 2012, 302:H1355-66; Lauzier et al., Arthritis Res. Ther. 2012, 14:R159; Verhaar et al., Neurochem. Int. 2011, 58:785-93; Schaertl et al., J. Biomol. Screen. 2010, 15:478-87; McConoughey et al., EMBO Mol. Med. 2010, 2:1-22; Kazemi-Esfarjani and La Spada, EMBO Mol. Med. 2010,

2:335-7

ZO11 Z-(D)-DON-Val-Pro-Leu-OMe 10 mg 450 €

Application: Non-inhibiting control to Z-DON-VPL-OMe (Z006)

 $IC_{50} \sim 20.000$ nM (compared to 20 nM for Z-DON-VPL-OMe) This compound is 1,000 fold less potent than the parent molecule Z-DON-VPL-OMe (Z006)

Inhibitors

2-[(2-oxopropyl)thio]imidazolium derivatives

Art. No.	Name	Unit	Price
D003	1,3-Dimethyl-2[(2-oxopropyl)thio]imidazolium chloride	100 mg	500 €
Synonym:	1,3-Dimethyl-2[2-oxo-propyl)thio]imidazol chloride, NTU283		/ Cr
Application:	Inhibition of transglutaminases		[N S Q
Reference:	Katt et al., Oncotarget. 2018, 9:34379-97; Algarni et al., Biochem. Pharmacol. 2017	, 128:55-73;	
	Sánchez-Lara et al., Vet Pathol. 2015, 52:513-23; Hugues et al., J. Biol. Chem. 2012,	287:18005-17;	
	Harrison et al., Br. J. Dermatol. 2007, 156:247-57; Skill et al., J. Biol. Chem. 2004, 2	279:47754-62;	
	Freund et al., Biochemistry 1994, 33:10109-19		

D004	1,3-Dimethyl-4,5-diphenyl-2-[(2-oxopropyl)thio]imidazolium	10 mg	550 €
	trifluorosulfonic acid salt)
Synonym:	L-683.685; 1,3-Dimethyl-2-(2-oxopropylthio)-4,5-diphenyl-1H-imidazol-3-ium		F ₃ C-SO ₃ -
	trifluoromethanesulfonate		7 11 4
Application:	Inhibition of transglutaminases; cell permeable*		
Reference:	*Basso et al., J. Neurosci. 2012, 9:6561-9;		
	Müller et al., PREPRINT 2022, doi 10.21203/rs.3.rs-1554384/v1; Lorand et al., Exp. Eye Res. 1998, 66:531-6;		
	Barsigian et al., J. Biol. Chem. 1991, 266:22501-9		



Application: Inhibition of transglutaminases

Reference: Bäuml et al., J. Med. Chem. 2019, 62:3513-23; Katt et al., Oncotarget. 2018, 9:34379-97; Kattula et al., Blood Adv. 2018, 2:25-35; Macrae et al., Clin. Invest. 2018, 128:3356-68; Aleman et al., PLoS ONE 2015, 10:e0124448; Aleman et al., J. Clin. Invest. 2014, 124:3590-600; Katt et al., Mol. Pharm. 2015, 12:46-55; Dodt et al., Anal. Biochem. 2013, 439:145-51; Basso et al., J. Neurosci. 2012, 9:6561-9; Van den Akker et al., PLoS ONE 2011, 6:e23067; Matlung et al., Atherosclerosis 2010, 213:77-84; Dale et al., Nature 2002, 415:175-79; Lorand et al., Exp. Eye Res. 1998, 66:531-6; Freund et al., Biochem. 1994, 33:11109-19; Barsigan et al., J. Biol.

Chem. 1991, 266:22501-9

Naturally occuring inhibitors

Art. No.	Name	Unit	Price
T087	Tridegin	200 µg	510€
	(recombinantly produced in E. coli , gene derived from Haementeria ghilianii)		
Application:	Inhibition of FXIII		
Reference:	Bäuml et al., Eur. J. Med. Chem. 2020, 201:112474 Böhm et al., J. Med. Chem. 2014	4, 57:10355-65;	
	Finney et al., Biochem. J. 1997, 324:797-805; Wallis et al., Blood Coagul. Fibrinolysis	. 1997, 8:291-5;	
	Seale et al., Thromb. Haemost. 1997, 77:959-63		

Michael acceptor (MA) inhibitors



Art. No.	Name	Unit	Price
A108	Ac-(D)-Asp-MA-Nle-Nle-Leu-Pro-Trp-Pro-OH	5 mg	500 €
Synonym:	ZED1301		
Application:	Site specific irreversible inhibitor of plasma transglutaminase	٠, ﴿	NH
	(factor XIII, FXIII). Peptidic inhibitor containing an electrophilic	 ┸┇┸┇┸╻	N OH
	Michael acceptor (MA) warhead		- V
Efficacy:	ZED1301 shows 30-fold selectivity for FXIII compared to tTG	MeO O	
	IC ₅₀ = 100 nM (FXIII, using fluorescent Assay Substance A101)		
	IC ₅₀ = 3000 nM (TG2, using fluorescent Assay Substance A101)		
Reference:	Stieler et al., Angewandte Chemie Int. Ed. 2013, 52:11930-4.		
B015	Biotin-Ahx-MA-QPL-OMe	10 mg	500 €
Application:	Site specific irreversible inhibitor of tissue transglutaminase;	0 × N	H ₂
	Peptidic inhibitor containing an electrophilic		OMe
	Michael acceptor (MA) warhead;]
	Biotinyl-analogon to Z013 (Z-MA-QPL-OMe)	MeOOO	
Z013	Z-MA-QPL-OMe	10 mg	500 €
Synonym:	ZED754	0 1	NH ₂
Application:	Site specific irreversible inhibitor of tissue transglutaminase;		OMe
	Peptidic inhibitor containing an electrophilic Michael acceptor (MA) warhead;) H
	Cbz-analogon (Carboxybenzyl, Z) to B015 (Biotin-Ahx-MA-QPL-OMe)	EtO	
Reference:	Protein Data Bank (PDB) entry: 3S3P;		

 $\label{eq:mulliminary} \mbox{M\"{\sc ii}ller et al., PREPRINT 2022, doi } 10.21203/rs.3.rs-1554384/v1$

Inhibitors

"Keillor TG2 Inhibitors" now commercially available at Zedira

Compounds AA9 (Z015), NC9 (Z016), and VA4 (Z017) were developed and produced by Dr. Jeffrey Keillor, Department of Chemistry and Biomolecular Sciences, University of Ottawa, Canada. The mechanism-based blockers carry an irreversibly acting acrylamide warhead linked to a lysine side chain. The NC9 and VA4 compounds are valuable tools shown to lock TG2 in the open conformation *in vitro* and in living cells and to abolish GTP binding. Further, the molecules halt the proliferation and invasion of cancer stem cells. Find more details in the respective product data sheet on our website.

The "Keillor TG2 Inhibitors" bear an acrylamide warhead, being attacked by the active site cysteine residue (1) to form an irreversible complex (2, 3).

"Keillor TG2 Inhibitors" (acrylamide compounds)

Kellior 1G2	innibitors" (acrylamiae compounas)		
Art. No.	Name	Unit	Price
Z 015	Keillor inhibitor AA9	10 mg	400 €
Application:	Site specific inhibitor of tissue transglutaminase		Î "
	$K_1 = 9 \mu M; k_{inoci}/K_1 = 0.10 \mu M^{-1} min^{-1}$		
Reference:	Akbar et al., J. Med. Chem. 2017, 60:7910–27	٩٤٠	
Z 016	Keillor inhibitor NC9	10 mg	400 €
Application:	Site specific inhibitor of tissue transglutaminase		
	$K_1 = 34 \mu M; k_{inoci}/K_1 = 0.08 \mu M^{-1} min^{-1}$	HN	^
Reference:	Akbar et al., J. Med. Chem. 2017, 60:7910-27;		
	Clouthier et al., Angew. Chem. Int. Ed. Engl. 2012, 51:124648;	~ -	~
	Kerr et al., Oncogene 2017, 36:2981-90; Fisher et al., Oncotarget 2015, 6:2	0525-39;	
	Adhikary et al., Oncotarget 2018, 9:34495505		
Z 01 <i>7</i>	Keillor inhibitor VA4	10 mg	400 €
Application:	Site specific inhibitor of tissue transglutaminase		0

Also new in Zedira's portfolio: LDN 27219

 $K_{l} = 13 \mu M; k_{inact}/K_{l} = 0.11 \mu M^{-1} min^{-1}$

Akbar et al., J. Med. Chem. 2017, 60:7910-27

Kerr et al., Oncogene 2017, 36:2981-90

Art. No.	Name	Unit	Price
D016	LDN 27219	10 mg	400 €
Application:	Reversible, slow-binding Transglutaminase 2 (TG2) inhibitor (IC ₅₀ = 0.25 μ M),		
	binding at the enzyme's GTP site	· · · · · · · · · · · · · · · · · · ·	N D H NH2
Reference:	Case and Stein, Biochemistry 2007, 46:110615;		- N 3 Nn ₂
	Duval et al., Bioora, Med. Chem. Lett. 2005, 15:1885-9		

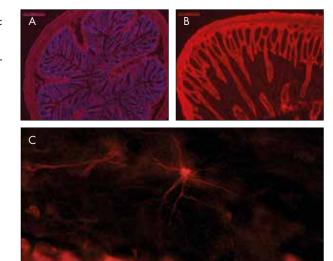
Reference:

Antibodies

Antibodies are important tools in many research and diagnostic applications.

Zedira offers antibodies – polyclonal as well as monoclonal – raised against:

- All human transglutaminases
- Guinea pig liver transglutaminase
- Bacterial transglutaminase
- The transglutaminase reaction product:
 N^ε-(γ-glutamyl)-L-lysine-isopeptide bond
- Fibrinolytic enzymes:
 Plasmin and its zymogen (plasminogen)
- Gliadin-variants



Indirect immunostaining

- (A) Anti-TG2 (A014): mouse colon section (1:100);
- (B) Anti-TG2 (A014): mouse small intestinal mucosa;
- (C) Anti-TG6 (A017): astrocyte in mouse corpus callosum.

(A/B) J. Knauer, Fraunhofer Gesellschaft Leipzig

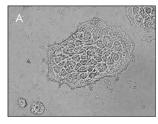
C) A. Schulze-Krebs, S. v. Hörsten, University Erlangen

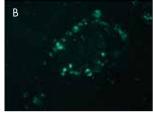
Antibodies labeled with fluorescent dyes

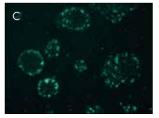
In many applications, the need for a fluorescently labeled antibody exists, ranging from fluorescence microscopy to fluorescence-activated cell sorting (FACS).

Zedira provides many of its polyclonal antibodies with a flourescent label like FITC or as a biotinylated version.

Of course, antibodies with other tags are available on demand. Just give us a call (+49 6151 66628 0) or send an e-mail (contact@zedira.com).







Direct immunostaining

Stimulated CaCo2 cells expressing TG2.

- (A) Transmitted light microscopy, magnification 1:40;
- (B) FITC-Anti-TG2 (A028): fluorescence microscopy, magnification 1:40;
- (C) FITC-Anti-TG2 (A028): fluorescence microscopy, magnification 1:20.

(A-C) W. Dieterich, University Erlangen-Nürnberg

Products

Antibodies against Transglutaminase 1

Art. No.	Name	Unit	Price
A018	Polyclonal antibody to human keratinocyte transglutaminase (TG1)	500 µg	400 €
Immunogen:	rec. human keratinocyte transglutaminase (T035), raised in rabbit		
Format:	Purified IgG		
Reference:	Landegren et al., PNAS 2021, 118:e2100687118; Algarni et al., Biochem. Pharma	col. 2017, 128:55	-73; Fischer
	et al., J. Invest. Dermatol. 2013, 133:1170-7; Itoh et al., J. Histochem. Cytochem. 2	013, 61:793-801	
A029	FITC-labeled polyclonal antibody to human TG1	200 µg	425 €
Format:	A018 purified via affinity chromatography on protein A, followed by FITC-labeling		
A042	Monoclonal antibody to human TG1 (clone XTG31)	200 µg	400 €
Immunogen:	rec. human keratinocyte transglutaminase (TO35), raised in mouse		
Format:	Purified IgG		
Reference:	Freedman et al., J. Invest. Dermatol.2021, 141:874-882.e6		
A043	Monoclonal antibody to human TG1 (clone XTG51)	200 µg	400 €
Immunogen:	rec. human keratinocyte transglutaminase (T035), raised in mouse		
Format:	Purified IgG		

Polyclonal antibodies against Transglutaminase 2

•			
Art. No.	Name	Unit	Price
A014	Polyclonal antibody to human tissue transglutaminase (TG2)	500 µg	400 €
Immunogen:	rec. human tissue transglutaminase (TO22), raised in rabbit		
Reference:	Landegren et al., PNAS 2021, 118:e2100687118; Dulay et al., Biosens. Bioelectron	. 2011, 26:3852-6	
A028	FITC-labeled polyclonal antibody to human TG2	200 µg	425 €
Format:	A014 purified via affinity chromatography on protein A, followed by FITC-labeling		
A053	Biotinylated polyclonal antibody to human TG2	50 µg	400 €
Format:	A014 purified via affinity chromatography on protein A, followed by biotin-labeling		
A072	Polyclonal antibody to mouse tissue transglutaminse	200 µg	400 €
Immunogen:	Mouse tissue transglutaminase (TO40), raised in rabbit		
A075	FITC-labeled polyclonal antibody to mouse TG2	200 µg	425 €
Format:	A072 purified via affinity chromatography on protein A, followed by FITC-labeling		



Monoclonal antibodies against TG2 domains

Name

Art. No. Price Monoclonal antibody to human TG2 (Catalytic Domain, clone XTG17) 400 € A033 200 µg

Unit

rec. human tissue transglutaminase (TO51), raised in mouse Immunogen:

Specificity: Mouse monoclonal antibody reacts with the Catalytic Domain of transglutaminase 2

(human, guinea pig, rat, mouse, and dog TG2)

> 95%, by SDS-PAGE Purity:

Kanchan et al., Cell. Mol. Life Sci. 2015, 72:3009-35 Reference:



400 € A034 Monoclonal antibody to human TG2 (Beta-Sheet Domain, clone XTG11) 200 µg

rec. human tissue transglutaminase (TO51), raised in mouse Immunogen:

Mouse monoclonal antibody reacts with the Beta-Sheet Domain of human transglutaminase 2 Specificity:

> 95%, by SDS-PAGE Purity:

Reference: Kanchan et al., Cell. Mol. Life Sci. 2015, 72:3009-35

A036 Monoclonal antibody to human TG2 (Beta Barrel 1 Domain, clone XTG21) 200 µg 400 €

rec. human tissue transglutaminase (TO51), raised in mouse Immunogen:

Specificity: Mouse monoclonal antibody reacts with the Beta Barrel 1 Domain of human transglutaminase 2

> 95%, by SDS-PAGE Purity:

Reference: Kanchan et al., Cell. Mol. Life Sci. 2015, 72:3009-35

400 € A037 Monoclonal antibody to human TG2 (Beta Barrel 2 Domain, clone XTG18) 200 µg

rec. human tissue transglutaminase (TO51), raised in mouse Immunogen:

Mouse monoclonal antibody reacts with the Beta Barrel 2 Domain of human transglutaminase 2 Specificity:

> 95%, by SDS-PAGE Purity:

Kanchan et al., Cell. Mol. Life Sci. 2015, 72:3009-35 Reference:

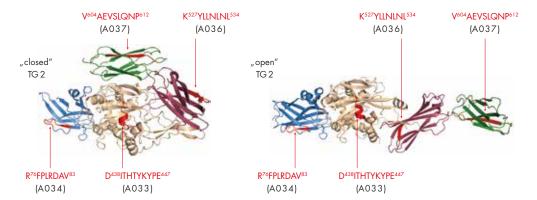


Figure: Epitopes of monoclonal antibodies to the four TG2-domains determined by peptide microarrays (see page 46),

marked in the "closed" and "open" conformation structure of TG2.

Antibodies against Transglutaminase 3

Art. No.	Name	Unit	Price
A015	Polyclonal antibody to human epidermal transglutaminase (TG3)	500 µg	400 €
Immunogen:	rec. human epidermal transglutaminase (T024) raised in rabbit		
Format:	Purified IgG		
Reference:	Csobán-Szabó et al., Int. J. Mol. Sci. 2021, 22:12448; Schulze-Krebs et al., Int.	J. Mol. Sci. 2021, Hi	etikko et al.,
	Acta. Derm. Venereol. 2018, 98:366-72; Algarni et al., Biochem. Pharmacol. 2	017, 128:55-73; Fisc	her et al., J.
	Invest. Dermatol. 2013, 133:1170-7		
A030	FITC-labeled polyclonal antibody to human TG3	200 µg	425 €
Format:	A015 purified via affinity chromatography on protein A, followed by FITC-labelin	g	
A078	Polyclonal antibody to human epidermal transglutaminase (TG3)	250 µg	400 €
	(Protein A purified)		
A082	Monoclonal antibody to human TG3 (clone XTG45)	200 µg	400 €
Immunogen:	rec. human epidermal transglutaminase (T024), raised in mouse		
Format:	Purified IgG		
Antibody ago	ainst Transglutaminase 4		
Art. No.	Name	Unit	Price

Art. No.	Name	Unit	Price
A022	Polyclonal antibody to human prostate transglutaminase (TG4)	500 µg	400 €
Immunogen:	rec. human prostate transglutaminase (TO42), raised in rabbit		
Format:	Purified IgG		
Reference:	Landegren et al., PNAS 2021, 118:e2100687118		

Antibodies against Transglutaminase 5

Art. No.	Name	Unit	Price
A008	Polyclonal antibody to human transglutaminase 5 (TG5)	500 µg	400 €
Immunogen:	rec. human Transglutaminase 5 (T086, inclusion body preparation), raised in rabbit		
Format:	Purified IgG		
A044	FITC-labeled polyclonal antibody to human TG5	200 µg	425 €
Format:	A008 purified via affinity chromatography on protein A, followed by FITC-labeling		

Antibodies against Transglutaminase 6

Name	Unit	Price
FITC-labeled polyclonal antibody to human TG6	200 µg	425 €
Purified via affinity chromatography on protein A, followed by FITC-labeling		
Monoclonal antibody to human TG6 (Catalytic Domain, clone XTG52)	200 µg	400 €
Protein G-affinity purified IgG		
Mouse monoclonal antibody reacts with the Catalytic Domain of human transglutamin	ase 6	
Monoclonal antibody to human TG6 (Beta Barrel 1 Domain, clone XTG39)	200 µg	400 €
Protein G-affinity purified IgG		
Mouse monoclonal antibody reacts with the Beta Barrel Domain 1 of human transglute	aminase 6	
Polyclonal antibody to human neuronal transglutaminase (TG6)	250 µg	400 €
(Protein A purified)		
rec. human neuronal transglutaminase (TO21), raised in rabbit		
Monoclonal antibody to human TG6 (Beta Barrel 2 Domain, clone XTG29)	200 µg	400 €
rec. human neuronal transglutaminase (TO21)		
Purified IgG		
	FITC-labeled polyclonal antibody to human TG6 Purified via affinity chromatography on protein A, followed by FITC-labeling Monoclonal antibody to human TG6 (Catalytic Domain, clone XTG52) Protein G-affinity purified IgG Mouse monoclonal antibody reacts with the Catalytic Domain of human transglutamin Monoclonal antibody to human TG6 (Beta Barrel 1 Domain, clone XTG39) Protein G-affinity purified IgG Mouse monoclonal antibody reacts with the Beta Barrel Domain 1 of human transgluta Polyclonal antibody to human neuronal transglutaminase (TG6) (Protein A purified) rec. human neuronal transglutaminase (T021), raised in rabbit Monoclonal antibody to human TG6 (Beta Barrel 2 Domain, clone XTG29) rec. human neuronal transglutaminase (T021)	FITC-labeled polyclonal antibody to human TG6 Purified via affinity chromatography on protein A, followed by FITC-labeling Monoclonal antibody to human TG6 (Catalytic Domain, clone XTG52) Protein G-affinity purified IgG Mouse monoclonal antibody reacts with the Catalytic Domain of human transglutaminase 6 Monoclonal antibody to human TG6 (Beta Barrel 1 Domain, clone XTG39) Protein G-affinity purified IgG Mouse monoclonal antibody reacts with the Beta Barrel Domain 1 of human transglutaminase 6 Polyclonal antibody to human neuronal transglutaminase (TG6) (Protein A purified) rec. human neuronal transglutaminase (TO21), raised in rabbit Monoclonal antibody to human TG6 (Beta Barrel 2 Domain, clone XTG29) 200 µg rec. human neuronal transglutaminase (TO21)

Antibodies against Transglutaminase 7

Art. No.	Name	Unit	Price
A040	Polyclonal antibody to human transglutaminase 7 (TG7)	200 µg	400 €
Immunogen:	rec. human Transglutaminase 7 (T011), raised in rabbit		
Format:	Purified IgG		
Reference:	Landegren et al., PNAS 2021, 118:e2100687118		

Antibodies against Factor XIII

Art. No.	Name	Unit	Price
A016	Polyclonal antibody to human factor XIII (A-subunit)	500 µg	400 €
lmmunogen:	rec. human blood coagulation factor XIII (TO27), raised in rabbit		
Reference:	Mitchell et al., Blood. 2014, 124:3982-90		
A032	FITC-labeled polyclonal antibody to human factor XIII (A-subunit)	200 µg	425 €
Format:	A016 purified via affinity chromatography on protein A, followed by FITC-labeling		
Reference:	Mitchell et al., Blood. 2014, 124:3982-90		
A052	Biotinylated polyclonal antibody to human factor XIII (A-subunit)	50 µg	400 €
Format:	A016 purified via affinity chromatography on protein A, followed by biotin-labeling		
A074	Polyclonal antibody to human blood coagulation factor XIII (B-subunit)	200 µg	400 €
Immunogen:	rec. human blood coagulation factor XIII B-subunit (T050), raised in rabbit		
A077	FITC-labeled polyclonal antibody to human factor XIII (B-subunit)	200 µg	425 €
Format:	A074 purified via affinity chromatography on protein A, followed by FITC-labeling		
A154	Monoclonal antibody to human factor XIII-A (Activation Peptide, clone XTG09)	200 µg	400 €
Specificity:	Mouse monoclonal antibody reacts with the Activation Peptide of human factor XIII		
A155	Monoclonal antibody to human factor XIII-A (Catalytic Domain, clone XTG02)	200 µg	400 €
Specificity:	Mouse monoclonal antibody reacts with the Catalytic Domain of human factor XIII		
Antibodies ag	gainst D-dimers		
Art. No.	Name	Unit	Price
A076	DD-XLink-mab	100 µg	400 €
	Monoclonal antibody against crosslinked fibrin ("D-dimer")		
Immunogen:	Human fibrin peptides cross-linked with plasma factor XIIIa, raised in mouse		
A079	Biotin-DD-XLink-mab	50 µg	400 €

Biotinylated monoclonal antibody against cross-linked fibrin ("D-dimer")

(product derived from A076)

Antibodies against Microbial Transglutaminase

Art. No.	Name	Unit	Price
A020	Polyclonal antibody to microbial protransglutaminase (pro-MTG)	500 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in rabbit		
A051	Biotinylated polyclonal antibody to microbial transglutaminase (MTG)	50 µg	400 €
Format:	Purified via affinity chromatography on protein A, followed by biotin-labeling		
A143	Monoclonal antibody to microbial transglutaminase (clone XM67, IgG1)	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in mouse		
Format:	Purified IgG		
A144	Monoclonal antibody to microbial transglutaminase (clone XM68, IgG2a)	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in mouse		
Format:	Purified IgG		
A145	Polyclonal antibody to microbial transglutaminase	200 µg	400 €
Immunogen:	Microbial protransglutaminase (T016), raised in rabbit		
Format:	Purified IgG		
Reference:	Stricker et al., J. Pediatr. Gastroenterol. Nutr. 2019, 68:e43-e50		

Antibody against Transglutaminase reaction product

Art. No.	Name	Unit	Price
A023	Monoclonal antibody to N ^e -(y-L-glutamyl)-L-lysine-isopeptide bond	100 µg	440 €
Immunogen:	N^{ϵ} -{ γ -L-glutamyl}-L-lysine-isopeptide, modified, raised in mouse		
Reference:	Wilhelmus et al., Anal Biochem. 2020, 592:113578; Armstrong et al., Acta Ci	r. Bras. 2018, 33	3:991-999;
	Scarnato et al., LWT - Food Sci. Tech. 2017, 81:101-110; Zhang et al., Mol. Ne	eurobiol. 2016, 50	3:5066-78;
	de Jager et al., J. Neurochem. 2015, 134:1116-28; Steppan et al., J. Am. Hear	t Assoc. 2014, 3	:e000599;
	Shrestha et al., Biomed. Res. Int. 2014,2014:651608; Nadalutti et al., Cell. Mol. Life	e Sci. 2014, 71:1	315-26; de
	Jager et al., Neurobiol. Aging. 2013, 34:1159-69; Shaik et al., Eur. J. Cell Biol. 201	2, 91:204-15; Elli	et al., Lab.
	Invest. 2011, 91:452-61; Wang et al., PLoS Pathog. 2010, 6:e1000763; Johnson	et al., J. Neurosc	i. Methods.
	2004, 134:151-8; Thomas et al., J. Immunol. Methods. 2004, 292:83-95; Kaartin	en et al., J. Bone	Miner. Res.
	2002, 17:2161-73		

Antibodies to gliadin are used in research as well as in diagnostics, e.g., for the detection of gluten in food samples. We offer a range of antibodies to gliadin differing in their specificity. The antibodies may be ordered as a set of 10 monoclonals (50 μ g each) (A086) or individually.

Antibodies to deamidated gliadin (A160, A161) are of special interest in the context of celiac disease, as they recognize an immunodominant epitope.

Antibodies against deamidated gliadin



Art. No.	Name	Unit	Price
A160	Monoclonal antibody to deamidated gliadin (clone ZDG-01)	100 µg	780 €
Immunogen:	Deamidated gliadin-related peptide Lys57-Glu65-[a-gliadin (58-73)] (KLQPFPQP	<u>E</u> LPYPQPQ)	
Specifity:	Specific for deamidated 33mer-alpha gliadin peptide (KLQPFPQP E LPYPQPQ)		
Reference:	Heil et al., J. Agric. Food Chem. 2017, 65:6982-90		



A161	Monoclonal antibody to deamidated and non-deamidated gliadin (clone ZDG-02) 100 µg	780 €
Immunogen:	Deamidated gliadin-related peptide Lys57-Glu65-[α-gliadin (58-73)] (KLQPFPQP E LPYPQPQ)	
Specifity:	Recognizes gliadin. Reacts with both the deamidated 33mer-alpha gliadin peptide (KLQPFPQPELPYPQPQ)	
	and the non-deamidated 33mer-alpha gliadin peptide (KLQPFPQPQLPYPQPQ)	

Antibodies against wheat gliadin

Name	Unit	Price
Monoclonal antibodies to gliadin (test sample set)	1 Set	600 €
(Set comprises 10 monoclonal antibodies, 50 µg each)		
XGY1, XGY4, XGY6, XGY7, XGY9, XGY10, XGY11, XGY15, XGY19, XGY24		
Monoclonal antibody to gliadin	500 µg	400 €
(Art. No. and Clones see set A086 and picture next page)	(each)	
Mouse monoclonal antibody raised against purified wheat aliadin		
	Monoclonal antibodies to gliadin (test sample set) (Set comprises 10 monoclonal antibodies, 50 µg each) XGY1, XGY4, XGY6, XGY7, XGY9, XGY10, XGY11, XGY15, XGY19, XGY24 Monoclonal antibody to gliadin	Monoclonal antibodies to gliadin (test sample set) (Set comprises 10 monoclonal antibodies, 50 µg each) XGY1, XGY4, XGY6, XGY7, XGY9, XGY10, XGY11, XGY15, XGY19, XGY24 Monoclonal antibody to gliadin (Art. No. and Clones see set A086 and picture next page) (each)

Antibody against barley hordein

Art. No.	Name	Unit	Price
A071	Monoclonal antibody to hordein (clone XH4)	500 µg	400 €
Immunogen:	Mouse monoclonal antibody raised against hordein (barley prolamin)		

Differences in gliadin antibody clones

Recombinant gliadin and deamidated gliadin peptides (G051-G055 and G005, G006, see section Celiac Disease Products) were analyzed using monoclonal antibodies to

gliadin. The picture below indicates the various antibodies, the corresponding clones, and their reactivity to gliadin and deamidated gliadin peptides.

Art. No.		AO	11	A	013	A)54	AC	56	A0	59	AO	60	A0	64	A0	67	AC	70	AC	85	Αl	60	Αl	61
Clone		XG	Y1	χo	GY7	ХС	GY6	ХG	Y11	ХG	;Y9	ΧG	Y10	ХG	Y4	ΧG	/15	ΧG	Y24	ΧG	Y19	n.	d.	n.	d.
Binds to [µg]		10	1	10	1	10	1	10	1	10	1	10	1	10	1	10	1	10	1	10	1	10	1	10	1
Wheat prolamin			0	0	0		0		0			0	0		0		0		0	0		-			
26mer gliadin peptide	Corres - 20mer - glodin	0	10									0	0	0				1				17)			8
26mer DGP	20me y-glodin, decemband		4			o						0		0									1	6	
33mer gliadin peptide	Care - glada					11						10		9								0		0	0
33mer DGP	Correct Street reginatio, decondared	-1				bi.	4					0	0	1	•						-		0	0	30
Carrier protein control	College												H									0	d		-
DGPx2	Street regiodis, decendand 20mer regiodis, decendand													0								0	0	Ď.	6
DGPx4	Steer eqlade, decordered 26ms replacie, decordered E0235 D0242					0	0					0		6					4			0	19		

Spotlight - Transglutaminase peptide microarrays for high resolution epitope mapping

Introduction

Poly- and monoclonal antibodies are important research tools for the elucidation of transglutaminase function in physiology and pathophysiology. Furthermore, auto-antibodies to TG2, TG3, or TG6, may be present in gluten-sensitive disorders and are used as diagnostic biomarkers.

Zedira and PEPperPRINT now offer peptide microarrays for high-resolution linear epitope mapping of monoclonal (mabs) and polyclonal antibodies (pabs). Further, the arrays may be used for the characterization of patients' sera containing antitransglutaminase auto-antibodies.

The PEPperCHIP® Transglutaminase Peptide Microarray is based on PEPperPRINT's unique peptide microarray platform: Transglutaminase sequences translated into 15 aa peptides are synthesized in duplicate with a maximum peptide-peptide overlap of 14 aa for full epitope coverage on a coated glass slide.

The following microarray formats are available for epitope characterization of your antibody or antiserum:

- Pan-Transglutaminase Peptide Microarray (P111): to determine the antibodies' epitopes in all human transglutaminases (FXIIIA, TG1, TG2, TG3, TG4, TG5, TG6, TG7, and EBP4.2)
- Transglutaminase 2 Microarray (P117): to analyze 5 samples (e.g., patients' sera) on one chip
- Custom Transglutaminase Microarray (P112): to design your microarray according to your specific requirements
- We further offer the analysis of your antibody: PEPperCHIP® Transglutaminase Microarray Service (P113)

Α	В		(
1.13.5	Peptide	Fluorescence	
	(TG2-derived)	intensity	
	VVTGPAPSQEAGTKA	0	
	VTGPAPSQEAGTKAR	6	
	TGPAPSQEAGTKARF	11	
	GPAPSQEAGTKARFP	8	
	PAPSQEAGTKARFPL	9	
	APSQEAGTKARFPLR	6	
	PSQEAGTKARFPLRD	19	
	SQEAGTKARFPLRDA	29	
800000	QEAGTKARFPLRDAV	4,785	
	EAGTKARFPLRDAVE	4,544	
	AGTKARFPLRDAVEE	7,466	-
	GTKARFPLRDAVEEG	3,646	
	TKARFPLRDAVEEGD	1,167	
	KARFPLRDAVEEGDW	598	
	ARFPLRDAVEEGDWT	1,080	
	RFPLRDAVEEGDWTA	1,671	
	FPLRDAVEEGDWTAT	11	
	PLRDAVEEGDWTATV	13	
	IND AVECODIA (TATIA)	10	1

С	D		
	TG2	2 Domain	Epitope consensus
			sequence
	1	catalytic	YLDSE
2.0	2	catalytic	DNNYGDGVSP
	3	catalytic	NEFGE I QG
	4	catalytic	QPGYEG
	5	catalytic	QALDPTPQEK
	6	catalytic	D İ THT
	7	catalytic	PEGSSEEREAFT
	8	Barrel 1	fah i tnntaee
	9	Barrel 2	LTEEQ
100	10	Barrel 2	EIPDPVEAG

Examples of epitope mapping

Epitope mapping of 4 monoclonal antibodies raised against full-length human TG2 and characterized for their domain-specificity by western blotting using recombinantly produced TG2-domains has been performed using the PEPperCHIP® Transglutaminase Peptide Microarray.

Epitope mapping of polyclonal rabbit anti-human TG2 antibody A014 has been characterized accordingly. Clear signals restricted to TG2-epitopes are given for all mabs as well as for pab A014. Cross-reactivity to other transglutaminase isoenzymes is not observed, confirming the specificity data obtained by Western

Figure 1A shows the fluorescence read out for mab A034 (specific to the TG2-beta-sheet domain). The fluorescence intensity of the epitope-containing peptide spots is given in figure 1B.

The fluorescence image of the microarray for pab A014 is shown in figure 1C. The deduced linear epitopes recognized by A014 are summarized in figure 1D.

Celiac disease patients' sera

blotting.

PEPperCHIP® Transglutaminase Peptide Microarray may also be used for the characterization of human patients' sera. As an example, the linear TG2 epitopes recognized by 3 celiac disease patients' sera (both IgA and IgG) are depicted in figure 2 (next page), where conserved epitope regions can be deduced. Interestingly, epitopes for domain-specific mabs as well as for pab A014 match those conserved epitope regions. Antibodies did not bind to catalytic site Cys277 and its neighboring amino acids, while the other catalytic triad amino acids (His335 and Asp358) are part of epitope regions. For the 3 sera analyzed, we found autoantibody binding epitopes all over the TG2-sequence.

For further information please go to: www.zedira.com

Figure 1: A) PEPperCHIP® Pan-Transglutaminase Peptide Microarray after incubation with mab A034 (1 μg/mL) and secondary antimouse IgG-antibody (DyLight680; red). Control: monoclonal anti-HA-antibody-DyLight800; green). B) Fluorescence intensity of the single spots around the A037 consensus motif RFPLRDAV (red). C) Microarray for pab A014 (10 μg/mL) revealing 10 clear epitope-like spot patterns with weak to strong intensity. D) Epitopes of polyclonal antibody A014.

PEPperCHIP® Microarray

Art. No.	Name	Unit	Price
P111	PEPperCHIP® Pan-Transglutaminase Microarray	1 Chip	475 €
	(Standard microarray)		
Content:	Human transglutaminases FXIIIA, TG1, TG2, TG3, TG4, TG5, TG6, TG7, and B4.2		
P117	PEPperCHIP® Transglutaminase 2 Microarray	1 Chip	475 €
Content:	Human transglutaminase 2		
Samples:	Analyze up to 5 samples with one chip		
P112	PEPperCHIP® Custom Transglutaminase Microarray	1 Chip	895 €
	(Customized transglutaminase microarray layout)		
P113	PEPperCHIP® Transglutaminase Microarray Service	1 Sample	695 €
	(Full service IgG and IgA analysis of one sample)		

PEPperCHIP® Accessories

Art. No.	Name	Unit	Price
P119	MAPIX Analyzer	3-Month License	295 €
	(Software for peptide microarray image analysis)	1-Year License	745 €
		Perpetual License	3500 €
P115	PEPperCHIP® Incubation Tray 3/1	1 Tray	325 €
	(Suitable for microarray P111)		
P116	PEPperCHIP® Staining Kit	1 Kit	95 €
	(Anti-HA (12CA5)-Cy5 or DyLight680)		
P118	PEPperCHIP® Incubation Tray 3/5	1 Tray	325 €
	(Suitable for microarray P117)		

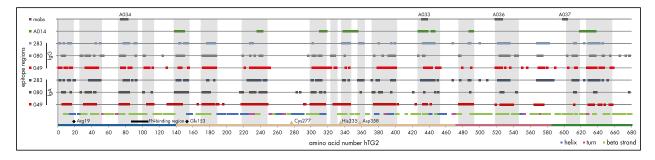


Figure 2: IgA- and IgG-epitope regions for 3 celiac disease patient sera (#283, #080, #049). In addition, epitopes for domain-specific mabs A033, A034, A036, and A037 as well as pab A014 are indicated. Common epitope regions are highlighted by rectangles.

Proteases

Relationship Proteases - Transglutaminases

Name

Human transglutaminases possess a catalytic triad and the reaction proceeds via a reactive intermediate linked to the nucleophilic cysteine of the enzyme. The mechanism is similar to the proteolysis reaction catalyzed by thiol proteases and obviously the enzyme classes even have an evolutionary relationship.

(Pro)thrombin from tested human plasma

The biology and physiology are also closely related. The serine protease **thrombin** (**T056**) activates factor XIII cleaving the activation peptide. Subsequently, **plasmin** (**P012**) degrades the fibrin clot. Therefore, proteases are important in transglutaminase research.

Unit

Price

Protease Substrates

Art. No.

,	· tame	•	
D005	Metalloprotease-Assay-Substance, DABCYL-Ser-Phe-EDANS	2 mg	325 €
Reference:	Weimer et al., Anal. Biochem. 2006, 323:110-9		
D017	Thrombin-Assay Substance, fluorescent, (D)-Phe-Pip-Arg-AMC	10 mg	200 €
Application:	Highly sensitive thrombin substrate, lower limit of detection: 5 pM (picomolar) thrombi	n	
Z020	Thrombin-Generation-Assay Substance, fluorescent, Z-Gly-Gly-Arg-AMC	25 mg	200 €
Application:	"Slow" acting thrombin substrate for determination of thrombin generation in plasma		
T004	Plasmin substrate Tosyl-GPKpNA, chromogenic	25 mg	350 €
Synonym:	N-(p-Tosyl)-Gly-Pro-Lys-pNA acetate		
Proteases			
Art. No.	Name	Unit	Price
P003	Prolylendopeptidase from Myxococcus xanthus (PEP, PEP-Mx), recombinant	150 U	400 €
Source:	Recombinantly produced in <i>E. coli</i>		
Reference:	Schulz et al., Adv. Mater. 2016, 28:1455-60		
P012	human Plasmin , recombinant (from Glu-Plasminogen, activated by Urokinase)	100 µg	450 €
Source:	Recombinantly produced in insect cells		
T056	Human alpha thrombin, highly active	2x 100 U	200 €
Synonym:	Coagulation factor IIa, $lpha$ -Thrombin		

Source:

Cereal Proteins

Background information

Cereals have a protein content of about 10%, which are classified by their solubility according to Thomas Burr Osborne (1919):

Albumin + globulin: soluble in saline
Prolamins soluble in ethanol

Glutelins: soluble in propanol/urea/DTE

Prolamins and glutelins like gliadin and glutenin from wheat play a crucial role in celiac disease pathophysiology.

Find in the table below the protein extracts of the most common cereals.



	Barley	Rye	Wheat	Wheat	Spelt	Oat	Millet (Sorghum)	Rice	Corn	Soy*
Albumin + globulin	G018	G021	G036 Leukosin + Edestin	G039	G030	G033	G045	G027	G024	G042
Prolamin	G019 Hordein	G022 Secalin	G037 Gliadin	G040	G031	G034 Avenin	G046 Kafirin	G028 Oryzin	G025 Zein	G043
Glutelin	G020 Hordenin	G023 Secalinin	G038 Glutenin	G041	G032	G035 Avenalin	G047	G029 Oryzenin	G026 Zeanin	G044

^{*} corresponding protein extracts

5 mg per unit - 250 €

Antibodies against gliadin and deamidated gliadin are also available, see Section: Antibodies

Other cereal protein products

Art. No.	Name	Unit	Price
P004	PT-Gluten	1 mg	250 €
Definition:	PT-Gluten is based on a wheat gluten preparation which has been	10 mg	1200 €
	proteolyzed by pepsin (porcine) and trypsin (porcine).		
Application:	PT-Gluten may be used in biochemical approaches, e.g. as substrate for transg	lutaminases or	
	as antigen for gliadin antibodies.		
Reference:	Elli et al., Hum. Immunol. 2012, 73:992-7		
G008	Omega-5 gliadin	500 µg	780 €
Source:	Recombinantly produced in <i>E. coli</i>		

Blood Coagulation

FXIII terminology

Blood coagulation Factor XIII (FXIII), also known as fibrin stabilizing factor (FSF), is a critical protein involved in the complex process of blood clotting or hemostasis. It plays a significant role in strengthening and stabilizing blood clots formed during the coagulation cascade.

The need for different terminologies when talking about Factor XIII (FXIII) arises from the existence of various forms or activated states of this protein. These different forms are denoted using various suffixes, such as "A $_2$ ", "a", or "B", to distinguish them from one another. Let us take a closer look at the examples.

FXIII-A₂B₂:

In the blood, plasma transglutaminase factor XIII (pFXIII) exists as an **inactive** heterotetramer, comprising two A subunits (FXIII-A) and two B subunits (FXIII-B). FXIII-A subunits are the catalytic subunit responsible for the cross-linking of fibrin upon activation. In contrast, the FXIII-B subunits stabilize the FXIII-A subunits and protect them from premature activation.

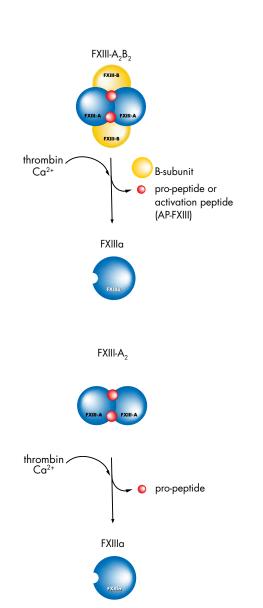
FXIII-A2:

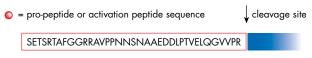
 ${\sf FXIII-A}_2$ specifically refers to the homodimeric **inactive** state of two ${\sf FXIII-A}$ subunits. Although the ${\sf FXIII-A}_2$ species practically does not exist in plasma, it has been described in various cell types such as platelets.

FXIIIa/FXIIIa°:

FXIIIa refers to the thrombin **activated** form of Factor XIII after cleavage of the pro-peptide (red ball) and subsequent binding of calcium ions. The active form FXIIIa is most likely monomeric as indicated by the x-ray structure of calcium-activated FXIIIa° in complex with the ZED1301 inhibitor (Stieler et al., Angew. Chem. Int. Ed. Engl. 2013, 52(45):11930-4). Artificially, FXIIIa° is formed without the prior cleavage of the pro-peptide in the presence of high concentrations of calcium.

The use of distinct terminologies such as FXIIIa and FXIII-A is essential in scientific discussions and medical contexts to avoid confusion between the different forms and subunits of Factor XIII. It allows researchers, clinicians, and healthcare professionals to be precise in their communication, helping to better understand the functions, interactions, and relevance of the protein in various physiological and pathological processes.





Zedira Art. No. A125

Products

T036

For more details see Section: Tro	ansglutaminases	
Name	Unit	Price
Human blood coagulation Factor XIII-A ₂	200 µg	400 €
Human blood coagulation Factor XIII-B subunit	200 µg	400 €
Human blood coagulation Factor XIII-A ₂ , Val34Leu -mutant	200 µg	400 €
Human Factor XIII a, Thrombin activated	200 µg	550 €
Coagulation factor XIII, recombinant human Factor XIII-A ₂	100 E	725 €
(Recombinant fibrin stabilizing factor)	250 E	1450 €
nibitors For more details see Se	ection: Inhibitors	
Name	Unit	Price
Ac-(D)-Asp-MA-Nle-Nle-Leu-Pro-Trp-Pro-OH	5 mg	500 €
ZED1301		
1,3-Dimethyl-4,5-diphenyl-2-[(2-oxopropyl)thio]imidazolium trifluorosulfonicacid salt	10 mg	550 €
Tridegin	200 µg	510 €
1,3,4,5-Tetramethyl-2[(2-oxo-propyl)thio] imidazolium chloride	10 mg	500 €
tivity Assays For more details see Section: Assays	and Substrates	
Name	Unit	Price
FXIII-Assay Substance, Abz-NE(CAD-DNP)EQVSPLTLLK-OH	10 mg	575 €
Fluorescent measurement of transglutaminase activity, optimized for FXIII		
FXIII-Assay Kit, Isopeptidase-Fluorogenic Assay, based on substrate A101		600 €
	Human blood coagulation Factor XIII-A2 Human blood coagulation Factor XIII-A2 Human blood coagulation Factor XIII-A2, Val34Leu-mutant Human Factor XIIIa, Thrombin activated Coagulation factor XIII, recombinant human Factor XIII-A2 (Recombinant fibrin stabilizing factor) ibitors Name Ac-(D)-Asp-MA-Nle-Nle-Leu-Pro-Trp-Pro-OH ZED1301 1,3-Dimethyl-4,5-diphenyl-2-[(2-oxopropyl)thio]imidazolium trifluorosulfonicacid salt Tridegin 1,3,4,5-Tetramethyl-2[(2-oxo-propyl)thio] imidazolium chloride ivity Assays For more details see Section: Assays Name FXIII-Assay Substance, Abz-NE(CAD-DNP)EQVSPLTLIK-OH Fluorescent measurement of transglutaminase activity, optimized for FXIII	Human blood coagulation Factor XIII-A2 Human blood coagulation Factor XIII-B subunit 200 µg Human blood coagulation Factor XIII-A2, Val34Leu-mutant 200 µg Human Factor XIIIa, Thrombin activated 200 µg Coagulation factor XIII, recombinant human Factor XIII-A2 (Recombinant fibrin stabilizing factor) For more details see Section: Inhibitors Name For more details see Section: Inhibitors Name 10 mg ZED1301 1,3-Dimethyl-4,5-diphenyl-2-[(2-oxopropyl)thio]imidazolium trifluorosulfonicacid salt Tridegin 200 µg 1,3,4,5-Tetramethyl-2[(2-oxo-propyl)thio] imidazolium chloride 10 mg ivity Assays For more details see Section: Assays and Substrates Name Unit FXIII-Assay Substance, Abz-NE(CAD-DNP)EQVSPLTILIK-OH 10 mg Fluorescent measurement of transglutaminase activity, optimized for FXIII

Transglutaminase Assay Kit ("DCC"), fluorescent, Casein, Dansylcadaverine



300 €

1 Kit

Blood Coagulation

Fibrin aggregation and clotting

Art. No.	Name	Unit	Price
F004	Fibrinogen, purified from human plasma	50 mg	125 €
Synonym:	Factor I		
F006	FITC-labeled Fibrinogen (product derived from F004)	5 mg	225 €
G101	Gly-Pro-Arg-Pro-amide	25 mg	375 €
Application:	Fibrin aggregation inhibitor peptide		
T056	Human alpha thrombin, highly active	2x 100 U	200 €
Fibrin clot de			
Art. No.	Name	Unit	Price
P012	human Plasmin , recombinantly produced in insect cells	100 µg	450 €
Antibodies	For more details see	Section: Antibodies	
Art. No.	Name	Unit	Price
A016	Polyclonal antibody to human factor XIII (A-subunit)	500 µg	400 €
A032	FITC-labeled polyclonal antibody to human factor XIII (A-subunit)	200 µg	425 €
A052	Biotinylated polyclonal antibody to human factor XIII (A-subunit)	50 µg	400 €

200 µg

100 µg

200 µg

50 µg

400 €

400 €

425 €

400 €

Polyclonal antibody to human factor XIII (B-subunit)

Monoclonal antibody against cross-linked fibrin ("D-dimer")

FITC-labeled polyclonal antibody to human factor XIII (B-subunit)

Biotinylated monoclonal antibody against cross-linked fibrin ("D-dimer")

"DD-XLink-mab"

Biotin-DD-XLink-mab

A074

A076

A077

A079

Transglutaminase saves lives!

Blood clot formation is a vital process to prevent life-threatening blood loss after trauma. The plasmatic part of the blood coagulation cascade can be divided into three steps:

- Cascade leading to activation of prothrombin
- Fibrinogen (F004) activation by thrombin (T056, T222) and fibrin aggregation (soft blood clot)
- Factor XIII activation by thrombin and cross-linking of fibrin fibers as well as covalent decoration with antifibrinolytics

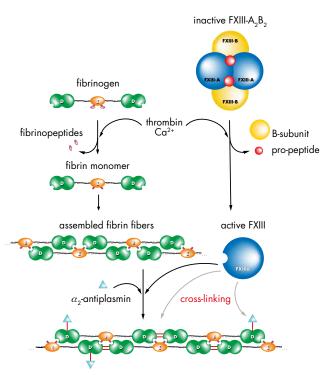
Plasma transglutaminase factor XIII (FXIII) plays an essential role in blood clot formation. In addition, factor XIII is unique in this process, as all the other enzymes involved are proteases. Factor XIII renders the blood clot stiff and resistant to fibrinolytic degradation. Because it is the only transglutaminase in the cascade, it offers the opportunity for a unique modulation of coagulation and promising approaches to prophylaxis of thrombotic events in at-risk patients.

An excellent historical account of factor XIII in blood clotting is given by Laszlo Lorand in "Factor XIII and the clotting of fibrinogen: from basic research to medicine" (J. Thromb. Haemost. 2005, 3:1337-48).

Novel compounds like ZED3197 developed by medicinal chemists at Zedira guide the way to small molecules selectively targeting coagulation factor XIII. In contrast to the currently available therapies, blocking factor XIII allows the formation of a weak fibrin clot. This prevents bleeding and therefore reduces the risk of life-threatening complications.

Zedira offers unique tools and biochemical reagents focusing on the interaction of plasma transglutaminase and fibrin:

- Factor XIII
- Factor XIII inhibitors
- Factor XIII activity assays
- Fibrin aggregation and clotting (Figure 1)
- Fibrin clot degradation (Figure 2)
- Antibodies.



cross-linked fibrin fibers decorated with α_2 -antiplasmin

Figure 1) In blood, the FXIII- A_2B_2 heterotetramer is bound to fibrinogen via its carrier B-subunits. Thrombin cleaves the fibrinopeptides forming the self-aggregating and polymerizing fibrin fibers. Concomitantly, thrombin activates FXIII in the presence of fibrin by the cleavage of the propeptide. The binding of calcium ions and dissociation of the B-subunits yield active FXIIIa. The active plasma transglutaminase covalently cross-links fibrin (red lines) and incorporates α_2 -antiplasmin (triangle) rendering the clot mechanically and biochemically stable.

Fibrinolysis by plasmin leads to the formation of fibrin degradation products as shown in Figure 2. The most important diagnostic marker is the so-called D-Dimer (compare to page 54/55).

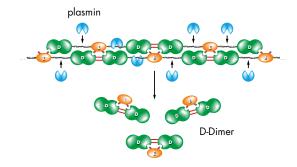


Figure 2) Clot degradation and lysis are mediated by plasmin. Plasmin degrades the coiled-coil structure of fibrin generating xFDPs (cross-linked fibrin degradation products).

Blood Coagulation

Spotlight - "DD-XLink-mab" directed against the cross-linked fibrin neoepitope

Introduction

For decades, coagulation factor XIII (FXIII) has been considered a scientifically valid target for the development of novel anticoagulants [1-3]. Inhibiting FXIII may lower the current bleeding risk in anticoagulation therapy since neither the thrombin level nor the platelet activation is affected.

Zedira developed small molecule inhibitors to modulate FXIII activity using structure-assisted drug design [4, 5]. To assess the efficacy in blood, we aimed to generate a monoclonal antibody directed against the isopeptide bond ("cross-link") within fibrin as a preferred biomarker. After proteolytic activation by thrombin, FXIIIa modifies the soft fibrin clot and thereby generates covalent bonds. First, cross-linking between abutting γ -chains of fibrin is catalyzed and subsequently α_2 -antiplasmin is incorporated to further increase the resistance against fibrinolysis (figure 1A). Plasmin catalyzes the retarded clot dissolution and the release of crosslinked fibrin degradation products (xFDPs/D-dimer).

When of blocking FXIIIa, only a soft clot is formed which may be rapidly hydrolyzed yielding non-cross-linked fibrin degradation products (FDPs, figure 1B).

SDS-PAGE of those degradation products reveals that the protein pattern differs remarkably under reduced and non-reduced conditions as shown in figure 2A.

Monoclonal "D-dimer" antibodies (e.g., DD-3B6/22) are commercially available and are used in *In Vitro* Diagnostics (IVD) to exclude thromboembolic events. However, these monoclonals do not detect the cross-link itself but address a portion of polypeptides within the D-domain after plasmin degradation that are conformationally reactive [8]. This hinders standardization and comparison of data obtained by different assays [9]. Therefore, we developed the "DD-XLink-mab" which directly recognizes the cross-linked fibrin neoepitope.

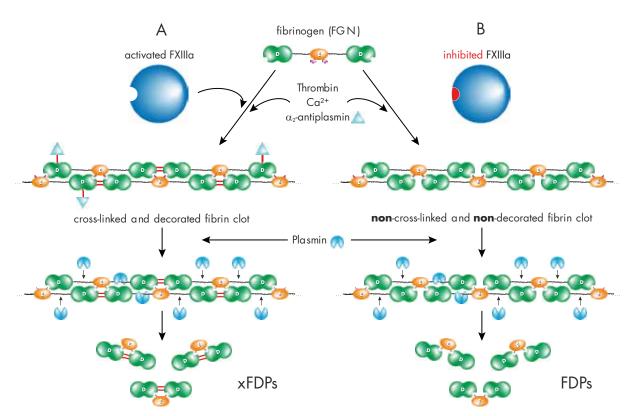


Figure 1: A) Upon clot formation, activated factor XIII (FXIIIa) modifies the soft fibrin clot by rapidly cross-linking γ -chains of fibrin and incorporating α_2 -antiplasmin. Thus, FXIIIa increases clot stiffness and resistance against fibrinolysis. Plasmin catalyzes the retarded release of cross-linked fibrin degradation products (xFDPs) and the characteristic "D-dimers".

Figure 1: B) Inhibition of FXIIIa leads to the fibrin fiber assembly without covalent modification. The so-called "soft clot" is highly susceptible to fibrinolysis leading to fibrin degradation products (FDPs).

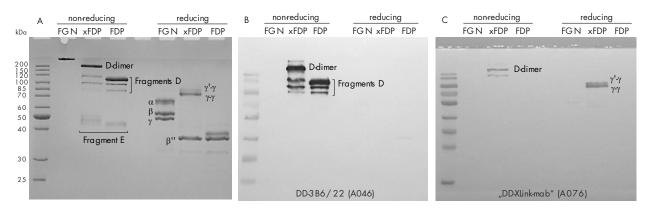


Figure 2: A) Coomassie-stained SDS-PAGE of fibrinogen, cross-linked fibrin degradation products (xFDPs), and non-cross-linked fibrin degradation products (FDPs) under non-reduced and reduced conditions. The most characteristic bands are referenced. Western blotting using B) "D-dimer" (DD-3B6, Zedira A046) and C) our novel "DD-XLink-mab" (Zedira, A076).

Synthesis of the antigen and immunization

A peptide sequence derived from human γ -fibrinogen containing Q398/Q399 and K406 was synthesized by standard solid-phase peptide chemistry. The purified peptide was subsequently crosslinked using thrombin-activated FXIII (FXIIIa, Zedira, T070). Mass spectrometry confirmed the formation of isopeptide bonds. After conjugation to Keyhole Limpet Hemocyanin (KLH), the conjugate was used to immunize three mice. Serum from one mouse showed mild reactivity against cross-linked fibrin degradation products (xFDPs), which was used as a readout both in ELISA and in Western blotting. Spleen-derived B-cells from this mouse were fused to myeloma cells yielding hybridoma cell lines. Separation and further screening led to a single clone producing a monoclonal antibody (named A076) with a substantial reactivity against xFDPs in ELISA.

Characterization of the monoclonal antibody (mab)

The specific requirement for the monoclonal antibody (mab) is to discriminate between cross-linked and non-cross-linked fibrin. In addition, selectivity against fibrinogen and other blood components is indispensable.

Production of xFDPs and FDPs: coagulation was simulated *in vitro* by adding thrombin to a mixture of human fibrinogen (Zedira, F005) and rhFXIII (Zedira, T027) in physiological concentrations either in the presence or absence of ZED3118, a direct-acting FXIIIa inhibitor. The insoluble fibrin clots were subsequently degraded by rhPlasmin (Zedira, P012) and the soluble proteins were separated by gel filtration chromatography. These protein preparations were used for ELISA and SDS-PAGE with subsequent Western blotting.

Immunostaining of xFDPs and FDPs by the commercially available "D-dimer" monoclonal antibody (DD-3B6/22) is shown in figure 2. The pattern reveals that in contrast to our novel "DD-XLink-mab" A076, both xFDPs and FDPs are recognized under non-reducing conditions only, in accordance with the literature [8]. Western blotting using the novel "DD-XLink-mab" indicates specificity for the cross-linked fibrin both under non-reducing and reducing conditions (figure 2c). The antibody shows no reactivity against fibrinogen or other plasma proteins.

Conclusion

We developed and characterized "DD-XLink-mab" (A076) directed against the major cross-link within the γ -chains of human fibrin. The recognized necepitope is clearly distinct from the one recognized by commercial "D-dimer" antibodies used in IVD for the exclusion of thrombotic events. We expect that the novel monoclonal antibody will be a valuable tool for basic hemostaseology and transglutaminase research. Further, evaluation in IVD, for clot imaging, and especially in the course of our FXIII drug development program is ongoing.

References

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- [8] Devine D.V. & Greenberg C.S., Am J Cin Pathol, 1988
- [9] Adam S.S. et al., Blood, 2009

Celiac Disease Products

Background information

Celiac disease affects about 1% of the population and therefore is the most common chronic inflammation of the small intestine triggered by cereal gluten/gliadin uptake in genetically susceptible individuals. The gluten-induced autoimmune disorder is characterized by autoantibodies to tissue transglutaminase (TG2), antibodies to deamidated gliadin, and villous atrophy in the final stage.

TG2 plays a central role in celiac disease. Besides being the primary autoantigen, it is involved in the pathogenesis. Under certain circumstances and in distinct environments such as in the inflamed gut, TG2 catalyzes deamidation of glutamine side chains in gliadin yielding glutamic acid. Deamidated gliadin (DGP) is subsequently recognized by receptors of the immune system breaking oral tolerance and triggering celiac disease. In addition, TG2 cross-links DGP to itself forming hapten-carrier-like complexes, thus breaking self-tolerance by anti-TG2-antibody production. Related gluten-induced autoimmune disorders are dermatitis herpetiformis/Morbus Duhring (autoantigen: epidermal transglutaminase, TG3) and neurological disorders like gluten ataxia (autoantigen: neuronal transglutaminase, TG6).

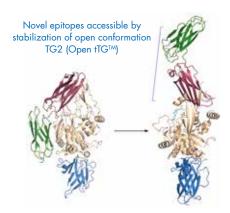
Open tTG - lift the celiac iceberg

Upon substrate binding, TG2 dramatically changes its structure (Pinkas et al., PLoS Biol. 2007). By reacting TG2 with a novel irreversible inhibitor, we could stabilize TG2 in the open conformation which we branded Open tTGTM.

Open tTGTM – it fits the antigen to the autoantibody – is the key to detect seronegative or borderline celiac disease patients. It is superior to the so far used closed conformation TG2, especially for patient sera with low or negative tTG autoantibody-titers (Lindfors et al., J. Clin. Immunol. 2011, 31:436-42).

Transglutaminase 6-ab ELISA kits

The ZediXclusive TG6-ab ELISA kits E103 and E104 are suitable for the detection of IgA or IgG type autoantibodies to TG6 in human sera, respectively.



For the purified protein products **Open tTGTM**, **Inhibited TG3**, and **Inhibited TG6** please refer to section Transglutaminases.

Get your serum sample measured for TG6 autoantibodies!

If **low sample numbers** do not account for buying an ELISA-kit, you may contact the following laboratories for sample measurement:

Northern General Hospital

Clinical Immunology and Allergy Unit care of Graeme Wild Herries Road, Sheffield S5 7AU, UK

E-mail: Graeme.Wild@sth.nhs.uk

Web: www.sth.nhs.uk/services/a-z-of-services?id=19

Praxis Prof. Dr. med. M. Kramer

Facharzt für Laboratoriumsmedizin Postfach 103320, 69023 Heidelberg, Germany

E-mail: m.kramer@praxis-dr-kramer-hd.de

Web: www.gluten-ataxie.de; www.gluten-ataxia.com

Products

Neuronal Transglutaminase (TG6) ELISA

TG6 is the novel autoantigen in gluten-sensitive neurological disorders like gluten ataxia.

Reference: Mulder et al., Dig. Liver Dis. 2018, 50:96-7; Zis et al., Dig. Liver Dis. 2017, 49:1196-200

Hadjivassiliou et al., Ann. Neurol. 2008, 64:332-43 and Lancet Neurol. 2010, 9:318-30



Art. No.	Name	Unit	Price
E103	ZediXclusive TG6-ab ELISA (IgA)	1 kit/96 wells	550 €
Antigen:	recombinant TG6, insect cells		
E104	ZediXclusive TG6-ab ELISA (IgG)	1 kit/96 wells	550 €
Antigen:	recombinant TG6, insect cells		

Celiac disease related diagnostic antigens

Name



Art. No.

Source:

T051	Open tTG™	250 µg	550 €
Source:	Recombinantly produced in insect cells	1 mg	1650 €
T010	Recombinant TG2 (<i>E. coli</i>)	250 µg	400 €
Source:	Recombinantly produced in E. coli	1 mg	1200 €
T021	Human neuronal transglutaminase	250 µg	500 €
	(TG6, recombinantly produced in insect cells)	1 mg	1500 €
T122	Recombinant TG2 (insect cells)	250 µg	400 €
Source:	Recombinantly produced in insect cells	1 mg	1200 €
T024	Human epidermal transglutaminase	200 µg	400 €
Source:	Recombinantly produced in insect cells		
T246	Recombinant human tissue transglutaminase	250 µg	400 €

(Cys-277-Ser, inactive mutant)

Recombinantly produced in **insect cells**

Unit

1 mg

1200 €

Price

Celiac Disease Products

Further products for celiac disease R+D

Art. No.	Name	Unit	Price
G001	Alpha2-gliadin, 33mer (aa56-88), biotinylated	5 mg	550 €
Sequence:	Biotin-LQLQPFPQPQLPYPQPQLPYPQPQLPYPQPQPF-OH		
Reference:	Galipeau et al., Am. J. Gastroenterol. 2014, 109:748-56, Qiao et al., J. Immunol. 20	04, 173:1757-62	
G002	Deamidated alpha2-gliadin, 33mer (aa56-88), biotinylated	5 mg	550 €
Sequence:	Biotin-LQLQPFPQPELPYPQPELPYPQPQPF-OH		
Reference:	Qiao et al., J. Immunol. 2004, 173:1757-62		
G003	Ac-PLQPEQPFPK(ε-Biotin), Deamidated gliadin peptide	10 mg	350 €
Reference:	Schwertz et al., Clin. Chem. 2004, 50:2370-5		
G004	Ac-PEQLPQFEEK(ε-Biotin) , Deamidated gliadin peptide	10 mg	350 €
Reference:	Schwertz et al., Clin. Chem. 2004, 50:2370-5		
G009	Alpha2-gliadin, 33mer (aa56-88)	5 mg	550 €
Sequence:	H-LQLQPFPQPQLPYPQPQLPYPQPQPF-OH		
Reference:	Qiao et al., J. Immunol. 2004, 173:1757-62		
G011	Deamidated alpha2-gliadin, 33mer, (Acetyl-aa56-88-amide, Q65E)	5 mg	550 €
Sequence:	Ac-LQLQPFPQP E LPYPQPQLPYPQPQLPYPQPQPF-NH2		
Reference:	Qiao et al., J. Immunol. 2004, 173:1757-62		
G013	QPFPQPQLPYPQPQ-amide, PepQ, alpha2-gliadin (aa60-73)	10 mg	350 €
Reference:	Heil et al., J. Cer. Sci. 2016, 70:47-56; Skovbjerg et al., Biochim. Biophys. Acta. 200	4, 1690:220-30	
G014	QPFPQPELPYPQPQ-amide, PepE, deamidated alpha2-gliadin (aa60-73)	10 mg	350 €
Reference:	Heil et al., J. Cer. Sci. 2016, 70:47-56; Skovbjerg et al., Biochim. Biophys. Acta. 200	4, 1690:220-30	
G057	Alpha2-gliadin, 33mer (aa56-88), TAMRA labeled	5 mg	600 €
Sequence:	TAMRA-LQLQPFPQPQLPYPQPQLPYPQPQPPF-OH		
G058	Alpha2-gliadin, 33mer (aa56-88), TAMRA and Biotin labeled	5 mg	750 €
Sequence:	TAMRA-LQLQPFPQPQLPYPQPQLPYPQPQPF-Lys(Biotin)-OH		

Art. No.	Name	Unit	Pric
G051	26mer gliadin peptide	250 µg	400
	(26mer-gamma gliadin peptide		
	(aa 59-84) fused to carrier protein)		
Sequence:	FLQPQQPFPQQPQQPYPQQPQQPFPQ		
G052	33mer gliadin peptide	250 µg	400
	(33mer-alpha gliadin peptide		
	(aa 57-89) fused to carrier protein)		
Sequence:	LQLQPFPQPQLPYPQPQLPYPQPQPPF		
G055	Carrier protein control	250 µg	400
	(Control for G051, G052,		
	G007, G054, G006, and G005)		
G007	DGPx1 (26mer DGP)	250 µg	400
	(26mer-deamidated gamma gliadin	1 mg	1200
	peptide (aa 59-84) fused to	•	
	carrier protein)		
Sequence:	FLQPEQPFPEQPEQPYPEQPEQPFPQ		
G054	33mer DGP	250 µg	400
	(33mer-deamidated alpha gliadin		
	peptide (aa 57-89) fused to		
	carrier protein)		
Sequence:	LQLQPFPQPELPYPQPELPYPQPQPF		
G006	DGPx2	250 µg	400
	(2 deamidated gliadin peptides	1 mg	1200
	fused to carrier protein) Carrier 33mer αgliadin, deamidated 26mer γgliadin, deamidated 26mer γgliadin 26mer	din, deamidated	
Sequence:	LQLQPFPQPELPYPQPELPYPQPELPYPQPQPF—FLQPEQPFPEQPEQPYPEQPFQ		
G005	DGPx4	250 µg	400
	(4 non-/deamidated gliadin peptides	1 mg	1200
	fused to carrier protein) Carrier 33mer ægliadin, deamidated 26mer ægliadin 26me	adin, deamidated – I	DQ2-γ1 DQ2
Sequence:	LQLQPFPQPELPYPQPELPYPQPELPYPQPQPF—FLQPEQPFPEQPEQPYPEQPEQPFPQ— PEQPQQSFPEQERP—GIIQPEQPAQL		
G017	Biotinylated DGPx1	100 µg	400
	(biotinylated 26mer-gamma deamidated gliadin peptide fused to carrier protein)		
G056	DGP and Gliadin peptides (Set No 1)	1 Set	780
	(G051, G052, G007, G054, and G055, 100 μg each)		

Services & Partnering

Services on Transglutaminase in Research and Development

Based on our profound expertise in transglutaminase, we offer to support industrial partners in their respective R&D efforts on a fee-for-service base. Zedira is your reliable partner with highly skilled, motivated, and experienced personal. Over the last decade, we successfully completed several projects with big or mid-sized Pharma, as well as with diagnostic companies.

Whatever you need — a product or a service around transglutaminase or related fields, please do not hesitate to contact us!

(+49 6151 66628 0 or send an e-mail to contact@zedira.com)

Service categories include, but are not limited to:

- Production of eukaryotic transglutaminases including mutants
- Manufacturing of microbial transglutaminases including mutants and tailor-made formulations
- Modification of transglutaminases (biotinylation, fluorescent labels, and specific conjugates)
- Development of transglutaminase assays for customer specific applications
- Determination of human and animal transglutaminase inhibition in drug development
- Organic synthesis of transglutaminase related small molecules (e.g. substrates, inhibitors, and labels)
- Scientific advice and experts opinion linked to transglutaminase.

Services on determination of Microbial Transglutaminase (MTG)

Microbial Transglutaminase is widely used in food applications. At Zedira, we provide services for determination and detection of MTG in your sample.

Please contact us for a quotation! (+49 6151 66628 0 or send an e-mail to contact@zedira.com)

Service categories include, but are not limited to:

- Determination of MTG activity in food preparations
- Determination of MTG **protein** in food preparations
- Determination of gluten/gliadin content in food and food preparations

Zedira is a reliable partner complementing the skills of pharmaceutical companies in the transglutaminase sector in order to create extra value and shorten development times. Please contact us for detailed information:

contact@zedira.com or +49 6151 66628 0



Zedi is in the lab now

... and wears a lab coat in an exemplary manner.

Spotlight - Toward Therapeutic Transglutaminase Inhibition

On July 1, 2021, a proof-of-concept study in celiac disease was published in the New England Journal of Medicine titled "A Randomized Trial of a Transglutaminase 2 Inhibitor for Celiac Disease" [1]. This publication marked a significant milestone in drug development.

For the first time, transglutaminase was clinically validated as a druggable target. These groundbreaking data bring hope to both patients with celiac disease and their physicians, addressing the strong, unmet medical need for a drug to support the gluten-free diet these patients must adhere to. The data suggest that inhibiting transglutaminase can particularly protect patients from hidden gluten. Alleviating patients' fear might improve the quality of life and health for millions.

This achievement reminds us of the wise words of George W. Merck: "We try to remember that medicine is for the patient. We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we have remembered it, the larger they have been".

Such a landmark trial indeed offers a moment to pause and reflect on our journey. The starting point was Zedira's tissue transglutaminase (TG2) blocker, ZED1227 — a small molecule inhibitor that selectively targets TG2 with strong potency [2]. After rigorous preclinical evaluations by our European licensee, Dr. Falk Pharma, ZED1227 entered phase 1 clinical trials in 2015, distinguishing itself as a first-in-class compound.

After successful safety evaluations of phase 1, ZED1227 entered phase 2a, a proof-of-concept study in 2018. Scientific data already had indicated that the mucosal immune response in celiac disease was orchestrated by TG2; however, the question remained: Could inhibiting transglutaminase activity mitigate the gluten-induced inflammation and translate into a clinical benefit? The results of the clinical study [1] answer this question with an unequivocal "yes"!

Moreover, data generated during the study provided new insights into the disease's pathogenesis. It was previously believed that gluten and TG2 interacted in the lamina propria. However, emerging data suggest that this might already be the case in the brush border membrane of the enterocytes [3].

ZED1227 is presently undergoing a phase 2b "real-life" study without additional gluten challenge. The team at Dr. Falk Pharma and Zedira has recently expanded through a collaboration with Takeda, which has secured licenses for the US and other territories. Together, we push the development of ZED1227, aiming to bring the drug to the patients as soon as possible. However, the clinical trials do not only yield data on safety and efficiency, but also provide additional knowledge on the disease mechanism. This may facilitate novel ideas for treatment, management, and diagnostic strategies for celiac disease.



What comes next at Zedira?

Eight transglutaminase enzymes exist in the human body. These multifaceted iso-enzymes fulfill a bundle of physiological functions but are also involved in disease states. Zedira developed and optimized drug candidates to address TG2, particularly in fibrotic disorders of the lungs, liver, and kidneys. We also designed tailor-made inhibitors aimed at the plasma transglutaminase FXIlla (F13a) to address thrombosis [4]. Blockers for TG3 and TG6 to target gluten-sensitive disorders dermatitis herpetiformis and gluten ataxia, respectively, are currently under development.

Further, an unprecedented assay platform to specifically detect transglutaminase iso-enzyme activity in biological specimens has been installed, holding potential for future companion diagnostics. In conclusion, the journey of therapeutic transglutaminase inhibition has just begun!

References

- [1] Schuppan et al., N. Engl. J. Med. 2021, 385:35-45
- [2] Buechold et al., Cells 2022, 11(10), 1667
- [3] Isola et al., Int. J. Mol. Sci. 2023, 24(13), 10815
- [4] Pasternack et al., J. Thromb. Haemost., 2020, 18(1), 191-200
- *The development of ZED1227 was supported by grants from the German Government.





Product List (alphanumeric)

	Name	Unit	Price	Page
A008	Polyclonal antibody to human transglutaminase 5 (TG5)	500 µg	400 €	40
A011	Monoclonal antibody to gliadin (clone XGY1)	500 µg	400 €	44
A013	Monoclonal antibody to gliadin (clone XGY7)	500 µg	400 €	44
A014	Polyclonal antibody to human tissue transglutaminase (TG2)	500 µg	400 €	38
A015	Polyclonal antibody to human epidermal transglutaminase (TG3)	500 µg	400 €	40
A016	Polyclonal antibody to human blood coagulation factor XIII (A-subunit)	500 µg	400 €	42, 52
A018	Polyclonal antibody to human keratinocyte transglutaminase (TG1)	500 µg	400 €	38
A020	Polyclonal antibody to microbial protransglutaminase (pro-MTG)	500 µg	400 €	15, 43
A022	Polyclonal antibody to human prostate transglutaminase (TG4)	500 µg	400 €	40
A023	Monoclonal antibody to N ^e -(y-L-glutamyl)-L-lysine-isopeptide bond	100 µg	440 €	43
A028	FITC-labeled polyclonal antibody to human TG2	200 µg	425 €	38
A029	FITC-labeled polyclonal antibody to human TG1	200 µg	425 €	38
A030	FITC-labeled polyclonal antibody to human TG3	200 µg	425 €	40
A031	FITC-labeled polyclonal antibody to human TG6	200 µg	425 €	41
A032	FITC-labeled polyclonal antibody to human factor XIII (A-subunit)	200 µg	425 €	42, 52
A033	Monoclonal antibody to human TG2 (Catalytic Domain, clone XTG17)	200 µg	400 €	39
A034	Monoclonal antibody to human TG2 (Beta Sheet Domain, clone XTG11)	200 µg	400 €	39
A036	Monoclonal antibody to human TG2 (Beta Barrel 1 Domain, clone XTG21)	200 µg	400 €	39
A037	Monoclonal antibody to human TG2 (Beta Barrel 2 Domain, clone XTG18)	200 µg	400 €	39
A040	Polyclonal antibody to human transglutaminase 7 (TG7)	200 µg	400 €	41
A042	Monoclonal antibody to human TG1 (clone XTG31)	200 µg	400 €	38
A043	Monoclonal antibody to human TG1 (clone XTG51)	200 µg	400 €	38
A044	FITC-labeled polyclonal antibody to human TG5	200 μg	425 €	40
A051	Biotinylated polyclonal antibody to microbial transglutaminase (MTG)	50 μg	400 €	15, 43
A052	Biotinylated polyclonal antibody to human factor XIII (A-subunit)	50 μg	400 €	42, 52
A053	Biotinylated polyclonal antibody to human TG2	50 µg	400 €	38
A054	Monoclonal antibody to gliadin (clone XGY6)	500 µg	400 €	44
A056	Monoclonal antibody to gliadin (clone XGY11)	500 μg	400 €	44
A059	Monoclonal antibody to gliadin (clone XGY9)	500 μg	400 €	44
A060	Monoclonal antibody to gliadin (clone XGY10)	500 μg	400 €	44
A064	Monoclonal antibody to gliadin (clone XGY4)	500 μg	400 €	44
A067	Monoclonal antibody to gliadin (clone XGY15)	500 μg	400 €	44
A070	Monoclonal antibody to gliadin (clone XGY24)	500 μg	400 €	44
A071	Monoclonal antibody to hordein (clone XH4)	500 μg	400 €	44
A072	Polyclonal antibody to mouse tissue Transglutaminase	200 µg	400 €	38
A074	Polyclonal antibody to human blood coagulation factor XIII (B-subunit)	200 µg	400 €	42, 52
A075	FITC-labeled polyclonal antibody to mouse TG2	200 µg	425 €	38
A076	DD-XLink-mab	100 µg	400 €	42, 52
A077	FITC-labeled polyclonal antibody to human factor XIII (B-subunit)	200 µg	425 €	42, 52
A078	Polyclonal antibody to human epidermal transglutaminase (TG3) Protein A	250 µg	400 €	40
A079	Biotin-DD-XLink-mab	50 µg	400 €	42, 52
A082	Monoclonal antibody to human TG3 (clone XTG45)	200 µg	400 €	40
A085	Monoclonal antibody to gliadin (clone XGY19)	500 µg	400 €	44
A086	Monoclonal antibodies to gliadin (test sample set)	1 Set	600€	44
A101	FXIII-Assay Substance, Abz-NE(CAD-DNP)EQVSPLTLLK-OH	10 mg	575 €	24, 51
A105	NQEQVSPLTLLK, alpha ₂ -Antiplasmin peptide (1-12)	25 mg	500 €	26
A106	(ATTO-488 TM)cadaverine	1 mg	275 €	20, 28
	Ac-(D)-Asp-MA-NIe-NIe-Leu-Pro-Trp-Pro-OH	5 mg	500 €	35, 51

Art. No.	Name	Unit	Price	Page
A109	ß-Amyloid peptide 1-42 (Aß 1-42)	1 mg	275 €	26, 28
A112	(ATTO-532™)cadaverine	1 mg	275 €	20, 28
A113	(ATTO-550™)cadaverine	1 mg	275 €	20, 28
A114	(ATTO-647N TM)cadaverine	1 mg	325 €	20, 28
A115	(ATTO-700™)cadaverine	1 mg	325 €	20, 28
A125	Factor XIII activation peptide	10 mg	475 €	11
A132	Microbial Transglutaminase (MTG)-substrate peptide Ac-M48	10 mg	350 €	27
A139	Monoclonal antibody to human TG6 (Catalytic Domain, clone XTG52)	200 µg	400 €	41
A140	Monoclonal antibody to human TG6 (Beta Barrel 1 Domain, clone XTG39)	200 µg	400 €	41
A143	Monoclonal antibody to microbial Transglutaminase (clone XM67)	200 µg	400 €	15, 43
A144	Monoclonal antibody to microbial Transglutaminase (clone XM68)	200 µg	400 €	15, 43
A145	Polyclonal antibody to microbial Transglutaminase	200 µg	400 €	15, 43
A152	3-Azidopropan-1-amine	100 mg	175 €	20
A153	4-Azidobutan-1-amine	100 mg	175 €	20
A154	Monoclonal antibody to human factor XIII-A (Activation Peptide, clone XTG09)	200 µg	400 €	42
A155	Monoclonal antibody to human factor XIII-A (Catalytic Domain, clone XTG02)	200 µg	400 €	42
A156	Polyclonal antibody to human neuronal transglutaminase (TG6)	250 µg	400 €	41
A158	Monoclonal antibody to human TG6 (Beta Barrel 2 Domain, clone XTG29)	200 µg	400 €	41
A160	Monoclonal antibody to deamidated gliadin	100 µg	780 €	44
A161	Monoclonal antibody to deamidated and non-deamidated gliadin	100 µg	780 €	44
A168	Abz-Peptide-Calibrator	10 mg	475 €	24
A169	(ATTO-542™)cadaverine	1 mg	350 €	20, 28
A171	N-Me- Abz-Peptide-Calibrator	10 mg	525 €	24
B001	Biotinyl-Thr-Val-Gln-Glu-Leu-OH	5 mg 25 mg	175 € 525 €	26
B002	N-{Biotinyl}cadaverine	25 mg 100 mg	175 € 475 €	20, 28
B003	Boc-DON-Gln-lle-Val-OMe, "Boc-DON"	10 mg	400 €	33
B007	Keratinocyte transglutaminase (TG1)-substrate-peptide K5	10 mg	350 €	27
B008	Tissue transglutaminase (TG2)-substrate-peptide T26	10 mg	350 €	27
B009	Epidermal transglutaminase (TG3)-substrate-peptide E51	10 mg	350 €	27
B010	Blood coagulation FXIII-substrate-peptide F11KA	10 mg	350 €	27
B013	Neuronal transglutaminase (TG6)-substrate peptide Y25	10 mg	350 €	27
B014	Transglutaminase 7 (TG7)-substrate peptide Z3S	10 mg	350 €	27
B015	Biotin-Ahx-MA-QPL-OMe	10 mg	500 €	35
B017	Microbial Transglutaminase (MTG)-substrate peptide M48	10 mg	350 €	27
C001	Z-Gln-Gly-OH	1 g	100 €	26
C001	Z-GIn-Gly-CAD-DNS	25 mg	175 €	21, 26
C002	Z-Oill-Oily-CAD-DING	100 mg	400 €	21, 20
C079	Z-Gln-Gly-PEG(3)-N ₃	25 mg	500 €	21
C090	Z-Gln-Gly-CADTAMRA	25 mg	500 €	21
C091	Z-Gln-Gly-CAD-Biotin	25 mg	350 €	21
C092	Z-Gln-Gly-(PEG1,088), monodisperse	25 mg	500 €	21
C093	Z-Gln-Gly-(PEG5,000), polydisperse	25 mg	500 €	21
C102	MTG Blocker	10 mg	250 €	15
		25 mg	425 €	
D002	N-(2,4-Dinitrophenyl)cadaverine	100 mg	175 €	28

Product List

Art. No.	Name	Unit	Price	Page
D004	1,3-Dimethyl-4,5-diphenyl-2-[(2-oxopropyl)thio]imidazolium	10 mg	550 €	34, 51
D005	Metalloprotease-Assay-Substance, DABCYL-Ser-Phe-EDANS	2 mg	325 €	48
D006	N-{Dansyl}cadaverine	100 mg	175 €	20, 29
D016	LDN 27219	10 mg	400 €	36
D017	Thrombin-Assay Substance, fluorescent	10 mg	200 €	48
E018	Zedi <i>Xclusive</i> Tissue Transglutaminase EIA	1 Kit	550 €	24
E021	Zedi <i>Xclusive</i> Microbial Transglutaminase (MTG) ELISA	1 Kit	425 €	16, 24
E103	Zedi <i>Xclusive</i> TG6-ab ELISA (IgA)	1 Kit (96 wells)	550 €	57
E104	Zedi <i>Xclusive</i> TG6-ab ELISA (IgG)	1 Kit (96 wells)	550 €	57
F001	Zedi <i>Xcite</i> 330/418 Fluorogenic FXIII-Assay Kit	1 Kit	600€	24, 51
F004	Fibrinogen, purified from human plasma	50 mg	125€	29, 52
F006	FITC-labeled Fibrinogen	5 mg	225 €	29, 52
F014	Zedi <i>Xcite</i> 330/418 Fluorogenic TG2-Assay Kit	1 Kit	600€	24
F015	Zedi <i>Xcit</i> e 330/418 Fluorogenic MTG-Assay Kit	1 Kit	600€	16, 24
F016	Zedi <i>Xcite</i> 360/460 Fluorogenic TG2-Assay Kit	1 Kit	600€	24
G001	Alpha2-gliadin, 33mer (aa56-88), biotinylated	5 mg	550 €	58
G002	Deamidated alpha2-gliadin, 33mer (aa56-88), biotinylated	5 mg	550€	58
G003	Ac-PLQPEQPFPK(ε-Biotin), Deamidated gliadin peptide	10 mg	350 €	58
G004	Ac-PEQLPQFEEK(ε-Biotin), Deamidated gliadin peptide	10 mg	350 €	58
G005	DGPx4	250 μg 1 mg	400 € 1200 €	59
G006	DGPx2	250 μg 1 mg	400 € 1200 €	59
G007	DGPx1	250 μg 1 mg	400 € 1200 €	59
G008	Omega-5 gliadin	500 µg	780 €	49
G009	Alpha2-gliadin, 33mer (aa 56-88)	5 mg	550 €	58
G011	Deamidated alpha2-gliadin, 33mer, (Acetyl-aa56-88-amide, Q65E)	5 mg	550 €	58
G013	QPFPQPQLPYPQPQ-amide	10 mg	350 €	58
G014	QPFPQPELPYPQPQ-amide	10 mg	350 €	58
G017	Biotinylated DGPx1	100 µg	400 €	59
G018	Barley albumin and globulin	5 mg	250 €	49
G019	Barley prolamin (Hordein)	5 mg	250 €	49
G020	Barley glutelin (Hordenin)	5 mg	250 €	49
G021	Rye albumin and globulin	5 mg	250 €	49
G022	Rye prolamin (Secalin)	5 mg	250 €	49
G023	Rye glutelin (Secalinin)	5 mg	250 €	49
G024	Corn albumin and globulin	5 mg	250 €	49
G025	Corn prolamin (Zein)	5 mg	250 €	49
G026	Corn glutelin (Zeanin)	5 mg	250 €	49
G027	Rice albumin and globulin	5 mg	250 €	49
G028	Rice prolamin (Oryzin)	5 mg	250 €	49
G029	Rice glutelin (Oryzenin)	5 mg	250 €	49
G030	Spelt albumin and globulin	5 mg	250 €	49
G031	Spelt prolamin	5 mg	250 €	49
G032	Spelt glutelin	5 mg	250 €	49
G033	Oat albumin and globulin	5 mg	250 €	49
	Oat prolamin (Avenin)	5 mg	250 €	

Art. No.	Name	Unit	Price	Page
G035	Oat glutelin (Avenalin)	5 mg	250 €	49
G036	Wheat albumin and globulin (Leukosin and Edestin)	5 mg	250 €	49
G037	Wheat prolamin (Gliadin)	5 mg	250 €	49
G038	Wheat glutelin (Glutenin)	5 mg	250 €	49
G039	Durum wheat albumin and globulin	5 mg	250 €	49
G040	Durum wheat prolamin	5 mg	250 €	49
G041	Durum wheat glutelin	5 mg	250 €	49
G042	Soy protein, saline soluble fraction	5 mg	250 €	49
G043	Soy protein, ethanol soluble fraction	5 mg	250 €	49
G044	Soy protein, propanol/urea/DTE soluble fraction	5 mg	250 €	49
G045	Millet (Sorghum) albumin and globulin	5 mg	250 €	49
G046	Millet (Sorghum) prolamin (Kafirin)	5 mg	250 €	49
G047	Millet (Sorghum) glutelin	5 mg	250 €	49
G051	26mer gliadin peptide	250 µg	400 €	59
G052	33mer gliadin peptide	250 µg	400 €	59
G054	33mer DGP	250 µg	400 €	59
G055	Carrier protein control	250 µg	400 €	59
G056	DGP and Gliadin peptides (Set No 1)	1 Set	780 €	59
G057	Alpha2-gliadin, 33mer (aa56-88), TAMRA labeled	5 mg	600€	58
G058	Alpha2-gliadin, 33mer (aa56-88), TAMRA and Biotin labeled	5 mg	750 €	58
G101	Gly-Pro-Arg-Pro-amide	25 mg	375 €	52
1001	Involucrine, recombinant human	500 µg	400 €	29
K004	"KxD", Boc-lys-en-DNS	10 mg	275 €	20, 29
L001	Substrate Finder Kit	1 Kit	390 €	19
L101	Biotin TGase Protein Q-Labeling Kit	1 Kit	550€	19
L102	PEG1,088 TGase Protein Q-Labeling Kit	1 Kit	550€	19
L103	PEG5,000 TGase Protein Q-Labeling Kit	1 kit	550 €	19
L104	ATTO-488™ TGase Protein Q-Labeling Kit	1 Kit	610€	19
L105	ATTO-532™ TGase Protein Q-Labeling Kit	1 Kit	610€	19
L106	ATTO-550™ TGase Protein Q-Labeling Kit	1 Kit	610€	19
L107	ATTO-647N™ TGase Protein Q-Labeling Kit	1 Kit	610€	19
L108	ATTO-700™ TGase Protein Q-Labeling Kit	1 Kit	610€	19
L201	Biotin TGase Protein K-Labeling Kit	1 Kit	550 €	19
L202	PEG1,088 TGase Protein K-Labeling Kit	1 Kit	550 €	19
L203	PEG5,000 TGase Protein K-Labeling Kit	1 Kit	550€	19
M001	MTG-ANiTA-Kit	1 Kit	610€	16, 25
M003	Tissue Transglutaminase Pico-Assay Kit	1 Kit	425 €	25
P003	Prolylendopeptidase from Myxococcus xanthus, recombinant	150 U	400 €	48
P004	PT-Gluten	1 mg 10 mg	250 € 1200 €	29, 49
PO10	(PEG1,088)amine, monodisperse	10 mg	200 €	20
PO11	(PEG5,000)amine, polydisperse	10 mg	200 €	20
PO12	human Plasmin, recombinant	100 µg	450 €	48, 52
P111	PEPperCHIP® Pan-Transglutaminase Microarray	1 Chip	475 €	47
P112	PEPperCHIP® Custom Transglutaminase Microarray	1 Chip	895 €	47
P113	PEPperCHIP® Transglutaminase Microarray Service	1 Sample	695 €	47
P115	PEPperCHIP® Incubation Tray 3/1	1 Tray	325 €	47
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Product List

Art. No.	Name	Unit	Price	Page
P116	PEPperCHIP® Staining Kit	1 Kit	95 €	47
P117	PEPperCHIP® Transglutaminase 2 Microarray	1 Chip	475 €	47
P118	PEPperCHIP® Incubation Tray 3/5	1 Tray	325 €	47
P119	MAPIX Analyzer	3-Month License	295 €	47
		1-Year License	745 €	
		Perpetual License	3500 €	
ROO1	N-(Tetrametylrhodaminyl)cadaverine	10 mg	200 €	20, 29
T002	Human tissue transglutaminase (TG2)	250 µg 1 mg	400 € 1200 €	6
T004	Plasmin substrate Tosyl-GPKpNA, chromogenic	25 mg	350 €	48
T009	Human keratinocyte transglutaminase (TG1)	150 µg	400 €	5
T010	Recombinant TG2 (E. coli)	250 µg	400 €	57
		1 mg	1200€	
TO11	Human transglutaminase 7	250 µg	400 €	9
T013	Human epidermal transglutaminase, Dispase activated	200 µg	550 €	8
T016	Microbial (bacterial) Pro-transglutaminase	250 µg	300 €	15
T018	Inactive human tissue transglutaminase	250 µg	400 €	6
		1 mg	1200 €	
T021	Human neuronal transglutaminase (TG6)	250 µg	500 €	9, 57
T		1 mg	1500 €	
T022	Human tissue transglutaminase (TG2)	250 µg 1 mg	400 € 1200 €	6
T024	Human epidermal transglutaminase (TG3)	200 µg	400 €	8, 57
T027	Human blood coagulation Factor XIII-A ₂ , recombinant	200 µg	400 €	10, 51
T034	Human tissue transglutaminase (TG2)	100 µg	400 €	6
T035	Human keratinocyte transglutaminase (TG1)	150 µg	400 €	5
T036	Transglutaminase Assay Kit ("DCC"), fluorescent, Casein, Dansylcadaverine	1 Kit	300 €	24, 51
T038	Rat tissue transglutaminase	250 µg	400 €	8
		1 mg	1200 €	
T039	Guinea pig liver transglutaminase, recombinant	10 U	410€	8
T040	Mouse tissue transglutaminase	250 µg	400 €	8
TO 10		1 mg	1200 €	
T042	Human prostate Transglutaminase (TG4)	100 µg	400 €	9
T050	Human blood coagulation Factor XIII B subunit	200 μg	400 €	10, 51
T051	Open tTG™	250 µg 1 mg	550 € 1650 €	6, 57
T056	Human alpha thrombin, highly active	2x 100 U	200 €	48, 52
T061	Mouse blood coagulation Factor XIII-A ₂	200 µg	400 €	11
T062	Dog blood coagulation Factor XIII-A ₂	200 µg	400 €	11
T063	Human blood coagulation Factor XIII-A ₂ , Val34Leu-mutant	200 µg	400 €	10, 51
T064	Inhibited human neuronal transglutaminase	250 µg	685 €	9
T065	Rat blood coagulation Factor XIII-A.	200 µg	400 €	11
T066	Pig blood coagulation Factor XIII-A ₂	200 µg	400 €	11
T067	Human tissue transglutaminase (TG2), endotoxin free	250 µg	450 €	6
	• • • •	1 mg	1350 €	
T070	Human Factor XIIIa, Thrombin activated	200 µg	550 €	10, 51
T072	Dog tissue transglutaminase	250 µg	400 €	8
		1 mg	1200 €	
T086	Human Transglutaminase 5	100 µg	400 €	9
T087	Tridegin	200 µg	510€	34, 51

Art. No.	Name	Unit	Price	Page
T092	Human blood coagulation Factor XIII-A ₂	100 µg	450 €	10
T101	1,3,4,5-Tetramethyl-2[(2-oxo-propyl)thio] imidazolium chloride	10 mg	500 €	34, 51
T106	Biotinylated human tissue transglutaminase (TG2)	100 μg 250 μg	400 € 800 €	6
T108	Cynomolgus tissue transglutaminase	250 µg	550€	8
T114	Blood Coagulation Factor XIII-Microassay Kit, colorimetric	1 Kit	470 €	25
T122	Recombinant TG2 (insect cells)	250 μg 1 mg	400 € 1200 €	57
T148	Biotinylated human Open tTG™	50 μg 250 μg	400 € 1600 €	6
T150	Biotinylated mouse open TG2	50 μg 250 μg	400 € 1600 €	8
T156	Biotinylated mouse tissue transglutaminase	250 μg 1 mg	550 € 1650 €	8
T167	Short human tissue transglutaminase, aa 1-465	250 µg	400 €	7
T168	Human tissue transglutaminase, C230A mutant	250 μg 1 mg	400 € 1200 €	7
T169	Human tissue transglutaminase, R580A mutant	250 μg 1 mg	400 € 1200 €	7
T173	Human tissue transglutaminase, R116C mutant	1 mg	1200 €	7
T184	Cat tissue transglutaminase	200 µg	400 €	8
T187	Factor XIII activation peptide, recombinant	500 µg	400 €	11
T197	Coagulation factor XIII, recombinant human Factor XIII-A $_{2}$	100 E 250 E	725 € 1450 €	10, 51
T246	Recombinant human tissue transglutaminase (Cys-277-Ser, inactive mutant)	250 µg 1 mg	400 € 1200 €	57
T250	Andracon™ – Recombinant Microbial Transglutaminase (HEPES-formulated, (frozen) liquid)	250 U 500 U 1000 U	2140 € 3750 € 7250 €	14
T255	Microbial transglutaminase with C-terminal His _è -Tag	25 U 10x 25 U 20x 25 U	400 € 3150 € 5550 €	15
Т300	Andracon™ – Recombinant Microbial Transglutaminase (HEPES-formulated, lyophilized)	25U 100 U 250 U 10x 25U 500 U 20x 25 U	270 € 975 € 2140 € 2140 € 3750 €	14
Z004	Z-Gln-Gln-Pro-Leu-OH	25 mg	325 €	26
Z006	Z-DON-Val-Pro-Leu-OMe, "Z-DON"	10 mg	425 €	33
Z009	Zedi <i>Xclusive</i> Microbial Transglutaminase Assay Kit	1 Kit	390 €	16, 25
Z010	Zedi <i>Xclusive</i> Tissue Transglutaminase Assay Kit	1 Kit	450 €	25
Z011	Z-(D)-DON-Val-Pro-Leu-OMe	10 mg	450 €	33
Z013	Z-MA-QPL-OMe	10 mg	500 €	35
Z015	Keillor inhibitor AA9	10 mg	400 €	36
Z016	Keillor inhibitor NC9	10 mg	400 €	36
Z017	Keillor inhibitor VA4	10 mg	400 €	36
Z018	Z-Glutamyl-Hydroxamate-Glycine	100 mg	150€	16
Z020	Thrombin-Generation-Assay Substance, fluorescent	25 mg	200 €	48



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Cover picture: Waldspirale, Darmstadt (translated: forest spiral)

The Waldspirale in Darmstadt, Germany, is an architectural masterpiece that captures the imagination with its unique and whimsical design. Built in the 1990s by the renowned architect Friedensreich Hundertwasser, this residential building stands as a true testament to his visionary style. The Waldspirale is characterized by its organic forms, vibrant colors, and abundance of vegetation. Its facade is adorned with irregular windows, golden onion domes, and a profusion of trees and shrubs, creating a harmonious blend of architecture and nature. Inside, residents enjoy a extraordinary living experience, with each apartment boasting its own distinctive layout. The Waldspirale stands as a remarkable symbol of Hundertwasser's philosophy, promoting a close connection between humans and the environment they inhabit.

Cover picture © Nicola Koch

