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REVIEW ARTICLE

Transdab wiki: the interactive transglutaminase substrate database on web 2.0 surface

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Abstract TRANSDAB wiki is a database of transglutaminase substrate proteins. This wiki is designed to provide quality content of all the details (including synonyms, structures, references) about transglutaminase substrate proteins and interaction partners. Currently TRANSDAB contains 243 articles about substrate proteins for 6 transglutaminase types in a user-friendly, editable format. Our aim was to collect structural information about substrate proteins and this information is provided in form of images, videos and links. The scientific community is invited to edit the database and besides providing up-to-date information, this wiki should serve as a platform for valuable discussions.

Keywords TG2 · Transglutaminase · Kinase · Deamidase · Interaction partners · Wiki

Abbreviations

ASAView	Web server for prediction of surface accessibility of proteins
GTP	Guanosine-5′-triphosphate
ID	Identification code
IUPred	Predictor for intrinsically unstructured regions in proteins
PDB	Protein databank
TRANSDAB	Transglutaminase Substrate Database
TRANSIT	Database of Transglutamination Sites
WHAT	Worldwide Happening Around Transglutaminase
VMD	Visual Molecular Dynamics software for molecular graphics

Availability TRANSDAB can be accessed from http://genomics.dote.hu/wiki/.

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Introduction

Transglutaminases (E.C. 2.3.2.13.) are a family of Ca^{2+}-dependent enzymes with various catalytic functions. They catalyze (1) the posttranslational modification of proteins forming epsilon (gamma-glutamyl)lysine bonds between the gamma-carboxamide group of glutamine residues and the epsilon-amine group of lysine residues or primary amines, (2) the deamidation of glutamine residues to glutamate in various proteins, (3) the hydrolysis of epsilon (gamma-glutamyl)lysine isopeptides as it was shown in the case of tissue transglutaminase (TG2) and blood coagulation factor XIIIa (FXIIIa), (4) the hydrolysis of certain esters such as *p*-nitrophenyl-acetate, and (5) the attachment of long-chain omega-hydroxyceramides to proteins by ester bond formation as it was shown in case of keratinocyte transglutaminase (TG1) (Lorand and Graham 2003; Nemes et al. 1999). TG2 promotes cell-matrix interactions binding to fibronectin and integrins and together with epidermal transglutaminase (TG3) have GTPase activity; in the presence of GTP TG2 functions as a G protein participating in signaling processes (Fesus and Piacentini 2002). TG2 has protein disulphide

isomerase activity (Hasegawa et al. 2003) and recently it was shown to have kinase activity phosphorylating several proteins (Mishra and Murphy 2004).

Transglutaminases can be found everywhere in living systems from bacteria to mammals and are implicated in various physiological functions from blood clotting, wound healing, extracellular matrix remodeling, to signaling, cell cycle regulation, apoptosis and inflammation. In mammals nine transglutaminase genes have been identified and eight of them code active enzymes. Blood coagulation factor XIIIa, TG1, TG2 and TG3 are well characterized enzymes while there is less information about the prostate enzyme (TG4), TG5, TG6 and TG7 (Griffin et al. 2002).

The identification of transglutaminase substrate proteins is critical for the establishment of the functional role of these enzymes in various cells and tissues. A large number of transglutaminase substrate proteins have been described and we have generated an interactive Transglutaminase Substrate Database, TRANSDAB, concerning the substrates of the transamidation, deamidation and phosphorylation reactions.

TRANSDAB contains 205 substrates for 6 types of transglutaminase enzymes: activated blood coagulation factor XIII, keratinocyte transglutaminase, tissue transglutaminase, epidermal transglutaminase, TG5 and microbial transglutaminase (TGM).

Our aim was to collect the transglutaminase substrate proteins reported in literature and to provide as much structural information as possible in an easy to find, user-friendly format. There exists another transglutaminase substrate database, TRANSIT (Facchiano et al. 2003), containing sequential information about 115 substrate proteins with entries which are not in browsable form.

Database content

Each article/entry of the TRANSDAB contains the substrate peptide name and its alternative scientific names, synonyms, the determination type (in vitro/in situ), the source organism where the protein was studied and the subcellular localization. The Swissprot entry for further information can be accessed via link through the Swissprot ID and for reference links to relevant scientific article(s) about determination of transglutaminase substrate proteins are also available through their PubMed ID.

The structural information is represented by a picture gallery of reactive glutamine and lysine residues and video image of the rotating molecule, all drawn with VMD (Humphrey et al. 1996) using the structural information from crystal structure files deposited in Protein Databank (PDB).

The crystal structure is also accessible via link to the Protein Databank (http://www.pdb.org/) through the PDBID. A sequence portion containing the substrate glutamine/lysine residues is also given, with reactive residues in italic, to ease the database searches. The surface accessibility data obtained with ASAView web server (Ahmad et al. 2004) for those substrate proteins where the modification site is known and the crystal structure contains these residues are also available in pdf and text formats.

For intrinsic disorder prediction there is a link to one of the most widely used predictor IUPred (Dosztányi et al. 2005). Other relevant information about substrate proteins, i.e., the change in activity upon transglutaminase action, are listed in Notes.

The entries/articles of the database can be browsed or searched by name and can be edited. Each substrate protein is a part of a category type making the information access very easy.

Our database contains links to TRANSIT and to WHAT (Worldwide Happening Around Transglutaminase).

Wiki

A wiki is a website designed for collaboration whose content can be edited by users who have access to it using a browser interface. The defining characteristics of wiki technology (Boulos et al. 2006) include the ease with which pages can be created and modified, tracking other users contributions, versioning capabilities, and article discussions. As wiki supports hyperlinks and has a simple text syntax for creating cross-links between articles, it can be used as a method of virtual collaboration. A wiki allows for regular updates as users can edit and comment articles simultaneously via a simplified interface. Therefore, a wiki is essentially a database for creating, browsing and searching information. Ward Cunningham, developer of the first wiki WikiWikiWeb (http://www.wiki.org/wiki.cgi?WhatIsWiki), described it as "the simplest online database that could possibly work". The best known example of a wiki Web site is Wikipedia (http://en.wikipedia.org), an online collaborative encyclopedia.

Who can edit this wiki?

Based on their scientific qualifications TRANSDAB users must be credentialed by the system administrator before they are allowed to edit or publish. All new users will be required to submit a detailed description of their research activities and scientific degree as well as current place of work; all credentialed users will be listed on the editorial board. This process excludes the possibility of anonymous

article creation as all articles are submitted by credentialed professionals.

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References

Ahmad S, Gromiha M, Fawareh H, Sarai A (2004) ASAView: solvent accessibility graphics for proteins. BMC Bioinformatics 5:51

Boulos MN, Maramba I, Wheeler S (2006) Wikis blogs and podcasts: a new generation of web-based tools for virtual collaborative clinical practice and education. BMC Med Educ 6:41

Dosztányi Z, Csizmok V, Tompa P, Simon I (2005) IUPred: web server for the prediction of intrinsically unstructured regions of proteins based on estimated energy content. Bioinformatics 21:3433–3434

Facchiano AM, Facchiano A, Facchiano F (2003) Active sequences collection ASC database: a new tool to assign functions to protein sequences. Nucleic Acids Res 31:379–382

Fesus L, Piacentini M (2002) Transglutaminase 2: an enigmatic enzyme with diverse functions. Trends Biochem Sci 27:534–539

Griffin M, Casadio R, Bergamini CM (2002) Transglutaminases: nature's biological glues. Biochem J 368:377–396

Hasegawa G, Suwa M, Ichikawa Y, Ohtsuka T, Kumagai S, Kikuchi M, Sato Y, Saito Y (2003) A novel function of tissue-type transglutaminase: protein disulphide isomerase. Biochem J 373:793–803

Humphrey W, Dalke A, Schulten K (1996) VMD—Visual Molecular Dynamics. J Mol Graph 14:33–38

Lorand L, Graham RM (2003) Transglutaminases: crosslinking enzymes with pleiotropic functions. Nat Rev Mol Cell Biol 4:140–156

Mishra S, Murphy LJ (2004) Tissue transglutaminase has intrinsic kinase activity: identification of transglutaminase 2 as an insulin-like growth factor-binding protein-3 kinase. J Biol Chem 279:23863–23868

Nemes Z, Marekov LN, Fésüs L, Steinert PM (1999) A novel function for transglutaminase 1: attachment of long-chain omega-hydroxyceramides to involucrin by ester bond formation. Proc Natl Acad Sci USA 96:8402–8407