Atomwise
Better medicines faster.

AIMS Award Application

1. Investigator Information

Your contact information is used to provide updates about your application.

NAME *

Principal
First

Investigator
Last

INSTITUTION *

University of Drug Discovery

DEPARTMENT *

Trending Drug Targets

JOB TITLE *

Professor

EMAIL *

p.investigator@udd.edu

PHONE

(123) 456-7890
(###)###-####

HOW DID YOU HEAR ABOUT US? *

Colleagues

- [x] I am eligible for the award

- [x] I agree to the terms and conditions

2. Project Information

Share your goals and explain the potential impact of your research project.

RESEARCH AREA *

Biotechnology

DISEASE OR CONDITION OF INTEREST *

Body Odor

PROTEIN TARGET OF INTEREST *

PepTSh (Peptide Transporter Staphylococcus hominis)

WHAT IS THE ROLE OR SIGNIFICANCE OF THE PROTEIN TARGET IN THE DISEASE? *

PepTSh is a member of the proton coupled oligopeptide transporter (POT) family found in staphylococcal bacteria. This transporter is known to import an odorless molecule that is secreted in human sweat, S-Cys-Gly3M3SH. Once inside the cell, this molecule is cleaved by bacterial enzymes to produce an extremely pungent thioalcohol, 3-methyl-3-sulfanylhexan-1-ol (3M3SH), which then diffuses out of the cell, generating an unpleasant odor.

WHAT IS THE PURPOSE OR POTENTIAL IMPACT OF A SMALL MOLECULE INTERVENTION? *

A small molecule inhibitor of the PepTSh transporter would prevent bacterial import and processing of the S-Cys-Gly-3M3SH precursor, thereby preventing the production of the 3M3SH molecule. Application of a PepTSh inhibitor should prevent one of the most unpleasant components of body odor aroma. For truly stubborn body odor, such a treatment could represent a technological breakthrough, bringing a breath of fresh air to crowded spaces like subways, concerts, and food courts.

3. Protein Information

Protein details tell us how to perform a virtual screen for your target.

UNIPROT ID: *

A0A1L8Y4Q3

Search at https://www.uniprot.org/

IS AN EXPERIMENTAL STRUCTURE (E.G. X-RAY CRYSTAL STRUCTURE, NMR, CRYO-EM) AVAILABLE FOR THE PROTEIN?

- (•) Yes
- ( ) No

PDB ID OR LINK:

6GZ9

Search at https://www.rcsb.org/

PROVIDE INFORMATION ABOUT THE LOCATION OF THE BINDING SITE IF KNOWN (DOMAIN OR RESIDUES).

The best site is likely near the valacyclovir ligand (TXC) in PDB 6GZ9.

PAPERS THAT DESCRIBE THE PROTEIN STRUCTURE, BINDING SITES, ETC.

Drop files here or Select files

Lin2015.pdf

Schlessinger2013.pdf
Minhas2019.pdf
Minhas2018.pdf

COMMENTS OR ADDITIONAL GUIDANCE

In addition to PDB 6GZ9, there are three other PDBs available with alternate ligands bound: 6EXS, 6HZP, and 6H7U. The Minhas2018 and Minhas2019 papers discuss these crystal structures. A 6-character "Reviewed" UniProt ID was not available for this target, so the "Unreviewed" UniProt ID associated with the PDB entries is provided instead.

4. Small Molecule Information

Help us deliver molecules with the properties you prefer.

ARE THERE KNOWN LIGANDS THAT BIND TO THE TARGET PROTEIN?

- (•) Yes
- ( ) No
- ( ) Don't know

IF THERE ARE ANY KNOWN LIGANDS, PLEASE LIST THEM HERE.

NCC(=O)CCC(O)=O
CC(C)[C@H](N)C(=O)OCCOCn1cnc2c1nc(N)[nH]c2=O
CCC[C@@](C)(CCO)SC[C@H](N)C(=O)NCC(O)=O

Please include information such as the name of the ligand, its SMILES code, and/or citations for papers describing the ligand.

IF THERE ARE ANY SPECIFIC PROPERTIES OF THE SMALL MOLECULE THAT ARE DESIRED, PLEASE DESCRIBE THEM HERE.

COMMENTS OR ADDITIONAL GUIDANCE

The attached Lin2015 and Schlessinger2013 review papers discuss the development of small molecule ligands for SLC transporters, including docking efforts, which may be relevant.

5. Assay Information

Tell us about the testing plan for the compounds you will receive.

WILL YOU TEST THE MOLECULES IN AN ASSAY THAT QUANTIFIES THE PROTEIN-LIGAND INTERACTION (I.E. KD, KI, IC50)? *

- (•) Yes
- ( ) No
- ( ) Don't Know

TELL US ABOUT YOUR ASSAY(S) THAT YOU WOULD USE TO TEST THE COMPOUNDS. PLEASE BE SPECIFIC AND AS DETAILED AS POSSIBLE. *

We will use a competition assay similar to what is described in Minhas2018. Briefly, proteoliposomes containing PepTSh will be prepared and placed in a buffer with tritiated 3H-di-alanine along with various concentrations of the test molecule. After an incubation period, the proteoliposomes will be filtered, washed, and analyzed with a scintillation counter to determine the percent inhibition of 3H-di-alanine transport relative to control. We also have an cell-based 3M3SH production assay.

COMMENTS OR ADDITIONAL GUIDANCE

SUBMIT

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