allied academies

4th International Congress on
DRUG DISCOVERY, DESIGNING AND DEVELOPMENT &
International Conference and Exhibition on
BIOCHEMISTRY, MOLECULAR BIOLOGY: R&D
November 02-03, 2017 Chicago, USA

An unexpected tolerance of silicatein activity to mutations revealed due to a novel water-soluble silica precursor

Natalia V. Povarova[1], Nikolay A. Barinov[2], Nadezda M. Markina[1], Mikhail S. Baranov[1], Valery B. Kozhemyako[3] and **Konstantin A. Lukyanov[1]**
[1]Institute of bioorganic chemistry, Russia
[2]Federal Research and Clinical Center of Physical-Chemical Medicine, Russia
[3]Pacific Institute of Bioorganic Chemistry, Russia

Silicateins play the major role in formation of silica skeletal structures in marine sponges. They are members of the cathepsin family of cysteine proteases with 65% homology with human *Cathepsin L.* The critical substitution that turns proteolytic activity to silica polymerization is supposed to be Cys to Ser substitution in the catalytic triad (Cys-His-Asn). We synthesized a novel silica precursor for silicateins – tetrakis(glycerol)orthosilicate (TGS). We have tested TGS as a substrate for silicatein A1 from the marine sponge Latrunculia oparinae. It effectively formed silica particles with and the amount of polymerized silica 1000-fold greater than previously described for silicatein alpha S.domuncula and tetraethyl orthosilicate. Then we investigated the activity of few silicatein point mutants – we substituted catalytic Ser and its flanking residues to the residues from its cathepsin homolog (S25C, Y26W, GAS23-25KSC). All the proteins retain silicatein activity. Alanine mutants of the catalytic triad (S25A, H163A, or N187A) still have silicatein activity. We hyposized that mechanism of silicatein enzymatic activity involves some other features of the protein and checked human cathepsin L for the presence of silicatein activity. And found that it is also capable to polymerise silica from TGS. So, new more available precursor allowed us to find new enzymatic activity of human cathepsin L and showed that our understanding of silicatein activity mechanism call for reevaluation.

e: povarovanv@gmail.com