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ORAL-POSTER

# In vitro selection of macrocyclic peptides against THG-1 for Esophagus Squamous Cell Carcinomas therapeutic lead compounds

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## Abstract

Ineffective current treatments for esophagus squamous cell carcinoma (ESCC) is one of the main reasons for its low 5-year survival (20%). Transforming growth factor beta-1 stimulated clone 22 - isoform 4 (Tsc22D4/THG-1) is overexpressed in 92.6% of ESCC specimens while strictly resided in mitotically active basal layer of normal squamous epithelial tissue. Knockout of THG-1 caused reduction in cancer cells growth, invasion and tumorigenesis. Experimentally, protein-protein interactions (PPIs) were identified as THG-1 mechanism to promote cancer progression. Well-known cellular regulators', Keap1, PHD2, TBLR1 and NRBP1, functional interactions are disrupted in the present of THG-1. To develop THG-1 PPIs antagonist, Random non-standard Peptide Integrated Discovery (RaPID) system was employed. In this system, D-stereochemistry, unusual side chains and N- methylation containing macrocyclic peptides was generated and screened against THG-1. High-specificity, flat-surface binding ability, rigidity make those peptides to be more advantageous for PPIs blocking compare to small molecules and antibodies. Herein, I discuss the process to identify potential lead compounds for ESCC therapeutic by blocking THG-1 PPIs.

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Esophagus, squamous carcinoma, macrocyclic peptide, RaPID system, therapeutic, THG-1, Keap1, PHD2, TBLR1

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## References