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"A SINGLE ATOM SUBSTITUTION IMPROVES THE PHARMACOLOGICAL PROPERTIES OF MACROCYCLIC PEPTIDES AND INCREASES PROTEIN STABILITY BY DESOLVATING AMIDE BOND"

February 21st, 2020 ~ 11:30AM
Life Science Center II, Room 130

Abstract: The hydrophilicity of the amide bond and its susceptibility to proteolytic degradation conspire to reduce the therapeutic efficacy of peptides in vivo. Thus, chemical modification that desolvates amide bond and shields it against proteolytic degradation, while retaining biological activity of the peptide is highly desirable. In this talk, I will elaborate how an oxygen to sulfur substitution results in markedly improved pharmacokinetic properties of macrocyclic peptides resulting in their enhanced plasma exposure following oral delivery in rats. I will also present our efforts in improving the thermal stability of proteins by this single atom substitution, which directly reveal an unappreciated property of thioamides.

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DR. SZOSTAK

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