"New RNA-binding peptidomimetic structures that repress HIV viral replication by specifically inhibiting transcriptional activation"

Abstract: The interaction between the human immunodeficiency virus (HIV-1) transactivator protein Tat and its response element TAR plays an essential role in viral replication by controlling HIV transcription. Previous attempts to inhibit this interaction have failed to yield molecules with sufficient potency and specificity to warrant pharmaceutical development. We have shown that conformationally constrained cyclic peptide structural mimics of Tat provide nM inhibitors of the Tat-TAR interaction. These peptidomimetics are proteolytically stable, penetrate cells efficiently and have no cytotoxicity. They specifically inhibit Tat-dependent activation of transcription in cells and repress replication of a wide variety of viral strains representing all the major HIV clades in primary human lymphocytes. The potency and selectivity observed for this family of peptides is unprecedented among Tat inhibitors and suggest that these types of compounds may be widely useful for the pharmacological inhibition of other protein-RNA interactions.

11:00 AM, Tuesday, March 18, 2008
Klaus Advanced Computing Building
Room 1116W