Lifeng Cai, J Antivir Antiretrovir 2011, 3:4
doi: http://dx.doi.org/10.4172/1948-5964.S1.6

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
VIROLOGY
5-7 September 2011 Baltimore, USA

Characterization of a T20-derived peptide with increased α-helicity and thermal stability

Lifeng Cai[1,2], Shuiyi Tan[2], Shibo Jiang[2] and Keliang Liu[1]

[1]Beijing Institute of Pharmacology & Toxicology, China
[2]Lindsley F. Kimball Research Institute, New York Blood Center, USA

T20 (enfuvirtide, Fuzeon) is the first approved HIV fusion inhibitor for salvage therapy of HIV/AIDS patients refractory to current antiretroviral drugs. Its unstructured character in physiological condition is considered accounting for its short *in vivo* half life with reduced activity. Increasing α-helical content and thermal stability is the main focus for next generation peptide HIV fusion inhibitor design. Here we reported the design and characterization of a helical T20-derived peptide T20Zip by substitution of the polar residues at *a*, *d* positions in T20 with hydrophobic residues in heptad registration. T20Zip had 80% α-helical content in physiological condition with a thermal transition temperature > 90°C. It showed similar activity as T20 to disrupt the secondary structure of N36 and N46 which contains NHR deep pocket; however, the mutation resulted in the lost of its activity to interact with T20's target N34. T20Zip's activity to disrupt fusogenic gp41 6-helical bundle formation as well as inhibit HIV-1 infection is significantly reduced, compared with T20; however, strong synergy was observed when combinational use of T20Zip with T20, or T1144, a next generation HIV fusion inhibitor with distinguished interaction model from T20. Therefore, T20Zip may be used as a lead for development of new generation HIV fusion inhibitors with different interacting model from the known HIV fusion inhibitors.

Biography

Lifeng Cai has completed his Ph.D from Peking University in 2003 and postdoctoral studies from Dental School in University of Pacific. He was Research Assistant Professor in 2007 at Touro University California and Assistant Member in 2008 at Lindsley F. Kimball Research Institute at New York Blood Center. He has been Associate Professor at Beijing Institute of Pharmacology & Toxicoloty since 2009.