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Molecular probe for visualization of HIV-1 protease inhibitor in living cells

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Abstract

The global human immunodeficiency virus infection/acquired immuno-deficiency syndrome (HIV/AIDS) epidemic is one of the biggest threats to human life. Mutation of the virus and toxicity of the existing drugs necessitate the development of new drugs for effective AIDS treatment. We designed molecular probes that utilize the Förster resonance energy transfer (FRET) mechanism to visualize HIV-1 protease inhibition within living cells to allow high content drug screening. We explored using AcGFP1 (a fluorescent mutant of the wild-type green fluorescent protein) as a donor and mCherry (a mutant of red fluorescent protein) as an acceptor for FRET microscopy imaging measurement of HIV-1 protease activity within living cells. The probes were designed by linking AcGFP1 and mCherry with an HIV-1 protease cleavable p2/p7 peptide. The cleavage of the linker peptide by HIV-1 protease leads to AcGFP1's separation from mCherry, quenching FRET between AcGFP1 and mCherry. In addition, by genetically engineering a probe with a tandem acceptor protein structure, a significant enhancement of FRET signal and FRET efficiency can be achieved as assessed by fluorescence lifetime imaging microscopy measurement. Our experimental results obtained in both *in vitro* and *in vivo* demonstrated that the molecular probes developed in this study would enable high-content screening of new anti-HIV agents through an automated FRET microscopy imaging measurement.

Biography

Dr. Sha Jin has completed her Ph.D. from Kyushu Institute of technology in Japan and postdoctoral studies from University of Pittsburgh School of Medicine. She is the Director of Disease Control and Treatment Engineering Laboratory in Biomedical Engineering Department at University of Arkansas. She has published more than 38 papers in peer-reviewed journals.