ABSTRACT

Project Code : BRG5480004
Project Title : Implement of novel strategy to interfere the assembly and maturation processes of human immunodeficiency virus (HIV-1) by artificial ankyrin repeat proteins
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Acquired Immune Deficiency Syndrome (AIDS) is a viral infectious disease that has threatened human lives for decades. Despite the attempts to fight this deadly disease, more than one-in-hundred adults in Thailand is infected with HIV. The attempts to cure the disease usually involve interruption of HIV life cycle which is a sequence of steps regulated both by viral and cellular proteins. The highly active antiretroviral therapy (HAART) in controlling HIV-1 is success. However, HAART is not totally effective in all cases especially in the multi-drug resistant, and has problematic side effects. Hence, several strategies have been emerged to apply as the novel therapeutic approaches including amalgamations of gene- and immune-therap. The most popular therapeutic molecules applied for this purpose are immunoglobulin fragments i.e. single chain variable fragment (ScFv) as intrabody format. However, due to the complex structures their intracellular functions are limited in certain compartments i.e. cytoplasm.

According to the increasing knowledge of protein-protein interactions and the development of advance selection technologies, novel binding molecules based on protein 'scaffolds' have been explored to mimic the binding principle of immunoglobulins with virtually target proteins. One of proteins in this architecture, the ankyrin repeat proteins, is very attractive scaffold to generate the specific molecular binders. These proteins mediate certain important protein-protein interactions in virtually all species and are found in all compartments of the cells indicating that these proteins can adapt for many different environments. In this study, the ankyrin repeat proteins will be created the artificial protein library and specific binding molecules to HIV-1 matrix and capsid domain (MA-CA) will be isolated. In contrast to ScFv intrabody, the isolated ankyrin binders will naturally fold and be active in cytoplasm. These binders will be applied to evaluate their intracellular function in the interference of viral life cycle. The successful innovation will be an alternative strategy for HIV gene therapy in the future.

Keywords: HIV, Ankyrin, intracellular, gene therapy