Abstract

HIV-1 is a dangerous retrovirus which represents one of the world's leading health problems. HIV-1 infection is incurable and without proper treatment by antiretroviral therapy it leads to death within several years. Despite intensive research, no HIV vaccine is currently available. This thesis presents a new and unique approach which has not been used for vaccine development yet. The promising strategy is based on small binding proteins that can elicit broadly neutralizing HIV-1 antibodies by mimicking their epitopes. The aim of this project was to select and characterize small binding proteins that can successfully mimic the surface of viral envelope glycoproteins that is recognized by the broadly neutralizing HIV-1 antibodies PGT121 and PGT126. Proteins were selected from a highly complex combinatorial protein library derived from a new type of scaffold called Myomedin. Firstly, the extent of the protein library was narrowed down using the ribosome display. Then the direct sandwich ELISA screening was applied to select scaffold variants that interact with the target antibodies. In total over 200 variants were tested and several promising candidates were found. These Myomedin variants were purified, biochemically and biophysically characterised and the best ones were used to immunize mice.

Keywords: protein engineering, HIV-1, broadly-neutralizing antibodies, protein mimicking, small binding proteins, ELISA