JAMES RENNIE BEQUEST

REPORT ON PROJECT

Project Title: High frequency stop codons in HIV-1 protease gene frame uniquely in patients exhibiting below detectable levels of plasma viremia during HAART

Travel dates: 02.06.2010 – 02.09.2010

Location: Westmead Millennium Institute, Westmead NSW 2145. Sydney. Australia.

Group Members: Magdalena Czubala

Aims: to identify and localize genetic mutations occurring in non-progressing HIV-1 patients.

HIV is very successful virus which takes more than a million lives worldwide each year. Untreated HIV patients relatively quickly progress to acquired immunodeficiency syndrome (AIDS). At that stage their immunological system fails and usually harmless microbe can lead to death. However, HIV patients undergoing Highly Active Antiretroviral Treatment (HAART), which consists of set of pills taken every few hours each day, show low levels of the virus in their bloodstream and do not progress to AIDS for many years. It seems that drugs used in HAART change genetic code of HIV, such it cannot longer replicate and spread within the body.

During 3 months-long summer placement in Westmead Millennium Institute in Sydney, we managed to amplify and sequence 560 base pair long HIV gag gene region from 83 patients, including 52 patients with below detectable levels (BDL) of HIV (<20-40 copies/ml plasma) and 31 patients with high viral levels (HVL). These sequences were align to reference HIV sequence and compared in order to identify significant mutations.

Our results had shown the presence of STOP codons in most of BDL patients at positions 16 and 157. These STOP codons resulted from conversion from tryptophan aminoacid (W) by so called “G-to-A hypermutation”, where guanine base becomes deaminated to adenin. Other STOP codons were also identified along the length of sequenced gene, giving a number of total 39 mutations in BDL. Interestingly, only one HVL patient had described hypermutation at position 157 and none of them shown significant changes at any other locations.
These results indicate that HAART therapy is able to keep low viral levels, most likely by interrupting coding region of essential viral genes. Presence of STOP codons halts progression of translational machinery what result in production of

not complete and useless proteins. Precise mechanism of this phenomenon requires further investigation.

The time spend in Sydney was not only the opportunity to develop my laboratory skills and gain new knowledge. It was also a huge chance to get to know the city and Australian culture. However, the most precious for me was to meet wonderful people from retroviral laboratory I was working in, who made me feel very welcome from the very first day. They also made my summer unforgettable memory.