The Adjuvant Study of New Saponins and MDP-Derivatives

Irina B. Andronovskaja[1], Yuri L. Krivorutchenko[2], Yuri S. Krivoshein[2],
Sergey S. Pertel[3], Vladimir I. Grishkovets[3], Vasily Ya. Chirva[3]

[1] *Taurican Ecology Institute, 333013, Sevastopolskaya street 76, Simferopol, Ukraine*
[2] *Crimean Medical University, 333670, Lenina Boulevard 5/7, Simferopol, Ukraine*
[3] *Simferopol State University, 333007, Yaltinskaya street 4, Simferopol, Ukraine*

In order to select an appropriate adjuvant for HIV-vaccines, three MDP-derivatives and three saponins have been evaluated for their ability to induce immune response in mice and to influence HIV-replication *in vitro*. Mice were immunised i/m with 1 μg of rgp 160 supplemented with 100 μg of the adjuvants per mice followed by three boosts.

Three saponins (3-O-α-L-rhamnopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-gentiobiosyl-hederagenin (Tauroside H_2), 3-ammoniumsulfat-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-gentiobiosyl-oleanolic acid (Tauroside I) and 3-O-β-D-glucopyranosyl-28-O-α-L-rhamnopy-ranosyl-(1→4)-O-β-D-gentiobiosyl-hederagenin (Tauroside St-K)) were isolated from Crimean Ivy *Hedera taurica* Carr. They demonstrated low capacity to induce T-cell proliferation and intermediate capacity to augment anti-rgp 160 antibody production. The highest anti-rgp 160 titres were detected for Tauroside I. Tauroside I also cause the strongest HIV-replication reduction (50-80%), followed by enchancing in the HIV-1 infectivity assay.

The examined group of MDP-derivatives included two α-anomers (N-[2-O-(butyl-2-acetamido-2,3-dideoxy-α-D-glucopyranosid-3-yl)-D-lactoyl]-L-alanyl-D-isoglutamine (α-butyl-MDP) and (N-[2-O-(butyl-2-acetamido-2,3-dideoxy-α-D-glucopyranosid-3-yl)-D-lactoyl]-L-alanyl-D-isoglutaminyl-(Nω-deoxycholyl)-L-lysine methyl ester (MDP-cholyl)) and one β-anomer (N-[2-O-(butyl-2-acetamido-2,3-dideoxy-β-D-glucopyranosid-3-yl)-D-lactoyl]-L-alanyl-D-isoglutamine (β-butyl MDP)).

Both α-anomers induced very small anti-rgp 160 antibody titres and high levels of HIV-1 replication. However, the difference in T-cell immune response was seen for these two α-anomers. MDP-cholyl induced T-cell response four times higher than α-butyl MDP.

The MDP derivative β-butyl MDP induced the strongest B- and T-cell responses to HIV-1 envelope glycoproteins. Moreover β-butyl MDP had no influence on the HIV-1 replication in JurKat-tat cells and seemed to be the most promising substance among others.