ABSTRACT

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Title of diploma thesis: In vitro evaluation of novel Toll-like receptor ligands I

Vaccination against preventable infections prevents millions of deaths each year. Their immunity enhancing activity is strengthened by the presence of vaccine adjuvants. Development of vaccine adjuvants leads to improved safety profile and also can play a vital role in the research of new vaccines against pathogens against which the vaccines currently do not exist. The main aim of this diploma thesis was to verify the ability of rationally developed small molecule ligands to influence Toll-like receptors and thus their potential to be utilized as vaccine adjuvants. The assay was carried out using modified cell lines continually expressing the human TLR4 or TLR8 whose activation leads to production of secreted embryonic alkaline phosphatase. Ten analyzed substances labelled as DM 001 – DM 010 were examined for their agonistic and also antagonistic properties while interacting with the TLRs. Immunomodulatory activity of these tested samples was then determined by quantification of secreted alkaline phosphatase with the help of a colorimetric enzyme reaction. The results of the analysis did not manage to prove a significant agonistic activity of any of the molecules, but some samples may exhibit potential antagonistic activity on hTLR8. More promising results were obtained with the hTLR4 agonist analysis, where three of the analyzed substances, namely DM 002, DM 005 and DM 008, showed stronger activity within the interaction with the receptor and they represent a foundation for further research.

Keywords

TLR; immunomodulators; in vitro evaluation; adjuvants; vaccine