# OPTIMIZIRANJE LASTNOSTI BIOLOŠKEGA ZDRAVILA ANSUVIMAB Z UPORABO PRISTOPOV RAČUNSKE KEMIJE

RAZISKOVALEC: Tevž Rus, 3. g

ŠOLA: Gimnazija Jožeta Plečnika ljubljana

MENTORICA: Lara Vertačnik - Gimnazija Jožeta Plečnika Ljubljana

SOMENTORJI:
Sebastjan Kralj - Laboratorij za fizikalno kemijo in kemijsko termodinamiko UM FKKT,
doc. dr. Marko Jukič - Laboratorij za fizikalno kemijo in kemijsko termodinamiko UM FKKT

KLJUČNE BESEDE:
molekularno modeliranje, računska kemija, protitelesa, virus Ebola, virus Marburg

POVZETEK NALOGE:

Virusa Ebola in Marburg, ki spadata v družino filovirusov sta že od svojega odkritja v drugi polovici 20. stoletja endemična, predvsem na območju Afrike. Virusna hemoragična mrzlica, ki jo povzročata, je hudo nalezljiva in pogosto smrtna bolezen, za katero je umrlo večje število ljudi.

Tekom raziskovalne naloge sem se želel podrobneje seznaniti z virusoma in preko raziskovalne naloge prispevati k razvoju učinkovitega zdravila. Raziskovalna naloga se je pričela s pregledom literature, ki je poglobila razumevanje o biokemijskem ozadju obeh virusov in o potencialnih možnostih za zaviranje delovanja virusov. Po osvojitvi potrebnega znanja o virusih, natančeneje filovirusih, protitelesih in proteinih ter proteinskih interakcijah, smo začeli z empiričnim delom naloge s pomočjo računalnika.

Osnovni namen naloge je bil poglobljeno razumevanje delovanja filovirusov, kot tudi vpliva mutacij na njihovo vezavo na protitelesa. S pomočjo literature in računalniških programov smo proučili delovanje in strukturo filovirusov ter protiteles ki zavirajo njihovo delovanje, opredelili ustrezne tarče za razvoj zdravila ter vizualizirali ustrezne proteinske komplekse glikoproteinov in protiteles. Na podlagi le-teh smo odkrili ustrezna skupna vezavna mesta obeh virusnih glikoproteinov ter ustrezne mutacije protiteles za močnejšo vezavo, ki smo jih kvantitativno ovrednotili.

ABSTRACT

Ebola and Marburg viruses, which belong to the filovirus family, have been endemic since their discovery in the second half of the 20th century, especially in Africa. The viral hemorrhagic fever they cause is a highly contagious and often fatal disease that has killed a large number of people.
During the research assignment, I wanted to learn more about viruses and through the research assignment contribute to the development of an effective medicine. The research task began with a review of the literature, which deepened the understanding of the biochemical background of the two viruses and the potential possibilities for inhibiting the activity of the viruses. After gaining the necessary knowledge about viruses, more specifically filoviruses,

antibodies, proteins and protein interactions, we started with the empirical part of the task with the help of a computer.
The basic purpose of the task was to gain a deeper understanding of the functioning of filoviruses, as well as the effect of mutations on their binding to antibodies. With the help of literature and computer programs, we studied the function and structure of filoviruses and antibodies that inhibit their function, defined suitable targets for drug development, and visualized the corresponding protein complexes of glycoproteins and antibodies. Based on these, we discovered the corresponding common binding sites of both viral glycoproteins and the corresponding antibody mutations for stronger binding, which were quantiatively evaluated.

KEYWORDS: molecular modeling, computational chemistry, antibodies, Ebola virus, Marburg virus, binding energy.