Brionna Jewel Tzaddi King
Third Year Medical Student
Louisiana State University Health Sciences Center-New Orleans School of Medicine– New Orleans, Louisiana
Mentor's Name: Giulia Monticone, Ph.D., Louisiana State University Health Sciences Center, Department of Genetics

"Adenosine analogs have immunomodulatory antiviral properties through the Adenosine A2A Receptor pathway"

The COVID-19 pandemic has unveiled an urgent need for novel antivirals to control emerging infectious diseases. Classic antivirals are often insufficient to clear infections in the absence of an effective immune response. Immunotherapy could complement the use of antivirals; however, its application to infectious diseases remains largely unexplored. Adenosine analogs (AAs) are antiviral drugs which resemble the structure of adenosine, a metabolite which suppresses the immune response through activation of the Adenosine A2A Receptor (A2AR) in immune cells. We hypothesized that selected AAs have previously unrecognized immunomodulatory properties by acting as A2AR antagonists. In this study, we used molecular docking modeling to screen AAs for their capacity to bind to A2AR and test AAs for immunomodulatory properties in cell-based and *in vivo* assays. We found that selected AAs restored T-cell functions from adenosine-mediated immunosuppression in T-cells, suggesting that they are endowed with immunomodulatory properties through A2AR antagonism, in addition to their intrinsic antiviral properties. These immunomodulatory functions contribute to the antiviral activity of the AAs as we found that the analogs could restore antiviral T-cell responses in COVID-19 models. In conclusion, selected AAs could be used as novel dual – immunomodulatory and intrinsic – antiviral drugs and could represent effective therapies against emerging viral diseases and future pandemics.