Institute of Molecular Biology and Genetics
NAS of Ukraine

ALL-UKRAINIAN CONFERENCE ON MOLECULAR AND CELL BIOLOGY WITH INTERNATIONAL PARTICIPATION

dedicated to the heroic struggle
of the Ukrainian people against russian invadors

June 15-17, 2022

CONFERENCE PROCEEDINGS

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24 th February 2022 Russia invaded Ukraine and this terrible war with destruction of civil infrastructure, including cultural, educational, and scientific objects interrupted the scientific work in our country. A lot of scientists were displaced within Ukraine or abroad. Our foreign colleagues immediately demonstrated great support and created a lot of opportunities for Ukrainian scientists in their countries. Despite this, most scientists stayed in Ukraine, some of them even in temporary occupied territories. Therefore, Young Scientist Council and in the Scientific Council of the Institute of Molecular Biology and Genetics NAS of Ukraine created the idea of All-Ukrainian conference with international participation with the aims to encourage Ukrainian scientists, to give the opportunity to colleagues from abroad to demonstrate their staunch support to Ukraine and to keep scientific process ongoing even on the background of the war.

The All-Ukrainian Conference on Molecular and Cell Biology with international participation was held as an online event on Zoom platform, from 15 th to 17 th of June 2022.

KEYNOTE SPEAKERS

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And **Vitaly Kordium (*Institute of Molecular Biology and Genetics, NAS of Ukraine, Kyiv, Ukraine) with* special *lecture***

IN SILICO STUDY OF COMPLEX FORMATION OF CHEMICALLY MODIFIED NUCLEIC BASES

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Aim. To study *in silico* in a fragment-to-fragment approach the possibility of the formation of stable [Het-BioM]-complexes with chemically modified nucleic bases by the π-stack mechanism and due to hydrogen bonding [HB]-complex.

Methods. The main characteristics of the electron structure of the studied compounds were calculated by DFT [wB97XD/6-31G(d.p.)] method (package GAUSSIAN 09).

Results. The introduction of fluorine in position 5 of uracil almost does not affect its affinity, does not change the nature of the S0-S1 transition, on the contrary, and reduces the S0-S2 transition energy (0.2 eV), increasing the possibility of [Het-BioM] complex formation by the π-stack mechanism and thymidylate synthase is blocked. The replacement of the fluorine atom by the chlorine atom in the uracil molecule (3) led to a change in the nature of the S0-S1 transition (n-pi* changed to pi-pi) and a decrease in the energy of this transition to 0.34 eV. Therefore, such a compound is primarily focused on the [Het-BioM] complex formation by the π-stack mechanism. The introduction of the electron-accepting sulfo group in position 5 of uracil (2) increases its electron-accepting properties without changing the nature of the S0-S1 transition (n-pi), increasing the probability of overlap of electron density with the second component of the [HB]-complex by 8 times. The S0-S2 (pi-pi*), transition energy remains approximately the same as in compound 1. Although the acceptor atoms of fluorine and chlorine have an inverse effect on the basicity of uracil, fluorine slightly increases the stability of the complex at 1.8 kcal/mol, and sulfo group stabilizes [HB]-complex at 2.5 kcal/mol. It can be assumed that such a replacement in the uracil molecule will have better therapeutic properties in the fight against cancer. The introduction of chlorine into the uracil molecule shows the low energy of stabilization of the [HB]-complex at 6.1 kcal/mol, because such a replacement will change the nature of the first electronic transition in molecule 3, and change the probable mechanism of complexation.

Conclusions. Thus, a detailed *in silico* study in the fragment-to-fragment approach shows that nitrogen π-conjugate molecules can form stable [Het-BioM] complexes with nucleic bases through π-stack interaction, as well as due to hydrogen bonding between LEP in twocoordinated nitrogen atom and proton of the functional groups of the nucleic bases. The possibility of complex formation by different mechanisms depends on the following quantum-chemical descriptors: parameter φ_0 of both components, as well as on the nature of their first electronic transitions. The introduction in the uracil of the acceptor sulfo group stabilizes the [HB]-complex at 2.5 kcal/mol, and the introduction of the chlorine atom at the same position changes the nature of the S0-S1, S0-S2 electron transitions so that such a molecule is characterized by the formation of a [π,π]-complex instead of [HB]-complex.