Emmanuelle BIGNON is a native of the south of France and earned her Ph.D. in computational biochemistry from Université Claude Bernard – Lyon 1, where she worked on characterizing the dynamics and reactivity of damaged DNA using molecular-level biophysics, under the supervision of Pr. Elise Dumont and Pr. Christophe Morell. After her Ph.D., she worked for two years as a postdoc in Pr. Elena Papaleo's group at the Danish Cancer Research Center in Copenhagen. In 2019, Dr. Bignon went on to receive a 18-month postdoctoral fellowship from Université Côte d'Azur to work at the Institut de Chimie de Nice. She is currently part of the GAVO project from the CNRS and works in the Laboratoire de Physique et Chimie Théoriques at Université de Lorraine as a postdoctoral fellow. She uses state-of-the-art computational methods to investigate the activity of enzymes interacting with nucleic acids in emergent viruses for the design of nucleoside-based antivirals. She authored 20 publications in rank A peer-reviewed journals and is the laureate of several young investigator prizes.

UNDERSTANDING THE DYNAMICS AND REACTIVITY OF NUCLEIC ACIDS TO FIGHT AGAINST PATHOLOGIES

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Although investigations on DNA damage and repair started several decades ago, the complexity and vastness of DNA damage chemical aspects still provide a broad matter of research as their underpinning molecular mechanisms remain poorly defined. The structural signature of DNA lesions is of major importance for their repair, but only few structural data are available from X-Ray and NMR studies. In order to gain insights into the formation and structure of damaged DNA, we investigated of a series of complex lesions within the double helix. The formation, structural signature and recognition by repair enzymes of oxidatively-generated damages (abasic sites, 8-oxoguanine, inter-strands crosslinks) and photo-lesions (cyclobutane pyrimidine dimers, pyrimidine 6-4 pyrimidone), isolated or embedded in mutiple damage sites, were charaterized within B- and nucleosomal DNA using molcular dynamics simulations and hybrid QM/MM methods. This allowed us to delineate the molecular mechanisms driving DNA damage formation and repair in a large panel of different cases, providing large perspectives in the field of cancer research.

Understanding the dynamics and reactivity of nucleic acids also opens new venues for the design of drugs against emergent viruses. Nucleoside analogs can be used to inhibit the replication of viruses (e.g., SARS-CoV-2 polymerase stalling provokes by Remdesivir incorporation). Molecular modeling tools allow to explore the interaction network perturbation between the nucleic acids and the targeted enzyme and to delineate the molecular mechanisms underlying the antiviral potential of the nucleoside analogs. Within the GAVO project funded by the CNRS, we investigate the translocation of RNA within SARS-CoV-2 polymerase by molecular dynamics simulations and free energy calculations, in order to characterize the structural changes induced by Remdesivir which lead to the blocking of the enzyme and therefore to the stopping the replication of the virus. This study provides a rationale for the Remdesivir action mechanism at the atomic scale and constitutes a framework for the prediction of the antiviral potential of other nucleoside analogs.

SARS-CoV-2 polymerase inhibition by Remdesivir