Cover Profile
doi.org/10.1002/chem.202002715

One Way Traffic: Base-to-Backbone Hole Transfer in Nucleoside Phosphorodithioate


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Invited for the cover of this issue are the groups of Roman Dembinski, Mehran Mostafavi, and Amitava Adhikary at the Polish Academy of Sciences, Université Paris-Saclay, and Oakland University. The image depicts a doughnut as a way of illustrating the hole transfer process. Read the full text of the article at 10.1002/chem.202000247.

What is the most significant result of this study?

Radiation-mediated charge (hole and electron) transfer processes are key steps that eventually translate to the lethal radiation damage to cells. Important precursors of the cellular damage are the sugar-phosphate backbone radicals, mostly sugar radicals. The rate and extent of hole (site of electron loss due to direct effect of radiation interaction) transfer from the sugar-phosphate backbone to the bases and from the bases to the sugar-phosphate backbone are critical processes that determine the yield of sugar radicals. Our work shows that replacement of oxygen atoms by sulfur in the phosphate group of the sugar-phosphate backbone changes the direction of the hole transfer process that takes place between base and phosphate. Without oxygen replacement (phosphate) or in phosphoro*mono*thioate, the typical hole transfer process occurs from backbone-to-base. This process reduces the type and extent of backbone damage which eventually lead to lethal damage for cells. However, direction of this hole transfer process reverses (i.e., base-to-backbone) if hole transfer occurs when two oxygen atoms in the phosphate group are substituted by two sulfur atoms (phosphorodithioate). This could be the key step in the mechanism of the phosphorodithioate-induced toxicity in humans.

What was the biggest surprise (on the way to the results presented in this paper)?

Our ESR, pulse radiolysis and theory results show that upon one-electron oxidation, first the guanine cation radical formation occurs and then by thermally-activated hopping, the hole (unpaired spin) transfers from guanine cation radical to the dithioate group in the phosphorodithioate moiety producing dithiyl radicals. ESR results show that these dithiyl radicals at low temperature undergo bimolecular reaction with the unreacted parent molecule to produce dimer anion radical. However, pulse radiolysis show that these dithiyl radicals at room temperature undergo dimerization to produce neutral S–S dimer.

What was the inspiration for this cover design?

The cover inspiration was to take something that is actually formless and represents a void space in the guanine electron cloud as the "hole," to give it a physical existence. To illustrate its "one way" direction, Ariela W. Kaspi-Kaneti chose a glazed doughnut for the hole in the middle. She made it look like a child leaving their parent's home, usually a path that goes in one direction, and suggested a car to represent the fast nature of this hole transfer process. Aditya Paul helped to integrate these ideas into the ultimate cover. The Polish and French part of the team lobbied for national "pączki" and "beignets" (no hole though) as high quality bakery products.