

Unraveling DNA Damage and Modifications Through Smart Nanobiotech Sensors

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Control and maintenance of genome integrity and the epigenetic landscape are of utmost importance in living organisms, especially in complex eukaryotes. Vertebrates possess an intertwined regulatory network that allows fine-tuned modulation of (epi)genome metabolism, in close interaction with nucleotide metabolism pathways. Recent findings in my lab indicate that the chemical space of DNA is even wider than thought and deoxyuridine moieties in genomic DNA may show a developmental pattern in vertebrate embryos, and may appear in a characteristically transient dynamic arrangement in cancer cell genomes. We are currently investigating the U-DNA developmental pattern in embryonal development and construct transgenic mouse models with combined knock-outs and knock-ins to study the role of U-DNA. We also are in the process to unveil the dynamic transient U-DNA patterns in cellular models (1,2).

These achievements are made possible only by relying on faithful, highly precise and quantitative techniques to follow the appearance and pattern of unusual bases in DNA (3). Such bases include the different oxidative products of methylcytosine – involved in gene expression control, base-modifications due to redox stress – induced by infections (4) and other diseases, and modified bases that appear as a result of anti-cancer chemotherapy – based on perturbation of nucleotide metabolism and DNA damage recognition and repair pathways.

The techniques we developed (1, 3) to get a critical insight into these processes rely on clever and innovative modifications of DNA-recognition enzymes. We transform these biocatalysts into highly specific receptors that bind to the modified bases but do not cleave them. We also equip these receptors with different conjugates to create the nanobiotechnological tools that we can apply in situ and in vivo experiments. We therefore are capable to provide a dynamic description of DNA damages in various physiological processes, as well as to evaluate the efficiency of chemotherapies (5,6).

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