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Spotlights on Recent *JACS* Publications

DNA DAMAGE, DOUBLE STRAND BREAKS, AND DEATH

Many anticancer drugs work by damaging DNA through oxidation, which can ultimately lead to cell death. Formation of an oxidized sugar, called 2-deoxyribonolactone, within the DNA strand backbone is one result of oxidation, but how this alteration leads to cell death is unclear. In an effort to explore the consequences of DNA oxidation in a more physiologically relevant setting, Chuanzheng Zhou and Marc Greenberg investigate the reactivity of 2-deoxyribonolactone in nucleosomal DNA (DOI: 10.1021/ja302993h).

Most studies investigating how 2-deoxyribonolactone affects the integrity of DNA have been conducted on free DNA, not nucleosomal DNA. However, in cells, DNA is packaged in particles called nucleosomes, which contain proteins called histones, and this packaging may influence the reactivity of DNA subjected to oxidation. The researchers found that, in nucleosomes, histone proteins actually increase strand scission by catalyzing the cleavage of the DNA strand containing the 2-deoxyribonolactone.

Their mechanistic studies of this process enhance our understanding of how these oxidizing agents cause single- or double-strand DNA breaks, the latter of which are particularly damaging to cancer cells. In addition, the insight gained into the role of nucleosomes in the DNA damage process could lead to new strategies for the design of anticancer drugs. **Eva J. Gordon, Ph.D.**

POLYMER NETWORKS MADE MALLEABLE WITH OLEFIN METATHESIS

For the first time, a team of scientists has demonstrated that rigid polymer networks can be made malleable at room temperature with the help of the Grubbs' second-generation ruthenium metathesis catalyst. Covalently cross-linked polymers are stable and resistant to solvents but cannot be further processed due to their inherent insolubility. On the other hand, thermoplastics can be processed repetitively, but often at the expense of integrity and performance.

Researchers led by Zhibin Guan have taken a step toward generating materials that combine the stability and insolubility of covalently cross-linked polymers with the processability of thermoplastics (DOI: 10.1021/ja303356z). The researchers introduced low levels of the Grubbs' catalyst to chemically cross-linked polybutadiene networks and found that the catalyst-infused polymers exhibited adaptive and malleable properties without compromising their mechanical properties.

The method allows catalyst deactivation after processing to permanently fix the desired properties of the polymer network. Given the abundance of olefin-containing polymers, the simple and efficient new method may be applied to develop insoluble cross-linked materials that are both strong and adaptive for a variety of industrial applications. **Christine Herman, Ph.D.**

SUICIDE ENZYME MAKES ESSENTIAL VITAMIN

Thiamin pyrophosphate (ThDP) is a ubiquitous metabolic cofactor that helps organisms combust sugars and synthesize amino acids. Tadhg Begley, Steven Ealick, and colleagues have characterized the unique biochemical pathway of the fungal *Candida albicans* enzyme (THI5p) that produces the pyrimidine half of the essential ThDP molecule from vitamin B_6 (pyridoxal phosphate) and a histidine amino acid in the enzyme (DOI: 10.1021/ja302474a).

Using isotopic labeling and mutagenesis of the protein's histidine residues, the researchers identified the active site His66 as the atom donor for formation of the pyrimidine ThDP precursor. Because THI5p in *C. albicans* loses His66 in forming the product, it can only engage in a single round of catalysis.

This identification of the histidine-derived-atoms donor paired with X-ray crystallographic analysis of the active site enabled Ealick, Begley, and colleagues to elucidate the unprecedented mechanism involved in forming the pyrimidine of ThDP in *C. albicans*. This work highlights some very unusual enzymology as well as the significant differences in the construction of ThDP between bacteria and yeast. Interestingly, the same researchers recently showed that THI4p, the enzyme responsible for biosynthesis in yeast of the thiazole half of the ThDP molecule, is also a suicide enzyme. Suicide enzymes are exceedingly rare, and the existence of two suicide enzymes in the same pathway is unprecedented. **Kenneth J. Moore**

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