Understanding and Improving Platinum Anticancer Drugs

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Abstract

Platinum compounds are a mainstay of cancer therapy. Barney Rosenberg's group at Michigan State University discovered the biological action of cisplatin in the late 1960's. Our laboratory subsequently established the chemical nature of events leading up to the binding of platinum anticancer drugs to DNA, their principal target in the nucleus of cancer cells. Platination of the genome evokes cell death pathways and attempts at damage repair. Binding of high mobility group (HMG) proteins to cisplatin 1,2-intrastrand d(GpG) cross-links blocks excision repair, an event that facilitates the ability of the drug to cure testicular cancer. This information has recently been used to sensitize additional cancer cell types to cisplatin by introduction of a particular HMG protein, HMGB4, which has the potential to cure cancer in humans without regard to tissue of origin. Details will be provided. This work was supported by a grant from the National Cancer Institute.