Metalloporphyrins in Cancer Chemotherapy: The Possible Role of Auger-Based Processes

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The possibility of exploiting Auger electron emission in cancer radiotherapy has been under study for many years. In the Auger process, irradiation of an atom results in release of an electron from one of the core shells. Outer shell electrons cascade toward the vacancy, resulting in the release of significant energy and the emission of a number of low energy electrons from the nucleus, leaving a polycationic center. Substantial local clustered damage to the DNA can result when the atom is localized near the DNA of a tumor cell.

It has been proposed that Auger therapy might be achieved using brachytherapy seeds as a source of radiation in conjunction with high Z metal-containing compounds which bind to DNA. The therapeutic effect will be most significant with a large number of high Z atoms bound to the DNA. Reduction of damage to the surrounding tissue is aided by localization of the carrier in the tumor. Cationic porphyrins are ideal metal carriers: they bind very well to DNA, can accommodate a wide variety of metal atoms in their central core, and have shown some specificity in binding to tumors.

Herein, we report studies of PtTMPyP4 and InTMPyP4, the indium and platinum chelates, respectively, of tetra-(*N*-methyl-4-pyridyl)porphyrin. Both molecules bind well to calf thymus (CT) DNA. Both have K or L shell energy levels appropriate for treatment with brachytherapy sources. Preliminary studies indicate that the combination of the metalloporphyrin and brachytherapy-based radiation is more effective than either treatment alone.

The success of the therapy depends on localization of the metal-containing porphyrin near the DNA. This in turn will depend on structural features of the porphyrin as well as the metal. Studies of the binding of a series of homologues of InTMPyP4 wherein the methyl group is replaced by ethyl, propyl, butyl, and benzyl groups, will be reported.