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Extensive biochemical and structural studies to develop potent DNA topoisomerase II inhibitors as anticancer drugs

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Human topoisomerases (topos) resolve DNA topological problems, unavoidably caused during DNA transcription, replication, recombination, and segregation of two identical copies of genomes in two daughter cells following replication. Topos can be grouped into two types according to the number of strands cleaved in one round of action. Topoisomerase type I (topo I) cleaves one strand of a DNA double helix while topoisomerase type II (topo II) cleaves both strands of one DNA duplex to make another noncleaved duplex pass through a transient, topo II-mediated break and then followed by reannealing the cleaved strands. Topo II is distinct from topo I in that topo II acts as a homodimer, requiring Mg (II) and ATP hydrolysis for enzyme turnover and rapid kinetics; this enables it to cut both DNA strands simultaneously. In addition, topo II is the only enzyme available to disentangle the topological problems in chromosomes, which must occur during DNA replication, and to decatenate the replicated chromosomes by introducing transient double strand breaks. Therefore, topo II has been targeted to develop chemotherapeutic drugs for long time. We have been studying to develop topo I- and/or topo II-targeting anticancer agents by synthesis of various flexible terpyridine derivatives with extensive biochemical evaluation and structural analysis. Our results are described in detail in this poster.

Biography

Y Kwon received a Ph.D. in chemistry from University of Houston in 2002 with studying on the determination of structure of DNA complexed with anticancer molecule, neocarzinostatin. She was a postdoctoral fellow at Baylor College of Medicine and extended her research interest into chemical genomics. She joined the faculty at College of Pharmacy, Ewha Womams University in 2005, where she is currently a Professor. She has published more than 82 papers in reputed journals and has been serving as an editorial board member of four reputed journals.

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