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The Rediscovery of UPI-928

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Abstract

In the 1980s UPI-928 was developed by a major international pharma. In the early 1990's with over 40 clinical trials, and a newly grant western European marketing and sales approval the company was sold, and then the purchasing company was sold. UPI-928 was apparently lost in the corporate shuffle and never marketed. As cytotoxic drugs were all that were known at the time, UPI-928 was found to have an acceptable tolerability profile in a maximum tolerated dose model of development, and demonstrated efficacy in AML, lymphoma, refractory breast cancer, and ovarian cancer. It was approved for human use for the treatment of AML. Subsequent work has shown that this class of drugs also has various immunogenic and other therapeutic properties, including the upregulation of DAMPs, induction of apoptosis, activation of T cells and myeloid cells, inhibition of HIF-1 expression, and UPI-928 has been found to activate Mφ capable of eliminating tumors in an allogeneic transplant model. Supernatants from activated Mφ were similarly found to be capable of extending survival in allogeneic mice with tumors. More recently, UPI-928 was found to bind to DNA at a specific site that disrupts telomere-telomerase interactions in a manner that dislocates telomerase binding proteins, causing immortalized cells to become senescent and die. UPI-928 may be an agent unique in its abilities to bridge cytotoxic, immune, and genomic mechanisms in a manner that makes it particularly suitable for combinatorial therapy.

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