

Experimental anti-cancer synthetic molecule targets tumor cell growth and angiogenesis

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A recent study conducted by three French CNRS (Centre National de la Recherche Scientifique) laboratories describes a new candidate anti-cancer drug, named HB-19. In contrast to conventional anti-cancer drugs, HB-19 has a dual mechanism of action by its capacity to target independently both tumor cell growth, as well as tumor angiogenesis (formation of new blood vessels which bring necessary nutrients and oxygen to the tumor mass). The molecular target of HB-19 is nucleolin expressed on the surface of all activated cells, in particular rapidly growing tumor cells and endothelial cells that play a key role in angiogenesis. The results of this work, directed by Ara Hovanesian, are published in the June 18 edition of *PLoS ONE*.

Nucleolin is one of the major proteins of the nucleus, but it is also expressed on the cell surface where it serves as a binding protein for variety of ligands implicated in cell proliferation, differentiation, adhesion, mitogenesis and angiogenesis. The specific binding of HB-19 to surface-expressed nucleolin leads to internalization of the complex followed by degradation of this multifunctional protein.

Using various in vitro and in vivo experimental models, the authors show that HB-19 is a potent inhibitor of tumor cell growth and angiogenesis. In mice grafted with human breast tumor cells, HB-19 treatment markedly suppresses the progression of tumor development, and in some cases eliminates measurable tumors while displaying no toxicity to normal tissue.

The in vivo antitumoral action of HB-19 in this mouse model (i.e. inhibition of tumor development) is comparable to that of 5-fluorouracil, a drug that is used to treat several types of human cancer. However, 5-fluorouracil has toxic effects on circulating white blood cells whereas HB-19 treatment demonstrated no observable toxicity in this study. Another possible advantage of HB-19 over existing anti-cancer drugs is its reproducible synthesis by conventional techniques to generate a stable product that is readily soluble in physiological solutions.

The direct action of HB-19 on tumor growth and angiogenesis fulfills the criteria for an efficient anticancer drug, since combination therapy targeting both of these events is considered an optimal strategy in cancer management. In view of such dual inhibitory action, reproducible synthesis, high stability, selective tissue retention, and in vivo lack of toxicity, HB-19 may be a promising candidate for evaluation in future clinical trials.

Source: Public Library of Science

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