

Histone H1 proteins: the human body's own oncolytic drug candidates

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The scope of biological functions of histone proteins, mainly identified with their structural and epigenetic interactions with DNA, has broadened extensively during the past two decades. The documented extranuclear and extracellular activities of histones comprise hormonal, regulatory and protective functions.

Especially linker histones exert pronounced cytotoxicity against microorganisms and tumor cells by selectively targeting and perforating the membranes of these cells and thus represent an important component of the innate immune system.

SymbioTec has developed the first recombinant derivative of human histone H1.3 for toxicology studies and clinical trials (applied trade name: ONCOHIST).

In vitro, the protein has shown cytotoxic activity against more than 60 tumor cell lines. Particularly haematological tumors proved to be very histone H1 – sensitive with IC50 values in the range of 2-5 μM which compares favourably with those of conventional cytostatic drugs. Healthy blood cells remain largely unaffected.

Toxicology studies in rats and dogs including 4 weeks multiple dose toxicity proved high tolerability and normal hemograms and clinical biochemistry. The protein thus appears safe. It is evenly distributed over all organs, does not accumulate and has a favourable half-life.

The first clinical phase I/II study with 22 patients with relapsed or refractory AML has been conducted in the Saarland University Hospital in Homburg/Saar (Principal Investigator: professor Michael Pfreundschuh). The results will be published elsewhere.

Tumor therapy using histone H1 proteins represents a completely novel therapeutic concept. ONCOHIST is the first oncolytic drug of human origin, characterized by inherent low toxicity and immunogenicity and a high therapeutic potential in a wide range of indications.

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