TECHNOLOGY OFFER

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Novel Gene Therapy Approach to cancer treatment

A hyper-active thymidine kinase mutant locally administered into the solid tumor via viral transfection drives tumour cells into cell cycle arrest and subsequent cell death. The effect requires very low to physiological substrate concentrations, which is expected to keep side effects at bay due to very low to no systemic exposure.

REFERENCE:
587.15

KEYWORDS:
- Oncology
- Biologic

AVAILABLE FOR:
- Development partnership
- Licence

DEVELOPMENT STATUS:
In vitro proof of concept

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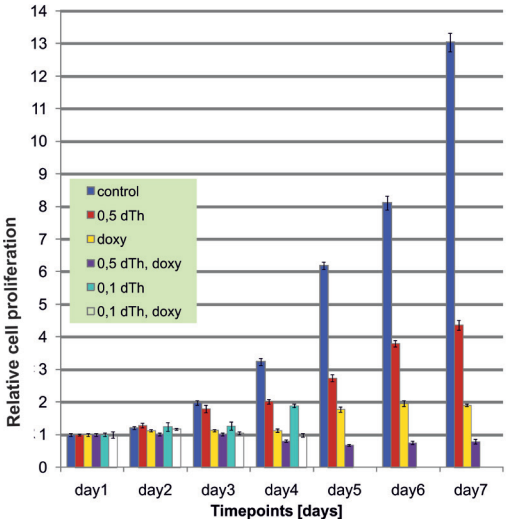
BACKGROUND

The cytosolic thymidine kinase 1 is a very well characterized enzyme essential for the provision of nucleotides for DNA synthesis. Whenever eukaryotic cells are exposed to higher levels of the substrate deoxythymidine, a cell cycle arrest occurs resulting in an inhibition of cell growth and proliferation. This is an elementary checkpoint in all mammalian cells, including cancer cells. Earlier attempts to use this effect to inhibit tumor growth were only partially successful as the required substrate concentrations also affected healthy cells.

TECHNOLOGY

PC-3 cells (primary prostate carcinoma) treated with **superTK1 plus/minus induction** with doxycyclin and **different dTh levels**



A super active human thymidine kinase 1 enzyme (superTK1), engineered by recombinant technology based on theoretical protein calculations, allows to dramatically reduce the growth inhibitory substrate levels of deoxythymidine to almost physiological substrate concentrations. The engineered enzyme is locally administered to tumor cells by AAV (adeno associated virus). Cytostatic as well as cytotoxic effects on tumor cells can be induced and maintained by very low deoxythymidine serum levels (< 0,1 mM). This avoids systemic exposure of high inhibitor concentrations to healthy cells and thus hardly entails any side effects. Combination treatment with cytostatics (e.g. 5-FU, AraC) is possible and expected to reduce concentrations of chemotherapeutics in a similar manner. Therefore lower side effects without diminishing treatment efficacy can be expected.

BENEFITS

- local administration into tumor, very low systemic exposure
- cytostatic and –toxic effects on normal cells highly reduced
- only local proliferating cells are targeted and harmed
- combination therapy with proven cytostatics facilitated

APPLICATIONS

- for solid tumors of any kind of origin and location
- AAV-based transfer affects all tumor cells equally
- no discrimination between tumor cell types
- repeated therapy regimens are easily possible
- method of choice for solid tumors inaccessible for surgery

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