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Abstract Book

Chemoembolisation Using Drug Eluting Beads: Magic Bullets Targeted by Arterial Guidance

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Transarterial chemoembolisation (TACE) is used in the treatment of hypervascularised tumours such as hepatocellular carcinoma (HCC) and involves delivering a drug into the hepatic artery followed by occlusion of the artery with an embolisation agent to starve the tumour of oxygen and nutrients. Although randomised studies have demonstrated a survival benefit for TACE (Llovet *et al.* 2002), the procedure varies vastly in clinical practise leading to inconsistent outcomes. Drug eluting beads (DEB) have been developed from sulfonate-modified polyvinyl alcohol hydrogel microspheres. These devices are capable of targeting tumours with drugs by flow-directed delivery down the feeding arteries and subsequent embolisation of the tumour capillary bed. The DEB affect intra-arterial delivery of chemotherapeutic agents over a sustained period in a controlled manner; deliver a high concentration of drug local to the site of the tumour; reduce the systemic exposure to free drug; occlude the tumour arterial blood supply. DEB have been well characterised *in vitro* with respect to loading and elution of drugs such as doxorubicin and the effects on the physical attributes of the beads related to catheter delivery (Lewis *et al.* 2006a; Gonzalez *et al.* 2007; Lewis *et al.* 2007). These drug-device combinations have been evaluated in a number of pre-clinical models that demonstrate the concept of high local delivery of the drug combined with lower systemic exposure (Hong *et al.* 2006; Lewis *et al.* 2006b). These data are supported by encouraging preliminary phase I/II clinical results in the treatment of HCC (Varela *et al.* 2007). This presentation will provide an overview the bench-to-bedside development of these drug-device combinations for the treatment of liver cancer.

Possibilities of Nonconventional Application of Streptokinase: Studies at the Molecular and Cellular Levels

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Background. Traditionally the preparations of streptokinase (SK) are used in clinical medicine for dissolution of thrombi, fibrin deposits.

In 1987-1991, we described pronounced superoxide dismutase-like activity of SK in chemical systems of superoxide radical generation, the inhibition of plasminogen-activating ability of SK by scavengers of superoxide radical (nitrotetrazolium blue, adrenaline), nucleotides (ATP, cAMP and NAD at rather high concentration: ≥ 0.01 M).

In 1993 we proposed the SK-containing composition for the treatment of patients with long-nonhealing wounds (a patent of the Russian Federation). Its local application in several surgical clinics of Minsk has yielded good results – the healing of such wounds was achieved in all cases.

In 1991, instillation of the SK solutions in eyes was used for treatment of guinea pigs with experimental herpetic keratoconjunctivitis (a patent of the USSR).

Since 1999, on the transplanted cells cultures of rat glioma C6 and human neuroblastoma IMR-32 the mitogenic effect of SK (10^{-11}–10^{-7} M), its stimulation of neuroblastoma cells as well as changes of intracellular contents of DNA, RNA and protein have been demonstrated. The exposition of rat pheochromocytoma PC12 cell culture with 5·(10^{-10}–10^{-6} M) only during 20 min was accompanied by significant changes of the level of ATP- and Ca^{2+}-activated intracellular proteolysis.

On organotypical and dissociated cultures of rat neocortex, sensory (spinal) and vegetative ganglia (on the nutrient mediums with deficiency of blood serum proteins), the neurotrophic effect of SK was established. It manifested itself by maintenance of vital activity of cells at deprivation of blood serum proteins, cold stress, damaging effect of anionic form of ATP, and stimulation of proliferation of glia, Schwann cells and other cells.

The cleavage of bovine fibrinogen in a thin layer of agar gel by washed cells of *Pseudomonas aeruginosa* hospital strain (grown up on plain agar) was inhibited by 20-100 % after SK additions to the cells on.

Conclusions. The scope of the results creates real preconditions for expansion of the medical application sphere of SK preparations, first of all, for stimulation of tissues' regeneration and, perhaps, for treatment of neurological pathology.