

Gene therapy of glioblastoma: Antisense/triple helix anti igf-i strategy

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Strategy of gene therapy based on antisense/triple helix anti IGF-I approach was investigated in the experimental treatment of Neuroglial derivatives using the model of mouse teratocarcinoma. This strategy, inducing immune anti-tumour response, has permitted to stop the development of teratocarcinoma's structures in tumour bearing animals. The effectiveness of anti - gene anti IGF-I therapy was evaluated in clinical treatment of brain malignant tumour - glioblastoma multiforme. The patients treated by classical surgery followed by radiotherapy were "vaccinated" by injection of genetically modified cancer cells: cultured cancer cells, originated from tumor removed during surgery, were transfected by antisense/triple helix anti IGF-I expression vectors. The PBL cells of treated patients have demonstrated an increasing level of T CD8+CD28+ cells with characteristic switch from CD8+11b+ to CD8+11b- after every of the three vaccinations. The minimum survival of treated patients was 19 months and maximum 24 months (using classical surgery and radiotherapy followed by chemotherapy, the median survival is generally 14 months, rarely 18 months). The described Phase I trial presents promising results - an increase in immune response goes together with life span. These results confirm the role of the immune phenomenon present in antisense anti IGF-I strategy investigated in previous preclinical experiments - suppression of animal glioma, hepatoma and teratocarcinoma tumours treated by the same cellular gene therapy inducing T CD8+ response.

Biography

J. Trojan has completed his Habilitation in 1981 in University Paris VI. In 1984 he has joined INSERM. His original contribution to biomedical science is as follows: 1. demonstration of the convergence existing between ontogenesis and carcinogenesis in relation with alpha-fetoprotein presence (Dev. Neurosci. 1984; 6: 25); 2. establishment of a new gene therapy of malignant tumours using anti - gene IGF-I technology (Science 1993; 259: 94). Between 2003 and 2007 he was the principal investigator of NATO Science Programme on gene therapy of tumours expressing IGF-I (USA, France, Poland, Germany; n° CLG LST 980517). Currently Dr Trojan is conducting research in cancer immuno-gene therapy.

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