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Cancer suicide gene therapy: Apoptosis of the ovarian cancer cells induced by EGFRvIII targeted delivery and cell nucleus targeted expression of the DNA-ase transgenes

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Malignant ovarian cancers are the most deadly of all diseases of the reproductive system. Radical oopherectomy in advanced cancer leads to complete infertility. Fertility sparing surgery followed by systemic therapies may result in infertility of the patients and/or the genetic mutations in oocytes potentially leading to genetic disorders of the offspring. The specific aim of this work was to refine our cancer suicide gene therapy, so the apoptosis is sharply restricted to the ovarian cancer cells only.

To attain this aim, we genetically engineered single chain variable fragments targeting EGFRvIII receptors, which are present on the cancer cells only. We also engineered the DNAase having the optimum for it activity at the cell nucleus environment, while having it expressed under the ovary specific promoters. We tested the specificity of delivery with the in situ PCR, immunoPCR, FCM, and NMR. We validated induction of apoptosis with the FCM, qPCR, EELS and EDXS.

Upon delivery to the mixed cell cultures spiked with the human ovarian cancers, the cell spheroids, and xenografts in nude mice, the transgenes were very selectively delivered only to the cells expressing EGFRvIII. Moreover, the transgenes were effectively expressed in the targeted ovarian cancer cells. The suicide transgenes induced effective degradation of the genomic DNA within the human ovarian cancer cells only.

We demonstrated that the cancer suicide gene therapy through targeted expression of recombinant DNAase is very specific in eliminating cancer cells, while leaving the healthy cells unharmed.

Biography

Marek Malecki MD PhD is currently an Associate Professor of Genetics, Genomics, and Gene Therapy at the Western University of Health Sciences, Pomona, CA. He acquired his expertise in molecular medicine during the fellowships at the Rigshospitalet, Copenhagen, Denmark and in molecular biology and genetics during the EMBO, Heidelberg, Germany funded postdoctoral fellowships. He is the author of the cancer suicide therapy. He is the inventor of the synthetic molecules facilitating genomic nanosurgery.

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