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Demonstration of anti-tumour bystander killing with prodrug-preloaded suicide gene-engineered tumour cells: a potential improvement for cancer therapeutics

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Abstract

Background: Therapeutic approaches for cancer rely on careful consideration of finding the optimal way of delivering the pro-drug for cellular-based cancer treatment. Cell lines and cell cultures have been used in these studies to compare the in vitro and in vivo efficacy of autologous vs. allogeneic tumour cellular gene therapy. Here we have investigated and are reporting for the first time the effect of prodrug ganciclovir (GCV)-preloading (pre-treatment) in suicide gene therapy of cancer.

Methods: This study examines the effect of GCV-preloading (pre-treatment) on a range of tumour cell lines in conjunction with suicide gene therapy of cancer. To determine the efficacy of this modality, a series of in vitro and in vivo experiments were conducted using genetically modified and unmodified tumour cell lines.

Results: Following co-culture of herpes simplex virus thymidine kinase (HSV-TK) modified tumour cells and unmodified tumour cells both in vitro and in vivo, GCV-preloading (pre-treatment) of TK-modified human and mouse mesothelioma cells and ovarian tumour cells allowed them to mediate efficiently bystander killing of neighbouring unmodified tumour cells in vitro. In contrast, GCV-preloading of TK-modified human and mouse mesothelioma cells and ovarian tumour cells abolished their in vivo ability to induce bystander killing of unmodified tumour cells, although there was some tumour regression compared to control groups but this was not statistically significant.

These results suggest that preloading TK modified tumour cells with GCV needs further study to define the most effective strategy for an in vivo application to retain their bystander killing potential after exposure to lethal doses of GCV in vitro.

Conclusions: This study highlights the promising possibility of improving the efficacy of pro-drug system to prevent any damage to the immune system and enhancing this type of suicide gene therapy of cancer, as well as the need for further studies to explore the discrepancies between in vitro and in vivo results.

Biography

DR Jehad Zeidi, lecturer in Cancer studies at the University of Liverpool Medical School, born and grew up in Jordan and received his Bachelor's degree from the University of Jordan. He obtained his master degree from London School of Hygiene and Tropical Medicine/University of London, and then obtained his PhD degree in 2000 from Kings College Medical School/University of London, in the field of Immune Gene Therapy of Cancer under the supervision of Professor Farzin Farzaneh. He then started his work as Postdoctoral Associate at the department of Immunology and Medicine at the University of Liverpool in 2002.

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