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Utilizing a foamy viral vector for engineering safer CD19CART cells

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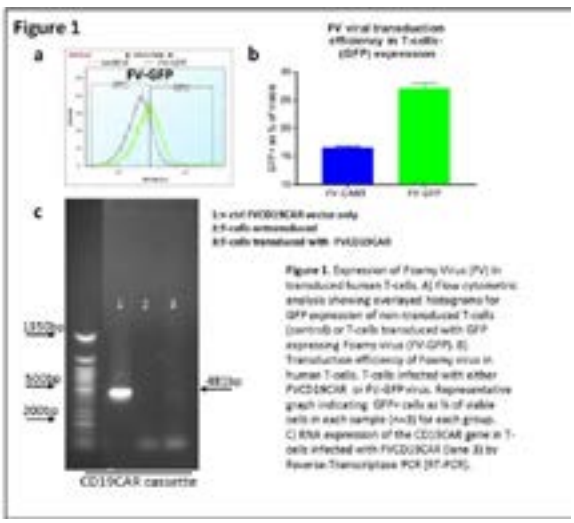
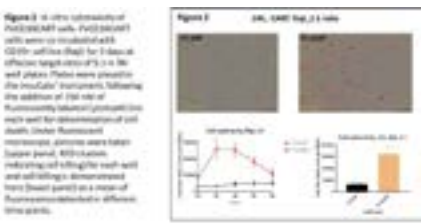
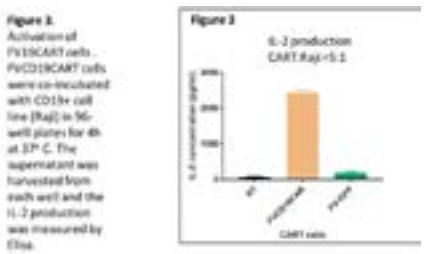
The recent advances in the field of Immuno-oncology has led to unprecedented clinical outcomes for several cancer patients and to the approval of CD19CAR cell based therapies both in the EU and the USA. In the clinical setting, gene delivery of CD19 Chimeric Antigen Receptors (CARs) in patient derived T-cells, has been achieved predominantly by the use of gamma-retroviral or lentiviral vectors. Despite their vast use in the field, these vectors however possess potential threat for patients due to the random integration events in the human genome and the possibility of mutagenesis. To address the safety issues in the delivery of CART cell therapies, we employed a spumaviral vector, namely Foamy Virus (FV) that has been credited with having safer properties for the host genome in gene therapy (3, 4). We used an FV vector to clone our CD19CAR cassette under the control of a human EF-1alpha promoter (FVCD19CAR). Peripheral blood was obtained from normal donors and T-cells were subsequently isolated from the buffy coat using magnetic beads. T-cells were transduced with our FVCD19CAR expressing vector and expanded for 1-2 weeks under cytokine stimulation before functional testing. RNA was extracted from FVCD19CART cells and the CD19CAR expression was verified by RT-PCR. We demonstrate the transduction of T-cells using FV-GFP vectors by flow cytometry. Functional evaluation of CART cells was performed in co-incubation assays with relevant CD19 expressing target cell line (Raji). CART cell activation was confirmed by a marked increase in cytokine levels as detected by Elisa in co-incubation assays. Moreover, we show increased cell death in FVCD19CART co-incubation assays compared to the control FV-GFP and non-transduced T-cells. Overall, our results indicate the feasibility of engineering safer CD19CART cells that retain their activation and *in vitro* tumor cell killing properties and could potentially be used as alternative vehicle for gene delivery.







Recent Publications

1. Hacein-Bey-Abina S et al. (2003) LMO2 associated clonal T cell proliferation in two patients after gene therapy for SCID-X1. Science. 302(5644):415-9.
2. Fischer A, et al. (2013) Gene therapy of primary T cell immuno deficiencies. Gene 525(2):170-3.
3. Trobridge G D, et al. (2006) Foamy virus vector integration sites in normal human cells. PNAS. 103(5):1498-503.
4. Jonah D Hocum, et al. (2016) Retargeted foamy virus vectors integrate less frequently near proto-oncogenes. Sci Rep. 6:36610.

Biography

Vasileios Atsaves has obtained his PhD in Cancer Signaling and Therapeutics at the University of Athens, School of Medicine, Athens, Greece in 2012. He has published more than 17 papers in reputed journals and has a research track of over 13 years working in universities inside US and EU on projects related to regulation of signaling pathways in cancer, small molecule inhibitors for targeted therapy and animal models of glomerulonephritis. From 2016, his interests shifted towards Immunology and Cancer Immunotherapy. As a Postdoctoral Researcher, he studied the transcriptional control of immune checkpoint molecules (PD-L1, PD-L2) in lymphoma and recently he began investigating the use of safer genetically engineered human CD19CART-cells for the treatment of human B-cell hematologic malignancies. He has now joined Ludwig Institute for Cancer Research in Lausanne as a part of the LabCore team and a member of the Professor George Coukos Lab.

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