Preclinical CAR T cell therapy; The Role of Graft versus Host Disease

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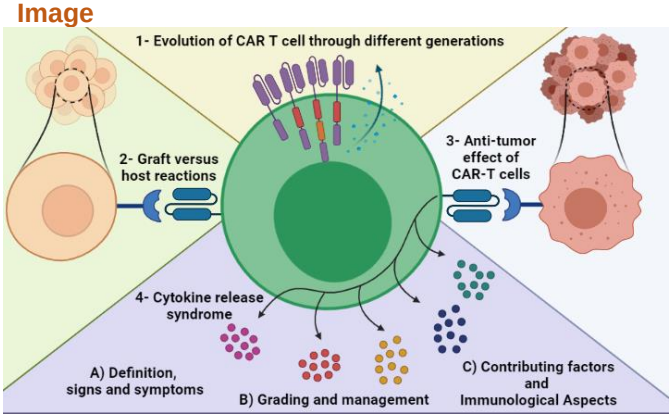
Abstract (300 word limit)

Chimeric antigen receptor (CAR) T cells are the forerunners of cancer immunotherapy, with many FDA-approved products to date. They have been significantly enhanced since their initial launch in 1993, and have demonstrated promising outcomes despite their unavoidable negative effects. Differential in histocompatibility antigens stimulates the xenogeneic CAR T cells' graft versus host disease (GvHD) impact against host cells in preclinical studies. it seems that balanced immunological reaction induced by CAR T cells in the form of cytokine release syndrome or GvHD is necessary for fostering good response, while hyperactivity of these reactions can potentially have higher efficacy but at the cost of threatening patient's life.

In this preclinical study, we sought to determine whether GvHD occurred following CAR T cell administration at common doses used in immunotherapy studies, and if so, how severe it was. The most common presentations of GvHD were hunched posture and ruffled fur, alopecia and scaling dermatitis. GvHD got more severe when higher doses have been administered. Transferred cell presence in blood was limited in non-fetal doses, while high fetal doses result in higher percentage of cells affecting the survival of mice.

CAR T cell administration at common preclinical immunotherapy doses is accompanied by GvHD. The concomitancy of xenogeneic GvHD effects and CAR-directed immune response should be considered when interpreting the results.

Image



Recent Publications (minimum 5)

1. Mansouri, Vahid, et al. "Recent advances in regenerative medicine strategies for cancer treatment." Biomedicine & Pharmacotherapy 141 (2021): 111875.
2. Arabi, Fatemeh, Vahid Mansouri, and Naser Ahmadbeigi. "Gene therapy clinical trials, where do we go? An overview." Biomedicine & Pharmacotherapy 153 (2022): 113324.
3. Sotoudeh, Masoud, et al. "Interpatient variability in mesothelin expression necessitates its evaluation before gastric cancer immunotherapy." Immunotherapy 14.7 (2022): 531-538.
4. Toutounchian, Samaneh, Naser Ahmadbeigi, and Vahid Mansouri. "Retinal and Choroidal Neovascularization Antivascular Endothelial Growth Factor Treatments: The Role of Gene Therapy." Journal of Ocular Pharmacology and Therapeutics (2022).
5. Mansouri V. X-Linked Retinitis Pigmentosa Gene Therapy: Preclinical Aspects [published online ahead of print, 2022 Nov 8]. Ophthalmol Ther. 2022;1-28. doi:10.1007/s40123-022-00602-y

Photograph



Biography (150 word limit)

Dr Mansouri, MD, has a background in immunology and interest in gene therapy and genetic interventions. As a result, engineered cell therapy and especially Chimeric antigen receptors (CAR) T cells is his field of interest in recent years. The double-sided effect of GVHD and GVT was among the emerging subjects that he has worked on. He is currently a post-doctoral researcher in gene therapy research center working on cell and gene therapy projects.

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Notes/Comments: