GIFT4-augmented B cells for melanoma immunotherapy

Jiusheng Deng, Emory University
Andrea Pennati, Emory University
Shala Yuan, Emory University
Ragini Kudchadkar, Emory University
David Lawson, Emory University
Jacques Galipeau, Emory University

Conference Name: Society for Immunotherapy of Cancer 29th Annual Meeting National Harbor, MD, USA
Publication Date: 2014-11-06
Type of Work: Poster
Publisher DOI: 10.1186/2051-1426-2-S3-P9
Permanent URL: https://pid.emory.edu/ark:/25593/s6n88

Final published version: https://jitc.biomedcentral.com/articles/10.1186/2051-1426-2-S3-P9

Copyright information:
© 2014 Deng et al.; licensee BioMed Central Ltd. This is an Open Access work distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

Accessed December 6, 2019 1:52 AM EST
GIFT4-augmented B cells for melanoma immunotherapy

Jiusheng Deng*, Andrea Pennati, Shala Yuan, Ragini Kudchadkar, David Lawson, Jacques Galipeau

From Society for Immunotherapy of Cancer 29th Annual Meeting
National Harbor, MD, USA. 6-9 November 2014

Melanoma is the most dangerous type of skin cancer and one of the fastest growing cancers in the USA. Immunotherapy, by enhancing patient’s immune system, has become an attractive approach for melanoma treatment due to the rapid drug resistance to chemotherapy. B cells are a heterogeneous cell population in the host immune system functionally as antibody-producers, antigen-presenting cells or regulatory cells. In the tumor microenvironment, B cells are among the heavy tumor-infiltrating immune cells. But B cell’s role in anti-tumor immunity remains controversial. Our lab has recently developed a novel GM-CSF and IL-4 fusion cytokine named GIFT4 (GMCSF and IL4 Fusion Transgene). This technology builds upon the successful development of “fusokine” platform [GIFT15] (Nature Medicine, 2009, 15: 1038-45). We discovered GIFT4 possess novel gain-of-function of immune activities, elicits robust B cell response and consequent killer T cell immunity against melanoma. GIFT4 protein has potent immune signaling activities, induces hyper-phosphorylation of STAT1, 3 and 5 in B cells, and reprograms B cells from melanoma patients into CD40+CD80+CD83+CD86+ antigen-presenting cells profiled by flow cytometry. Luminex assay reveals that GIFT4-B cells secrete substantial amount of IL-2, innate cytokines IL-6 and GM-CSF, chemokines CCL2, CCL3, CCL4 and CCL5, and adhesion molecule ICAM-1, but not IL-10 and IFN-γ. Those GIFT4-B cells robustly promote sustained ex vivo expansion of tumor-killing T cells that are IFN-γ+, NKG2D+ Granzyme B+ and granulysin+, and produce Fas ligand and TRAIL. Moreover, human GIFT4-B cell licensed cytotoxic T cells kill human melanoma cells in vitro and in NSG immune deficient mice. We expect that GIFT4, as an anti-melanoma agent, will provide a novel strategy and opens a new avenue for human B cell-based immunotherapy against melanoma. We propose that GIFT4-B cells from melanoma patients could serve as a potential immunotherapeutic agent for personalized melanoma cell immunotherapy.

Published: 6 November 2014

doi:10.1186/2051-1426-2-S3-P9