Breakthroughs of 2015-Personalized Immunotherapy Based on Individual GWAS and Biomarkers

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We at Biomarkers Journal had opportunity to report "a clue of persoanlized immunotherapy" [1]. In the late 1980s, Rosenberg and his colleagues initially administered autologous T-cells to treat malignant melanoma (such as tumor-infiltrating lymphocyte, TIL). After that, TIL, nature killer cells, cytokine-induced peripheral blood mononuclear cells (lymphokine activated killer, LAK; cytokine-induced killer cells, CIK; dendritic cells and cytokine-induced killer cells, DC-CIK), and macrophage have been greatly developed into adoptive immunotherapy. Initially, TIL had some responses to treat tumor patients, however, the cells only achieved 11-30% partial and complete responses (PR and CR) as left photo. In order to increase immunotherapy effect, two subspecialties have been developed during the last twenty years: (1) genetically engineering some special substances such as TNF-α, TGF-β, IL-2, IL12 and IFN-γ have been largely developed into T-cells; (2) genetically engineering some higher affinity substances between tumor cells and T-cell such as modified TCR (T-cell receptor) and chimeric antigen receptors T-cell (CAR-T cells) have been also successfully applied to B-cell leukemia/lymphomas. When human genome sequence decoded after 2004, scientists and physicians have largely studied workflows from genomic profile to system modeling in silico until cell engineering in/ex vivo. Moreover, Rosenberg reported efficacy of T-cell personalized immunotherapy for different patients related with individual GWAS in 2015 [2]. Personalized immunotherapy has been increasingly emerged in the new generation immunotherapy. Our manual in Biomarker Journal supported the concept of personalized immunotherapy based on individual genomic data. Personalized immunotherapy based on system modeling and/or GWAS has at least four advantages to contrast genetically-modified adoptive immunotherapy: (a) induced T-cells are based on system biology rather than any genetic modification performance so that personalized immunotherapy can keep T-cells good proliferation during culture; (b) CD8+cell culture based on personalized genomic profiles with their network also can release some special substances (such as TNF-α and IFN-γ) or inhibiting some genes expression (such as inhibiting TGF-β) after the functional T-cell in vivo infusion as **(Figures 1A and 1B)**; (c) Functional inducing or inhibiting T-cells could be much safer than genetically-modified T-cell immunotherapy cells to treat patients with a good efficacy as **(Figure 1C and 1D)**; (d) Once new antibodies, antigens, cytokines, growth factors and receptors are discovered such as antibody to anti-PD-1 and anti-cytotoxic T-lymphocyte antigen-4 (CTLA-4), individual T-cell genomic profiles related to network to link the new compounds can be quickly applied to personalized immunotherapy for different patients.
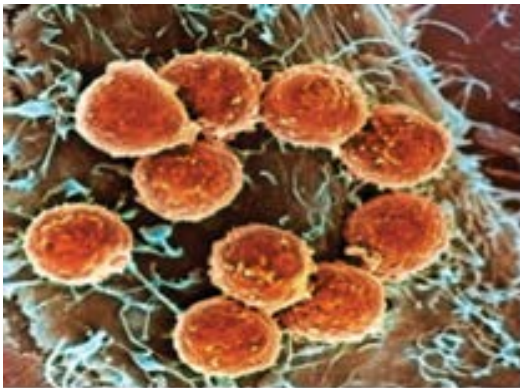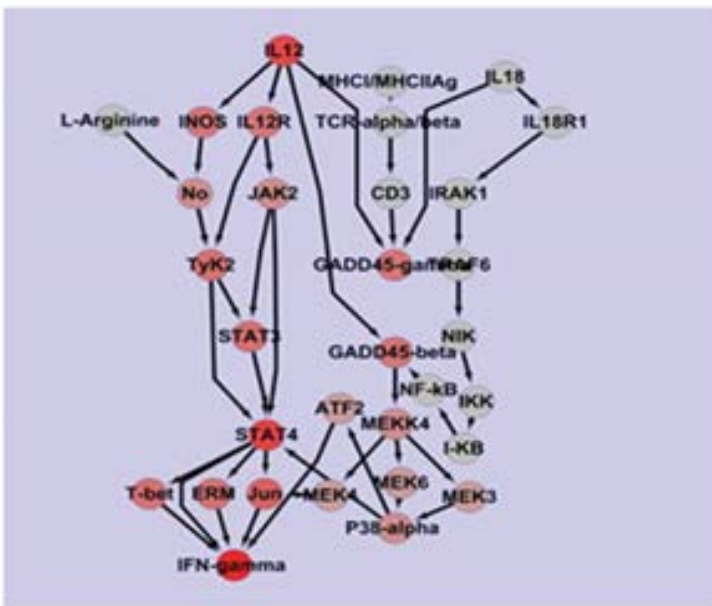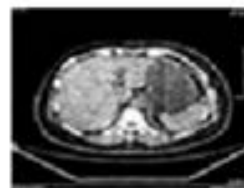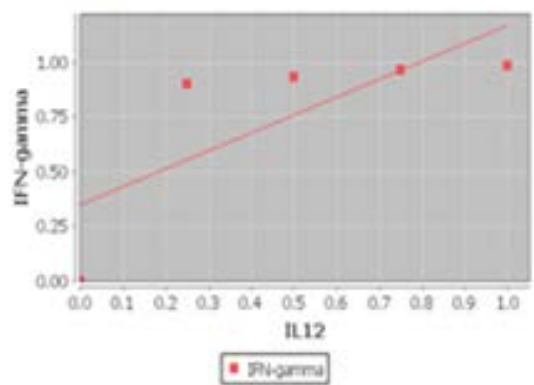
Figure 1 A. Network and layout from patient genomic biomarkers. Red colour indicates inducing network; B. IL12 can induce γ-IFN higher expression in the patient; C. A primary hepatocellular cancer (51 years old, female) with size about 8x9 cm mass before treatment; D. Tumor mass decreased to 6x7 cm with liquefaction after 5 months of personalized immunotherapy.

References

1   Biaoru Li, George Liu, Hongliang Hu, Jianqing Ding, Jie Zheng and Alex Tong (2015) Biomarkers Analysis for Heterogeneous Immune Responses of Quiescent CD8+cells -A Clue for Personalized Immunotherapy. Biomarkers Journal 1: 3.

2   Rosenberg SA et al. (2015) Adoptive cell transfer as personalized immunotherapy for human cancer. Science 348: 62-68.