EXPRESSION OF ION CHANNELS IN CAR T-CELL GENERATIONS

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Cancer immunotherapy partly relies on the reprogramming of host immune cells to recognize and eliminate cancerous cells. Genetic modification of T cells CAR (CAR T-cells) could be utilized in the treatment of hematological malignancies. Ion channels of T-cells participate in the regulation of activation via modulation of Ca^{2+}-dependent pathway. Moreover, ion channels play role in various effector functions inevitable for target cell abolition. Consequently, modification of ion channels' function can contribute to the successful immune therapy. However, no study reported about the expression of CAR T-cells ion channels expression so far.
In cooperation with the Cellular and Molecular Therapy Group at our department we created generation 1, 2 and 3 CAR T-cells. We used whole-cell patch-clamp technique and FURA-2 based Ca^{2+}-imaging to assess the expression level of Kv1.3/KCa3.1 and CRAC level in CAR T-cells, respectively.
We showed that Kv1.3 expression was the same in all groups, while KCa3.1 expression increased gradually from generation 1 to 3 CAR T-cells: generation 2 and 3 cells had almost doubled KCa3.1 expression. Motivated by this, we determined the KCa3.1 and Kv1.3 level in CD4/CD8 population of generation 3 CAR cells: 1) the KCa3.1 expression in $CD8^+$ CAR cells was higher than in $CD8^+$ control, 2) the Kv1.3 expression level in CD4+ CAR cells was higher compared to control. Thapsigargin-induced Ca^{2+}-response of CD8+ CARs was the lowest as compared to other CD4/CD8 groups. We suppose ion channels can facilitate outcome of immunotherapy and further experiments needed to clarify their functional role.

CAR: chimera antigen receptor, CD4/8: cluster of differentiation 4 or 8, Kv1.3: Shaker-type K^+ channel, type 1.3, KCa3.1: Ca^{2+}-activated K^+ channel, type 3.1, CRAC: Ca^{2+}-release activated Ca^{2+} channel