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Editorial

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Novel CAR-T cells to eliminate cancer

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We are excited to start a first issue of online journal *Trends in Cancer Research and Chemotherapy.* The journal will be focused on all aspects of cancer research and chemotherapies.

Recently immunotherapy became very important type of therapy to decrease cancer growth. In particularly, CAR (chimeric antigen receptor) therapy [1-3] demonstrated remarkable results leading to two novel FDA-approved drugs. Cellular immunotherapy such as CAR -T cell therapy is a highly promising approach for the treatment of hematological and solid cancers [4-6]. CAR-T cell therapy is efficacious against B cell malignancies including leukemia (acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), diffuse large B cell lymphoma, follicular lymphoma and mantle cell lymphoma and others [7-9]. **In addition, CAR-T cells effectively eliminate solid tumor cancer [10].**

The CARs contain an extracellular single-chain variable fragment (scFv) specific for the tumor surface antigen, along with a transmembrane domain and intracellular co-stimulation and activation domains [5-7]. In clinical trials, CD19-specific CAR-T cells targeting CD19-positive hematological cancers have yielded response rates of 80-90% in acute lymphoblastic leukemia and 50-80% in refractory lymphomas [11]. In solid tumors, there are more challenges exist on the road to achieve high response rate in patients [12].

Recently we demonstrated that the addition of a FLAG (DYKDDDDK) tag to the CD19 CAR did not affect its cytotoxic function against cancer cells *in vitro* or *in vivo* [13]. In addition, the FLAG tag reduced the levels of cytokines produced by the CAR-T cells, which might be advantageous for clinical studies (for example, limiting cytokine release syndrome). The FLAG tag can be used for detection, sorting the CAR-T-positive cells and for imaging the CAR-T cells after injection into the patient. Importantly, the FLAG tag is not immunogenic in primates [14], suggesting that it can be used for human studies.

FLAG-tagged CAR-T cells are not limited to hematological cancers, but can also be used for solid cancers. We recently found that FLAG-tagged CAR-T cells specific for mesothelin were as effective as non-tagged mesothelin-specific CAR-T cells. As with CD19, mesothelin-FLAG CAR-T cells were effectively detected with the anti-FLAG antibody.

In addition, we developed novel CD47-CAR-T cells targeting CD47 tumor antigen and demonstrated that CD47-CAR-T cells effectively killed ovarian, pancreatic, lung, melanoma cancer cell lines *in vitro* and blocked pancreatic xenograft tumor growth *in vivo* [15,16]. We also developed humanized CD47 CAR-T cells that will be tested in future *in vivo.*

Thus, novel CAR-T therapies will be developed in future against hematological and solid tumor targets.

I would like other authors to submit their novel data to our journal.

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