Armed T cells with CAR for cancer immunotherapy

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The development of genetic engineering has enabled the modification of stem cells and somatic cells. T cells exert immune responses against cancer cells. Efforts to redirect T cell specificity of a chimeric antigen receptor (CAR) to a desired antigen began in the 1990s (Gross et al., 1989; Kuwana et al., 1987). In 2006, the first clinical trial using carbonic anhydrase IX CAR-T cells to fight renal cancer was conducted (Lamers et al., 2006). Until 2011, Porter et al. exploited CD19 CAR-T to treat refractory/relapsed chronic lymphoid leukemia (Porter et al., 2011). Subsequently, trials using CD19 CAR-T to treat hematological malignancies, including acute lymphoid leukemia (Grupp et al., 2013), lymphoma (Brentjens et al., 2013; Lee et al., 2015), and even multiple myeloma (Garfall et al., 2015) revealed a positive response rate. In 2013, along with antibodies targeting immune checkpoints, CAR-T therapy reached a scientific breakthrough. A 93% complete response rate of CD19 CAR-T based cancer immunotherapy for acute lymphoid leukemia was reported at the most recent American Society of Hematology (ASH) meeting. Currently, more than 70 clinical trials are recruiting patients for CAR-T-based cancer immunotherapy.

In China, CAR redirected T cells have been widely investigated (Wang et al., 2009; Wang et al., 2013). Several antigens recognized by CAR-T cells have been exclusively studied in China (Deng et al., 2015; Tang et al., 2014). Gao et al. completed preclinical studies of using glypican-3-specific CAR-T cells to treat hepatocellular carcinoma (Gao et al., 2014); these clinical trials are currently in

the recruitment stage. Han et al. registered the first CD138 CAR-T therapy for multiple myeloma (NCT01886976). Recent results from clinical trials in China showed substantial efficacy for treating hematological malignancies (Dai et al., 2015; Zhang et al., 2015; Zhang et al., 2016). To date, 29 clinical trials to evaluate the safety and efficacy of CAR-T therapy are being conducted in China and are expected to provide support for the safety and efficacy of CAR-T cells for further applications.

It is my great honor to guest-edit this special topic focused on CAR-T in *Science China Life Science*. In this issue, I present my understanding of the current status of CAR-T therapy in China and worldwide. To expand the therapeutic benefit for cancer patients in China, three aspects of CAR-T therapy must be addressed: (i) Regulatory guidelines specific for CAR-T therapy must be established to facilitate the commercialization of this cancer immunotherapy by pharmaceutical companies. (ii) Enhancing the therapeutic efficacy of CAR-T therapy for solid tumors is an important task. (iii) Enhancing the efficacy and safety of CAR-T therapy and searching for antigens specific to tumor cells is suggested, particularly using genome-wide sequencing to identify unique mutations related neo-antigens for CAR design. Once these aspects are resolved, CAR-T-based cancer immunotherapy is expected to provide multiple benefits to cancer patients.

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Biographical Sketch

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