

Bispecific Antibodies: Bright Way for Cancer Therapeutics

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Editorial

Antibody based cancer therapeutics show great beneficial to more and more patients and the antibody drug market is growing fast. As Removab[®] approved in 2009 and Blincyto[™] approved in 2014, bispecific antibodies with combination of two antigen binding specificities shed new light on antibody based cancer therapeutics especially when new technologies for engineering and manufacturing are available.

Currently, most of approved antibody for cancer therapy is monospecific with limited binding to one antigen. Drug resistance and cancer relapsed are the biggest obstacle for monoclonal antibody (mAb) therapy [1,2]. Bispecific antibodies with two functional “arms” simultaneously addressing two different antigens or epitopes are sufficient to target two pathways involved in cancer pathogenesis showing advantage over the mAb therapy (for example, targeting EGFR and IGFR) [3]. With the combination of specificity of two different antibodies, bispecific antibodies have inherent specificity towards target. Moreover, some clinical studies have shown that the expression level of targeted receptor is decreased or even lost after mAb therapy, such as anti-CD20 therapeutics [4-6]. Bispecific antibodies could be worthwhile to try to push CD20 targeting therapy back to the right path.

The major advantage of bispecific antibodies is harnessing immune effector cells to kill cancer cells. Cytotoxic T lymphocytes play a critical role in immunosurveillance and anti-cancer immunity. Bispecific antibodies redirect cytotoxic T cells to cancer cells to form a cytolytic synapse followed by T cell activation, proliferation and cancer cell lysis. Besides blinatumomab, several bispecific antibodies engaging T cells show promising anti-cancer efficacy in clinical trials [7,8]. Moreover, targeting innate immune system by bispecific antibodies is another attractive strategy which has been gaining more and more interest. As an important member of innate immune system, natural killer (NK) cells play a major role in antibody dependent cytotoxic activity (ADCC) through FcγIIIa receptor (CD16A). So far, lots of excellent work has been made to enhance the effector function of therapeutic mAb by Fc mutation or glycosylation engineering. Bispecific antibodies are much more straightforward to bridge NK cells to cancer cells via CD16A receptor and clinical studies show that NK cell engager indeed demonstrates potent cancer killing effect [9]. As a bispecific fusion protein targeting NKG2D showing potent efficacy against human multiple myeloma, NKG2D could be an ideal target for bispecific antibodies to redirect and activate NK cells in cancer immunotherapy [10].

With the technological breakthrough in bioengineering, more and more novel platforms for bispecific antibodies are emerging. And the revival of bispecific antibodies gains the attention of biopharmaceutical companies. There is no doubt that bispecific antibodies will likely lead the antibody market in the next few years based on the encouraging clinical results in cancer immunotherapy.

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