

Antibody Conjugates: The Future Is Now

The 1955 short film *The Future Is Now* highlighted inventions for the future, predicting home movies projected on television and videophones, automatic doors, solar power, and radiolabeled medicines. These ideas, seemingly farfetched at the time, are now everyday tools. This issue of *CCR Focus* offers, in many ways, a similar projection of future potential. Building upon ever-improving technology to identify specific antibodies for specific tumors and arming those antibodies to deliver toxic molecules to cancer cells has seemed for many years an impossibly optimistic strategy, despite the earlier approval of radiolabeled antibodies. However, the reality is that this strategy is in the clinic, and it is likely here to stay. As this issue of *CCR Focus* went to press, the U.S. Food and Drug Administration (FDA) approved SGN-35, brentuximab vedotin. The drug consists of a monoclonal antibody targeting CD30 linked to several molecules of monomethyl auristatin E, a highly potent antitubulin agent. This FDA approval follows by a decade the accelerated approval of gemtuzumab ozogamicin for acute myelogenous leukemia. In 2010, the latter was withdrawn from consideration for regulatory approval in the United States, following inferior results in a clinical trial in first-line therapy, albeit a different clinical setting from that upon which the accelerated approval was based. These advances represent a version of "personalized medicine" for the future, one in which a patient's tumor could be studied for surface expression patterns that could be targeted by antibody conjugates. If we view the current molecules in development as prototypes, as in the 1955 film, then there is room for considerable excitement and optimism. With expert Beverly Teicher as Guest Editor, this issue of *CCR Focus* reviews a series of these molecules, many already in the clinic, and highlights both successes and challenges in development. Steiner and Neri discuss antibody-radionuclide conjugates, both old and new; LoRusso and colleagues describe the development of T-DM1, the trastuzumab-maytansine conjugate, in breast cancer; Katz, Janik, and Younes introduce data underlying the recent approval of brentuximab vedotin; Ricart highlights inotuzumab ozogamicin, an anti-CD22 conjugated to a derivative of calicheamicin; Blanc and colleagues discuss SAR-3419, a CD-19 antibody conjugated to a maytansine derivative; and Kreitman and Pastan describe the long march toward approval of moxetumomab pasudotox, an anti-CD22 monoclonal antibody conjugated to a fragment of *Pseudomonas* exotoxin. The only disappointment is that so many of the conjugates are directed toward antigens found on lymphoid cells; only T-DM1 targets a solid tumor. This, then, is the challenge ahead: identifying unique antigens on the solid tumors in oncology that cause the majority of death and suffering. As with every issue of *CCR Focus*, this issue is meant to be accessible to those interested but not experts in the topic, to stimulate the thinking of those in the field, and to highlight concepts for future research.

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