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Translation

Chugai's Novel Antibody Engineering Technology Published in Nature Biotechnology

- Enabling single antibody molecule to block the function of target antigen multiple times -

October 18, 2010 (Tokyo) - Chugai Pharmaceutical Co., Ltd. ("Chugai") [Head Office: Chuo-ku, Tokyo. President: Osamu Nagayama] announced today that Chugai has established a innovative antibody engineering technology that enables a single antibody molecule to block the function of target antigen multiple times, which was previously impossible for conventional monoclonal antibody. This technology has been published online in Nature Biotechnology November edition, which can be accessed from October 17(BST) on its website. (http://www.nature.com/nbt/journal/v28/n11/index.html)

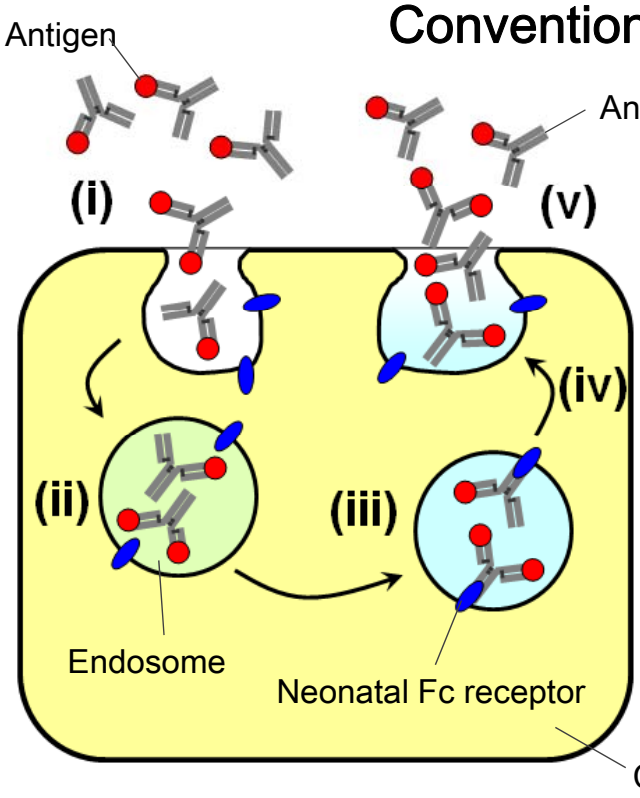
Monoclonal antibodies can specifically bind to a target antigen and selectively block its function. Most of the currently approved monoclonal antibody therapeutics exert their therapeutic efficacy by binding to the disease related target antigen and blocking its function. However, in case of conventional antibodies, a single antibody molecule could bind to the target antigen and block its function only a single time. Utilizing the technology published in Nature Biotechnology, this novel monoclonal antibody is capable of binding to the target antigen multiple times. This novel technology is characterized by the fact that once the antibody binds to the target antigen in plasma and delivered into the endosome (one of the cellular organelles), the target antigen is released from the antibody within the endosome. As a result, the target antigen is transferred to the lysosome (cellular organelles responsible for degradation) and rapidly degraded, whereas the antibody is recycled back extracellularly and able to bind to another target antigen. By repeating this cycle of binding to the antigen in plasma and releasing the antigen in the endosome, the antibody can bind to the target antigen multiple times and repeatedly block its function.

Chugai has successfully applied this technology to Actemra®, a humanized anti-human IL-6 receptor monoclonal antibody, to generate a second generation anti-IL-6 receptor antibody capable of repeatedly blocking IL-6 receptor function multiple times. By applying this technology, preclinical studies have demonstrated that duration of IL-6 receptor blockade has improved more than 4-fold compared to Actemra®. Reduction of injection dose and/or frequency could be achieved only by applying this novel technology, but not by conventional antibody engineering technologies. Therefore, significant improvement in patients' convenience is expected by this technology. In addition, this technology can be applied to monoclonal antibodies targeting various disease related antigens other than IL-6 receptor, and thus we believe that this novel technology would lead to the generation of innovative antibody therapeutics which cannot be achieved by conventional monoclonal antibodies

Chugai, as a leading company in the biotechnology field, will continue working to develop innovative technology and apply such technology to drug discovery, in order to contribute to the human health around the world.

(Reference)

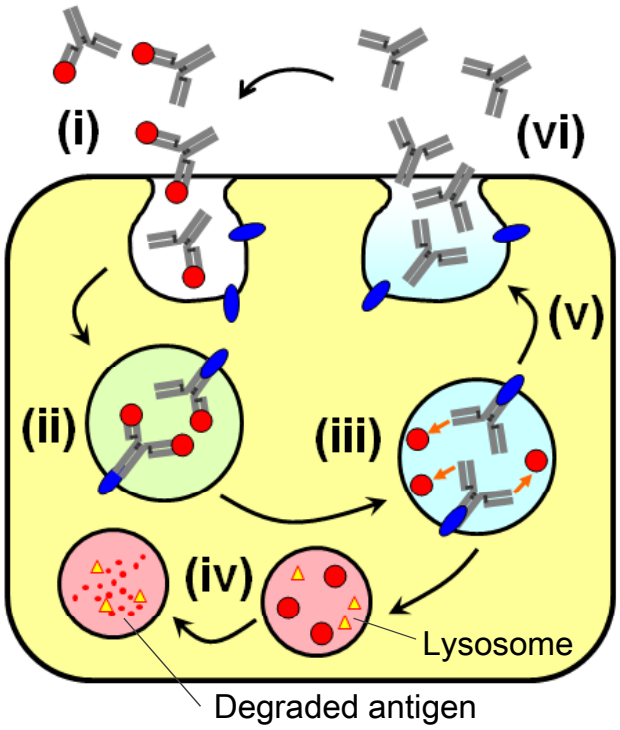
Conventional antibody



(i) Conventional antibody binds to the target antigen in plasma, and (ii)-(iii) delivered into the endosome while the target antigen is bound to the antibody. Then, (iv) antibody is extracellularly recycled back as an antigen bound form. Therefore, (v) the recycled antibody cannot bind to the next antigen.

Conventional antibodies can bind to the antigen only single time by single antibody molecule.

Antibody generated by novel technology



(i) Antibody generated by novel technology binds to the target antigen in plasma, and (ii) delivered into the endosome. Within the endosome, (iii) the target antigen is dissociated from the antibody. Then, (iv) antigen dissociated from the antibody is degraded within the lysosome, whereas (v) the antibody is extracellularly recycled back as an antigen non-bound form. Therefore, (v) the recycled antibody can bind to the next antigen.

By repeating this binding and dissociation, antibodies generated by novel technology can repeatedly bind to the target antigen multiple times by single antibody molecule.