EL7. *In Vivo* Application of Radiolabeled Monoclonal Antibodies

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One day one surgeon brought one monoclonal antibody with him to our laboratory. He told me that he developed the murine monoclonal antibody that reacted with human colorectal tumor cells. He was proud of saying that his antibody could be potential for targeting tumors. We labeled his monoclonal antibody with I-125, and then injected it to nude mice bearing human colorectal cancer. We were happy to see that I-125-labeled antibody was localized to tumor specifically. We had believed that we could open the door toward the "magic bullets." It was about fifteen years ago. Now what is going on with this targeting concepts?

In this overview recent news from the newcomer is presented, including general remarks regarding antibodies, labeling techniques, radionuclides, and biological considerations.

(1) Monoclonal antibodies

Many monoclonal antibodies have been developed. Whatever they react with, the reaction should be specific with high affinity. Antibodies should react with some antigens which are present in targeting cell surface or targeting tissue vessels. Chimeric or humanized antibodies are preferable for clinical use because they are less immunogenesity that makes repeated administration possible. Fragmentation of an antibody has been well studied. Small fragments, such as single Fv chain, are cleared from the body very rapidly. The tailor-made antibodies are now possible to be produced by recombinant technology.

(2) Radionuclides labeled

I-131, In-111, and Tc-99m are popular radionuclides for labeling antibodies. Labeling techniques have been exclusively studied. The point is how to retain radionuclides in the targeting tissues with high amount and in the normal tissue with small amount. Pre-targeting procedure, using bifunctional antibodies or avidin-biotin is of promise for decreasing the nonspecific uptake especially in the liver. I-131, Y-90, and Re-186 are good candidates for radioimmunotherapy. Their physical properties such as their LET, as well as their biopharmacological characterization such as their biodistribution, influence the results of radioimmunotherapy of cancers.

(3) Targeting tissues

As long as the monoclonal antibody is specific for the disease, the labeled antibody injected should reach any disease, such as tumors, inflammation, or infarction. The point is how to deliver radionuclides efficiently. The vascularity and permeability of the targeting tissues are major factors. The antigen density of targeting tissues also influenced the uptake of radiolabeled antibodies. Pretreatment with some drugs such as Interferon and Interleukin-2 have been successful for efficient targeting.

(4) Clinical situation

A huge cases have been reported about radioimmunoscintigraphy. Some of them have played the important role for the patient management. Cancer transplanted in nude mice could be well treated with radioimmunotherapy. Clinical radioimmunotherapy of cancer have, however, been less successful than we might have expected. The recent success of radioimmunotherapy of B-cell lymphoma with I-131-labeled antibody has encouraged us to go on clinical applications. It also made some points clear to succeed radioimmunotherapy.