NOBEL SYMPOSIA

Report from the lecture presented by Richard Lerner

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Antibody molecules with its programmable binding specificity has emerged as an important tool for chemistry and medicine. Today at least 17 different antibodies have been approved for therapeutic use and hundreds more are in clinical trials.

One major problem when developing antibodies outside the human body is the immune response to the antibody itself when introduced as a vaccine. In addition, some patients cannot or should not be immunized for various reasons. To overcome these problems, antibodies can now be "raised" outside of the body and endowed with affinities, and selectivity that the patient's immune system might not be able to produce.

A large variety of such antibodies are prepared in combinatorial human antibody libraries and specific antibodies that bind to specific targets are then selected. The use of combinatorial libraries that contain many more antibodies to each antigen permits selection of antibodies with an increased selectivity and avidity. The approach also allows the ability to create and select antibodies that do not exist in nature the access to the entire diversity of the immune system such that one can harvest any antibody no matter how rare. Indeed, one can access any antibody that an individual has ever made irrespective of whether it is currently being produced while avoiding the immune response in humans. In addition, the combinatorial library allows production of antibodies without immunization. Another advantage is that these antibodies can be conjugated to toxins to destroy target cells. Furthermore, antibodies can be designed to carry catalytic activity such that covalent bonds are made upon binding to their antigens. In addition to offering new ways to destroy antigens such antibodies can lend long "antibody half-lives" as compared to shorter-lived drugs and peptides. In cancer therapy, covalent antibodies can give immune effector function to cell-specific molecules that are otherwise not sufficiently toxic to remove tumor cells.

One example of the application of this technique is the human antibody “Humira” to treat Rheumatoid Arthritis. Another example is production of human antibodies that bind to metastatic breast cancer cells but not the parental tumor. These antibodies block the process of metastasis and kill metastatic foci that are already established.