《招待講演 2》

Nuclear Immunology: At the Crossroads of Immunology and Nuclear Medicine

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Localisation of radiolabelled antibodies was first described by Pressman and Keighly 45 years ago (1948) in animals. However, first success with this technique did not occur *in vivo* but by combination of the specificity of immunologic reactions with the sensitivity of radioactive tracer methodology *in vitro* (radioimmuno assay technique in the fifties). This interface of two specialities of medical science (unclear medicine and immunology) had an enormous and still growing impact on the practice of medicine. To date, most assays, particularly for hormones, rely on *monoclonal* antibodies which have provided increased sensitivity. Another very important practical application of monoclonal antibodies is the immunohistochemical characterization of various tissues and bone marrow purging.

Since 1965, when Gold and Freedman detected the carcinoembryonic antigen (CEA)—which is nowadays still the most widely used tumor-associated antigen (NCA was described also at that time by von Kleist and Burtin and has recently gained a very important new application in immunoscintigraphy of inflammation and for bone marrow imaging by *in vivo* labelling of granulocytes via anti-NCA antibodies)—dramatic basic discoveries have been made in immunology. The *monoclonal antibody technology* (Köhler and Milstein, 1975) enabled the characterization of innumerable new tumor-associated and even tumor-specific antigens. Intact antibodies have been fragmented into smaller, less immunogenic molecules. *Genetic engineering technology* was applied for the production of chimaeric (mouse-human), humanized (reshaped CDR grafted) and human monoclonal antibodies. Hybrid molecules (bispecific antibodies, chemically synthetized bispecific monoclonal antibody conjugates, antibodies linked to immunomodulators, enzymes, cytotoxic drugs etc.) were created, which held great promise for the future.

The next revolution is just to come: Genetic engineering technology enables antigen-binding fragments to be made by exploiting repertoires of variable domain genes derived from immunized animals and expressed in bacteria (E. coli) or yeast (F_v cloning by PCR). Looking ahead, animals might even be bypassed and antibody production *in vitro* might be possible by making repertoires of antibody genes and selecting those with antigen-binding activity or by using computer graphic techniques to build specific antigen-binding sites ("designer antibodies"). It might well be that in a few years from now on, only small sized, molecular engineered "smart" peptides (molecular recognition units, only few amino acids of length) will be used (instead of the large proteins currently applied), similar to receptor-recognizing substances which have already proven their great potential in nuclear medicine practice. Furthermore, during the last ten years, *labelling techniques of monoclonal antibodies* have also been dramatically improved. Especially the introduction of a simple, fast and efficient technique for Technetium-99m labelling of proteins was a decisive step towards to the routine establishment of immunoscintigraphy. Improved nuclear imaging systems, e.g. multihead gamma cameras, single photon (SPECT) and positron emission tomography (PET), will enable us to detect disease in an earlier stage and with higher resolution. Highly specific tracers, like monoclonal antibodies and molecular recognition units on the one hand, and sophisticated imaging technologies on the other, will make it possible to fully use the potential of immunology and unclear medicine by combining specificity with sensitivity.

Since Dec. 1984, nearly 2,500 patients with various malignant and benign diseases have been studied at our institution with radiolabelled monoclonal antibodies. The main clinical indications (colorectal cancer, ovarian carcinomas and head and neck tumors as well as *in vivo* cell labelling and detection of myocardial necrosis will be discussed in detail and are excellent examples that in clinical practice the concept of Nuclear Immunology is established and works.

In the future, therapeutic applications of this fascinating concept (radioimmunotherapy, immunotherapy) might become a new avenue emerging from the crossroads of Nuclear Medicine and Immunology.