

Beatrix Kotlan Scientific Research Summary

She was a most dedicated and independent research scientist, with great enthusiasm and responsibility. A rare and outstanding Clinical Immunologist specialized in both Transplantation and Cancer Immunology. As a transplant immunologist, she studied ways and means to downregulate antibodies, while as a Tumor immunologist to develop immunotherapeutic strategies to augment antibodies to kill tumor cells.

At the beginning she focused on chimerism and induction of tolerance in transplant recipients, realizing “the need to get rid of complications from immunosuppressive treatment, and escape from symptoms related to chronic rejection” (*VOX Sang* 2002; 83, (SUPPL. 1): 159-165). Even after two decades, her work is being cited extensively (Beatrix Research Gate Citation index 31.74 on the day of her demise).

Working in the frame of the Hungarian healthcare system, in a governmental hospital, always presented real challenges to researchers: from the very beginning she had to manage all kinds of tasks from several independent experiments, through developing and standardizing novel assays up to project application writing and getting support for her research. She did much of her bench to bedside research herself. In the course of the years she learned and became skilled in a number of high-quality complicated research techniques.

She had to take considerable part in different patient-related diagnostics (functional immunological assays for immune deficiencies and bone marrow transplantation, phenotyping of leukemia patients, constant on call service for kidney transplantation-related immunology). Her scientific results and presentations in Hungary and abroad were highly appreciated, and helped her building international collaborations independently, getting scholarships and developing her own favorite projects of interest.

Regarding the state of woman researchers at international level Beatrix was very upset about the fact that woman scientists over forty were pretty much neglected, there were no more scholarships available for them and they had to fight twice as much to succeed.

From the very beginning she very actively researched histocompatibility (HLA) in the field of immunogenetics.

She soon became intensively involved in the strenuous international kidney transplantation night duty service, enabling to find the right donor kidney for the patient. This took many valuable years from her research.

Later on, she successfully applied immunotherapy (intravenous immunoglobulin, IVIg) for the treatment of recurrent spontaneous abortion. She was the first in Hungary to launch and develop a nationwide translational research project in reproductive immunology to help couples bring to life healthy babies with the help of Interferon, resulting in the birth of healthy newborns in 88,6% of 26 patients.

She also intensively researched cytotoxic T-lymphocyte precursor frequency with acute and chronic GVHD in matched sibling bone marrow transplantation.

Her in-depth studies on IVIg led her to join a team to define the critical hurdles in cancer immunotherapy (*J Transl Med.* 2011; 9: 214).

As a first step, she has focused and developed a novel panel assay to define tumor-associated antigen-binding antibodies in patients with metastatic melanomas with potential diagnostic value (*Immunol Res.* 2015; 61(1-2):11-23). Her second approach was to develop challenging tumor immunological techniques to track cancer stem cells in malignant melanomas and other solid tumors (*Contemp Oncol (Pozn).* 2018;22(1A):41-47). The third step of her primary research was to investigate the repertoire of antibodies against tumor-associated disialylated glycosphingolipid antigens in melanoma patients. Serendipitously, she has deciphered a bi-directional regulatory mechanism between B Cells and the tumor (*Frontiers Immunol.* 2019; 10: 650).

Moreover, Beatrix Kotlan has developed a novel approach and could define important tumor associated membrane structures in breast carcinomas. She became very skilled in antibody engineering and high throughput molecular genetic techniques and successfully obtained grants and scholarships (Fulbright, NATO CLG, Eotvos, etc) for her project. Her results in breast cancers served as “proof of principle” in revealing tumor antigens by tumor infiltrating B cells.

As a result of Beatrix’ Hungarian and international applications (OTKA T030380, OTKA T048933, Eotvos, NATO CLG, Fulbright) an immunological reagent was developed for the diagnosis of tumor patients, to reveal micro metastases in the course of the metastasis process. She managed to biochemically identify the target molecule of the reagent’s specific binding. She could prove that the reagent is important not only for breast tumors, but for other solid tumors also.

Another important project was the immunoglobulin repertoire analysis based on DNA sequence analysis, which is the foundation of the genetical identification and biotechnological feasibility of the protein molecules targeting the tumor cell.

Beatrix’ other main activity was the detailed DNA- and tumor-cell-level analysis of immunocompetent cells originating from breast cancer, melanoma and other solid tumors, aiming at diagnostical use.

The tumor reactive antigen derivatives can be developed thanks to a novel approach, which promise further therapeutic use at international level.

She strongly believed that the genetic information inherent to the immune cells within the tumor might one day be useful in cancer therapy.

Will A Foster has said: “Quality is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives, the

cumulative experience of many masters of craftsmanship. Quality also marks the search for an ideal after necessity has been satisfied and mere usefulness achieved.” Beatrix’ last paper in *Frontiers in Immunology* (2019; 10: 650) says it all.

Her many friends and colleagues find it very hard to bid farewell to Beatrix. This is the time to emulate her and continue the research journey with her spirit in our thoughts.