

Van Loghem Laureate Jannie Borst: A fascination for the complexity of life



Prof. dr. Jannie Borst (1957) is honored to join the ranks of the Van Loghem Laureates and to deliver the Van Loghem Lecture 2009. “All of my predecessors are outstanding scientists who have significantly contributed to the field of immunology. To follow in their footsteps feels as a recognition for a life-time effort to make a difference.” With her impressive list of contributions, one can only conclude that Jannie Borst succeeded in this ambition. But success did not come easy, says Borst: “It required hard work and perseverance.” An interview with the laureate.

Jannie Borst had no grand design to become an immunologist. “Not at all. When I left high school, I was fascinated by the complexity of life and the impact of mankind on nature. I still am, by the way. Biology seemed the right study for me, but I was afraid it would be a little bit soft and not challenging enough. Therefore I opted for a Master in Biology with Chemistry at Leiden University.” She focused on biological insect control, a new topic in the mid seventies. But eight months of counting aphids in a greenhouse proved to be a little boring. “I was not so much interested in how many parasitic wasps were needed in order to reduce the number of aphids to acceptable levels. I was more intrigued by the mechanisms at work on a molecular level. And so I chose to specialize in biochemistry, in protein molecules.”

Novel approach

Jannie Borst obtained her Master in Biology with Chemistry in 1980 with outstanding notes, alongside the ambition to start a scientific career. Unfortunately for her, a large number of young professors had recently been appointed for life. Her career perspective in The Netherlands was therefore virtually non-existent at the time. “I still think it has been an unwise policy in the seventies to appoint a generation of professors who hardly had to prove themselves, like the generations after them had to”, she says. But Jannie Borst turned this disadvantage into an advantage. She was forced to look beyond the Dutch borders and one of her professors recommended her at the Dana-Farber Cancer Institute in Boston. “When I applied, I was unaware of the fact that the institute was part of the renowned Harvard Medical School”, she admits. “I did the major part of my PhD work under the supervision of biochemist professor Cox Terhorst and entered the world of immunology. We studied T lymphocytes, a central factor in disease control. We focused on how T cells are able to recognize that cells have been invaded by a virus. Certain molecules on infected cells transmit pieces of virus protein. These are recognized by specific T cell receptors – after which the T cell starts to multiply in order to destroy the infected cells. With the help of monoclonal antibodies I discovered the CD3 gamma, delta and epsilon subunits of the human T cell receptor. These subunits are responsible for transmitting the signal that puts the T cell to work.” By then, it was a novel approach to use monoclonal antibodies to discover these molecules. “A very exciting time.”

Two main research lines

Life became a roller coaster ride for the young PhD student, publishing in Nature and cited by the crème de la crème in immunology. In 1984 she returned to the Netherlands to work with immunologists dr. Jan de Vries and dr. Hergen Spits. “They were able to culture human T cells, something few people could do in those days.” In 1985 she obtained her PhD degree from Leiden University and in 1987 she started an independent career with the aid of a 5-year personal fellowship from the Netherlands Organization for Scientific Research (NWO). This was followed by a staff scientist position at the Netherlands Cancer Institute (NKI-AVL) in 1992, up to now her employer. In 1999 she was appointed professor in Experimental Oncology at the University of

Amsterdam and in 2002 she became head of the Immunology division at the NKI. “Since 1984 I have been working on improving immunotherapy of cancer. Sustaining survival of activated lymphocytes is expected to improve anti-tumor immunity. At the same time, the mechanisms we elucidate may be exploited to block undesired immune responses, as in auto-immunity and transplant rejection. One main research line therefore focuses on the role of anti-apoptotic TNF receptor family members in control of the T cell response. The second aim of our work is to contribute to the design of novel anti-cancer therapies by exploiting apoptotic pathways. To this end, a second main research line targets on pro-apoptotic signaling by TNF receptor family members and DNA damaging anti-cancer regimens.”

Endlessly fascinating

Over the years, Jannie Borst not only discovered the CD3 complex, but also a novel human T cell subset expressing T cell receptor gamma/delta. Another highlight was the discovery of the signal transduction complex associated with human membrane immunoglobulin (BCR) and the implication of various signaling molecules in the BCR pathway. The list of key contributions by her group also mentions the identification of TNF receptor family member CD27 and its ligand CD70 as an important T cell costimulatory system, the elucidation of the mechanism underlying ceramide production in response to apoptotic stimuli and the discovery of a novel mechanism of ubiquitination that regulates apoptotic signaling by death receptors.

Research is endlessly fascinating, Borst says. At the same time it can be depressing, because of the never ending fight for research funding. “And just like in top sport, researchers have to cope with many disappointments”, she says. “It is the occasional highlight that keeps us going.” Teaching helps, says Borst: “I find it stimulating. It's important to share our knowledge, and I am happy to meet young people, who are enthusiastic about science. It makes me feel useful.”

In her oration she explained why it is so difficult to battle cancer. But, she says: “Over the past years researchers have come to understand the molecular basis of cancer which has allowed completely novel approaches to fight it. We have made incredible progress.”

Sustainable society

As devoted as she is to her work, she still finds the time to do sports, to read and to enjoy the company of close friends. From time to time she can be found in South Africa, where her partner lives. “My life there is the opposite of my life here in Amsterdam: our house lies secluded, surrounded by nature, overlooking the ocean. Just maybe, in ten years or so, I might start a life over there. I don't think that I could stay content by just hanging around. But I can imagine myself returning to my biology roots: protecting nature, striving for a sustainable society.”