

Healthcare industry BW

Joining forces to develop anti-cancer immunotherapies

No cancer therapy is currently achieving such promising results as immunotherapy. The German Cancer Research Center and Bayer HealthCare have established a joint laboratory to develop novel immunotherapies that selectively reactivate the body's own immune system and incite it to attack tumour cells, thereby supporting the faster translation of concepts from the laboratory into clinical application.



Prof. Dr. Philipp Beckhove, head of the Department of Translational Immunology at the German Cancer Research Center
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“None of our other medical approaches is currently achieving such impressive results in cancer treatment as immunotherapy,” said PD Dr. Jürgen Krauss, scientific director of the “32nd Heidelberg Spring Symposium - Immunotherapy in oncology – new standards and future strategies” that will be organised by the National Centre for Tumour Diseases (NCT) in February 2015.

“Immunotherapy will become a solid pillar of tumour therapy in the future”, says Professor Philipp Beckhove, head of the Department of Translational Immunology at the German Cancer Research Center (DKFZ). The Heidelberg-based NCT, which is specifically focussed on combining ongoing cancer research with clinical patient care, is making a huge contribution towards achieving this.

Bayer and DKFZ extend strategic research alliance

Beckhove is also director of the Joint Immunotherapy Laboratory that was jointly established by the DKFZ and Bayer HealthCare at the NCT in 2013. Its aim is to extend the partners' successful strategic research alliance that has existed since 2008 and also focus their activities on the field of immunotherapy. The partners will invest a total of up to 3 million euros a year.

In June 2013, at the official opening of the laboratory, Prof. Dr. Otmar D. Wiestler, Chairman of the



Official opening of DKFZ's and Bayer HealthCare's "Joint Immunotherapy Laboratory" on 25th June 2013 by Prof. Dr. Philipp Beckhove (DKFZ), Prof. Dr. Guido Adler (University Hospital Heidelberg), Prof. Dr. Dr.h.c.mult. Otmar D. Wiestler (DKFZ), Dr. Karl Ziegelbauer (Bayer), Prof. Andreas Busch (Bayer) (from left to right).
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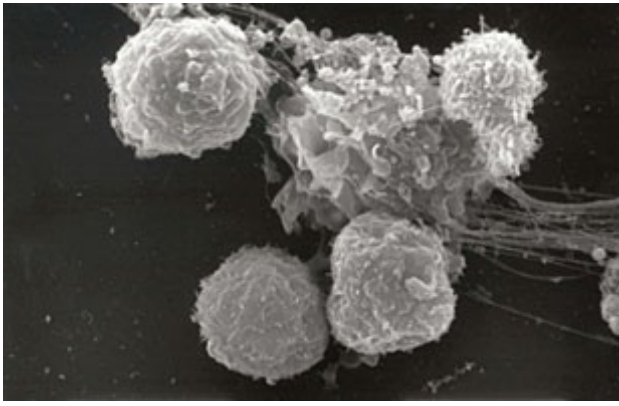
DKFZ's Management Board, and Prof. Dr. Andreas Busch, member of Bayer HealthCare's Executive Committee and head of Global Drug Discovery, declared their ambitious goal of identifying at least two new drug candidates in the field of cancer immunotherapy and moving them towards clinical trials. The partners will jointly work on the review processes of individual projects, the allocation of resources and have an equal share in the right to research results.

The joint laboratory accommodates several staff, including four post-docs. Around half of the staff is on Bayer's payroll and the other half is paid by the DKFZ. They work together on the projects. The close cooperation facilitates the rapid translation of basic oncological research results, which is the work done by the DKFZ, into clinical studies and the development of pharmaceutical compounds, which is where Bayer contributes its expertise.

Checkpoint inhibitors

Instead of attacking the tumour directly, cancer immunotherapy seeks to reactivate the body's own immune system and incite it to attack tumour cells. In general, tumour cells are recognised and eliminated by the immune system. However, the problem is that tumour cells that lead to cancer have effective mechanisms that they use to protect themselves against immune cells.

"Each tumour that manages to manifest itself in patients, has activated "brakes" in the patient's immune system which ensure that the body's own cells are not attacked," explains Beckhove. The mechanisms underlying these "brakes" are now quite well understood.



Dendritic cell with T lymphocytes
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CTLA-4 (cytotoxic T-lymphocyte antigen 4), a protein receptor found on the surface of cytotoxic T cells (ed. note: T cells that destroy virus-infected cells and tumor cells) and a kind of “checkpoint”, acts as such a brake, turning off the immune attack of T cells when stimulated. This brake can be released with a humanised monoclonal antibody (checkpoint inhibitor) that is directed against CTLA-4 and the immune reaction is subsequently directed against the tumour cells.

This involves antigen-presenting dendritic cells which present a “police photo” of the tumour cells to the T cells, thus directing the immune system attack to the tumour. The checkpoint inhibitors that are directed against the PD-1 (“programmed death-1”) receptor, which is involved in the regulation of the apoptosis (programmed cell death) of T cells, seem to be even more effective.

PD-1 is activated by the binding of immunomodulatory ligands (PD-L1 and PD-L2) which are expressed on tumour cells, thereby blocking an immune response to the cancer cells. Antibodies against PD-1 or its ligands reverse the blockade and enable the immune system to attack the tumour cells effectively.

Researchers around the world are working intensively on such immune checkpoint inhibitors and many studies are under way. Many companies are involved in drug development. The DKFZ’s and Bayer HealthCare’s Joint Immunotherapy Laboratory is also specifically focussed on identifying immunosuppressive molecules on the surface of tumour cells. The aim is then to block these molecules with antibodies and induce a specific immune response against the tumours.

A good start with an as yet uncertain end

At the end of 2013, the renowned scientific journal *Science* referred to the advances in immunotherapy as a turning point in cancer treatment. Finally, after decades of research, it now seems to be possible to activate the body’s own immune system against tumours. The first immunotherapies for the treatment of inoperable black skin cancer (ed. note: malignant melanoma) have already been given marketing authorisation. Other immunotherapies are undergoing testing in clinical trials, including for the treatment of kidney and lung cancer. Spectacular tumour remissions have been observed in these trials; Prof. Dr. Jäger, director of the Department of Medical Oncology at the NCT, reported on one such trial in January 2015.

However, it is still too early to judge whether such therapies are able to achieve the long-term suppression of the tumour or even cure the cancer. Some patients do not respond to immunotherapy at all, and it is currently not understood why this is so. There are no effective immunological treatment options for many tumours. As *Science* stated, the application of immunotherapy for

cancer treatment is the start of a new book; however, nobody knows how it will end.

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Boosting the immune system can improve cancer prevention and treatment

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