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Overcoming Tumor Resistance to Immunotherapy: The European Research Council awards international project led by Heidelberg Medical Faculty

IIn the PRECISION-ImmunoRad project, a multidisciplinary team of scientists from Heidelberg, USA, and Cyprus will unite their expertise to develop novel curative therapeutic strategies for currently hard-to-treat cancers. These strategies will integrate high-precision ion beam therapy with genetically engineered immune cells therapies (CAR-T cells), personalized cancer vaccines, and the targeted reprogramming of the tumor immune microenvironment. The European Research Council (ERC) awarded the Synergy Grant, coordinated by Heidelberg Medical Faculty at Heidelberg University, a total of €14 million over six years. Of this, €5.5 million is allocated to projects in Heidelberg.

An international research project by the Heidelberg Medical Faculty of Heidelberg University in collaboration with the German Cancer Research Center (DKFZ), the University of Pennsylvania (UPenn), USA, and the Cyprus Cancer Research Institute (CCRI) has been awarded the prestigious ERC Synergy Grant from the European Research Council (ERC) for their joint project "PRECISION ImmunoRad." The aim of this project is to translate the successes of immune cell-based therapies in curative treatment of blood cancers to the field of solid tumors. The investigative team has delineated the key immune evasion mechanisms underlying the resistance of solid tumors to immunotherapies, such as CAR-T cell-based therapies. Consequently, the team of scientists aims to reprogram the tumor immune microenvironment so that immune cells can more effectively eliminate tumor cells. To this end, the team of scientists will leverage the full synergistic potential of high-precision ion beam radiotherapy and CAR-T cell therapy, two of the most promising strategies in modern precision cancer medicine. In addition, personalized cancer vaccines and molecular engineering methods will be employed to modulate and reprogram the tumor immune microenvironment, creating an immunopermissive niche.

The ERC Synergy Grant is considered one of the most competitive awards in European science. Through this funding program, the ERC supports outstanding researchers in realizing groundbreaking ideas that can only be implemented by the collaborative efforts of specialized teams. The grant provides €14 million in funding over six years.

The coordinator of this international collaboration is Prof. Dr. Dr. Amir Abdollahi, Heidelberg Medical Faculty of Heidelberg University, Heidelberg University Hospital and Managing Director of the National Center for Tumor Diseases (NCT) Heidelberg. "With this unique combination of ion beam therapy, cell-based interventions, and immunotherapy strategies, our goal is to set the foundation for a new era of precise, personalized cancer treatments—empowering the immune system itself to become the most powerful ally against otherwise therapy-resistant tumors," says Prof. Abdollahi. "The close collaboration between leading research centers clearly demonstrates how international scientific excellence can jointly pave the way for new approaches to tackling hard-to-treat cancers more effectively in the future."

The subprojects are led by:

- Prof. Dr. Dr. Amir Abdollahi, W3-Professor of Translational Radiation Oncology at the Heidelberg Medical Faculty of Heidelberg University and the head of the eponymous Clinical Cooperation Unit of the German Consortium for Translational Cancer Research (DKTK) at the German Cancer Research Center (DKFZ). He is a renowned expert in the fields of ion-beam therapy and targeted reprogramming of the tumor immune microenvironment.
- Prof. Dr. Dirk Jäger, Medical Director of the Department of Medical Oncology at Heidelberg University Hospital (UKHD) and NCT Heidelberg, and Head of the Clinical Cooperation Unit Applied Tumor Immunity at the DKFZ. He is an expert specialist in the field of personalized immunotherapies.
- Prof. Dr. Constantinos Koumenis, currently Endowed Professor of Radiation Oncology at the University of Pennsylvania (UPenn), Philadelphia, USA, will establish a research group at the Cyprus Cancer Research Institute (CCRI) in Nicosia, Cyprus, as part of the project. He is an expert in FLASH proton therapy and the stress responses triggered by radiation in tumors and their microenvironment (integrated stress response).
- Prof. Dr. Carl H. June, Director of the Center for Cellular Immunotherapies at UPenn, is considered a pioneer in immune cell engineering and the father of CAR T cell therapy.

“As the Faculty of Medicine, we are delighted about this fantastic award for the research team granted by the European Research Council,” says Prof. Dr. Michael Boutros, Dean of Heidelberg Medical Faculty. “The transatlantic collaboration, which will be funded by the ERC Synergy Grant for the next six years, is particularly noteworthy.”

Ion-Beam Radiotherapy and “molecular engineering” are intended to support immune cells in fighting tumors

Particularly aggressive tumors such as pancreatic cancer have so far shown little to no response to conventional forms of treatment. Not only are they resistant to radiation and chemotherapy, they also evade the immune system by forming protective scar tissue (remodeling), releasing immunosuppressive substances into the immediate environment, or specifically reprogramming immune cells so that they no longer attack or tolerate the tumor. These factors limit the efficacy of modern immunotherapies.

The aim of “PRECISION ImmunoRad” is to overcome different tumor immune evasive mechanisms. Prior work of the consortium indicate that this can be achieved through the combined use of ion beam therapy, CAR-T cell therapy, targeted application of immune activating agents in the tumor environment, and personalized cancer vaccines.

Ion beam therapy—using protons, helium, carbon, or oxygen ions, for example— effectively destroy tumor cells with high precision while sparing surrounding healthy tissue. At the same time, it breaks down tumor structures and stimulates immune responses, making the tumor visible to the immune system. By destroying immune-suppressing cells and signaling pathways in the tumor, the irradiation prepares the ground for CAR-T cell therapy. For this purpose, the body's own immune cells are isolated and genetically armed outside the body so that, once back in the patient's body, they recognize and attack the tumor. Thanks to the preparatory effect of ion beam therapy, CAR-T cells should in future also be able to reach tumors that were previously shielded from the immune system. " To conquer cancer, we will harness the full synergistic potential of two Cancer Moonshots: high-precision particle therapy and immune cell therapy”, says Prof. June. ”This transatlantic alliance between Heidelberg University and the University of Pennsylvania unites two world-leading programs with a shared mission to transform cancer care."

Combination with personalized cancer vaccines to build immune memory

This approach is complemented by personalized cancer vaccination. This involves identifying characteristic molecules – known as tumor antigens – from the respective tumor. Based on this information, scientists generate a vaccine consisting of an individualized set of antigens tailored to each person, which specifically “trains” the body's own immune system to recognize specific tumor characteristics. “We hope that with these vaccines, in combination with precision radiotherapy and immune cell therapies, will enable the formation of immune memory for long-lasting tumor defense. This would be a pivotal milestone in developing highly individualized, effective cancer therapies” says Prof. Jäger. Prof. Koumenis' team will identify new targets for both CAR T cells and personalized vaccines. “The goal is to make new findings available to the consortium for rapid clinical translation so that patients can benefit from this collaboration at an early stage,” says Prof. Koumenis.

"I am deeply impressed by how the pioneering work in ion therapy in Heidelberg has grown far beyond the original goal of anatomical precision. Now it has the potential to enable new treatment options for widespread use in cancer medicine, not only in terms of precise radiation, but also as a door opener for immune cell therapy" says Prof. Dr. Dr. Jürgen Debus, Medical Director of the Department of Radiation Oncology and Radiation Therapy and Chairman of the Board of the UKHD. Under his leadership, the worldwide unique Heidelberg Ion Beam Therapy Center (HIT) was established in 2009.

Press release

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Source: Heidelberg University Hospital

Further information

- Heidelberg University Hospital