St. Anna Kinderkrebsforschung
CHILDREN'S CANCER RESEARCH INSTITUTE

MEDIZINISCHE UNIVERSITÄT WIEN

Press Release

Natural Killer Cells in the Fight Against Neuroblastoma

A recently published review in *Cancer and Metastasis Reviews* highlights promising therapeutic strategies utilizing natural killer (NK) cells to combat neuroblastoma, an aggressive pediatric tumor of the sympathetic nervous system. Researchers from St. Anna Children's Cancer Research Institute and the Medical University of Vienna emphasize that NK cells play a crucial role in the tumor microenvironment and hold significant potential for innovative treatment strategies.

Natural killer (NK) cells are vital components of the innate immune system, capable of detecting and eliminating stressed or transformed cells without prior sensitization. Unlike T-cell-based therapies, NK-cell therapies do not require personalized approaches since NK cells lack T-cell receptors. "This opens the door for so-called 'off-the-shelf' immunotherapies, which can be made available more quickly and cost-effectively," explains Sabine Taschner-Mandl, Principal Investigator at St. Anna Children's Cancer Research Institute (St. Anna CCRI).

Challenges in Neuroblastoma Treatment

Neuroblastoma is among the deadliest solid tumors in children, particularly in high-risk groups, where mortality rates exceed 50%. While NK-cell immunotherapies have been successful in treating blood cancers, they face considerable challenges in solid tumors like neuroblastoma. The tumor microenvironment (TME) plays a key role in modulating immune responses, often suppressing effective immune attacks.

The TME in neuroblastoma is poorly immunogenic, characterized by low infiltration of T and NK cells. This reduced immunogenicity is partially due to the tumor's low mutation burden. "Low-risk neuroblastomas show increased infiltration of T and NK cells, correlating with better clinical outcomes," says Irfete Fetahu from the Medical University of Vienna. However, in high-risk neuroblastomas, immune checkpoint molecules, stromal, and myeloid cells contribute to immune suppression.

Innovative Therapeutic Approaches and Advances

Despite these challenges, significant advancements have been made. One of the leading immunotherapeutic strategies for neuroblastoma involves antibodies targeting the tumor-associated disialoganglioside GD2. NK cells can recognize the Fc fragments of these antibodies and eliminate tumor cells via antibody-dependent cellular cytotoxicity (ADCC). Clinical trials with the anti-GD2 antibody dinutuximab have shown substantial improvements in survival rates for neuroblastoma patients and have become standard treatment.

Another breakthrough is the development of genetically engineered NK cells equipped with chimeric antigen receptors (CAR). These CAR-NK cells are designed to better recognize and target tumor-specific receptors. “CAR-NK cells have the potential to be safer and more effective than CAR-T cells, as they persist in the body for a shorter duration and cause fewer side effects,” notes Magdalena Rados from St. Anna Children’s Cancer Research Institute.

However, a major hurdle remains the limited immune surveillance by NK cells. Tumor cells often develop mechanisms to evade immune detection, such as downregulating MHC class I molecules, which NK cells typically recognize. Researchers are actively exploring strategies to enhance NK-cell function in the tumor microenvironment and overcome these immunosuppressive mechanisms.

A particularly promising approach is the combination of NK-cell therapies with existing treatments, such as chemotherapy or other immunomodulatory agents, to improve long-term efficacy. Preliminary preclinical studies indicate that administering NK cells alongside anti-GD2 antibodies significantly enhances survival rates in high-risk neuroblastoma cases, according to Rados.

Conclusion

The role of NK cells in tumor defense is highly complex, and their therapeutic application in solid tumors like neuroblastoma is still in its early stages. Nevertheless, ongoing research is paving the way to unlocking their full therapeutic potential and integrating them more effectively into clinical practice. “The coming years will be crucial in determining how NK-cell-based therapies evolve in clinical settings,” emphasizes Taschner-Mandl.

About the St. Anna Children's Cancer Research Institute

The St. Anna Children's Cancer Research Institute (CCRI) is an international, interdisciplinary research institution dedicated to advancing diagnostic, prognostic, and therapeutic strategies for the treatment of children and adolescents with cancer through innovative research. Addressing the specific characteristics of pediatric tumors, research groups work across the fields of tumor genomics and epigenomics, immunology, molecular biology, cell biology, bioinformatics, and clinical research. Their goal is to bridge the latest scientific findings with clinical needs, ultimately improving the well-being of young patients.

For more information: www.ccri.at & www.kinderkrebsforschung.at

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