St. Anna Kinderkrebsforschung
CHILDREN'S CANCER RESEARCH INSTITUTE

MEDIZINISCHE UNIVERSITÄT WIEN

## Press Release

# Nerve healing: neighboring cells become police force - and could make tumors benign

(Vienna, 15.09.2022) **Scientists from St. Anna Children´s Cancer Research Institute (St. Anna CCRI) discovered a completely new function of the cells that surround nerve fibers: so-called Schwann cells not only attract immune cells to initiate nerve healing, but also behave like a "police force" themselves. Among other things, they shut down the immune response in time during the nerve repair process to protect the nerve fibers. The authors hypothesize that similar mechanisms could prevent benign childhood nerve tumors from growing.**

Schwann cells are known to protect and repair nerve cells. Until now, however, it was not known that they themselves take over functions of certain immune cells during nerve healing. For example, they produce signaling molecules that can activate other immune cells. In particular, however, they are able to stop inflammatory reactions in order to prevent excessive tissue damage and allow the nerve to regenerate.

"This is essential, because inflammation releases free radicals against which nerve fibers cannot protect themselves. Therefore, the inflammation must be cleared quickly, which is precisely what Schwann cells do," explains Dr. Sabine Taschner-Mandl, who designed the study and heads a research group at St. Anna CCRI. The new results, in which the Medical University of Vienna is also significantly involved, were published in the journal *Glia*.

### Do Schwann cells protect against malignancy?

How are these results related to tumor growth? After nerve injury, Schwann cells adopt a "repair" mode that is also found in benign infantile nerve tumors. There, it causes the tumor cells to mature and thus reach a stage where they lose their aggressive properties and no longer divide unchecked (*Weiss T., Taschner-Mandl S., et al., Nat Commun 2021*).

"Based on the current results, we now suspect that the immune cell functions of Schwann cells also become effective in childhood nerve tumors. This is because in cancer, there is always a kind of inflammation bubbling away that never comes to a halt. In benign nerve tumors, ganglioneuromas, the accompanying chronic inflammation could be stopped by Schwann cells similar to nerve healing, because unlike malignancies, benign nerve tumors have many Schwann cells in their microenvironment. We also see that a lot of immune cells migrate into these tumors, for which the Schwann cells could also be responsible," says Sabine Taschner-Mandl.

### Healthy Inflammation: First Activate, Then Shut Down

In particular, the current study shows that Schwann cells can influence certain immune cells, so-called T cells, which play an important role in the defense against cancer. Schwann cells - both those in nerve regeneration and those in benign tumors - carry MHC-I and MHC-II molecules on their surface that are important for T-cell regulation. Via these molecules, Schwann cells present recognition features of material they have previously taken up from their environment.

We mimicked an inflammatory response in the laboratory and detected a whole range of additional stimulatory and inhibitory surface molecules that are also necessary for T cell activation," explains Jakob Berner, MSc, co-first author of the study and interim PhD student in Kaan Boztug's group at St. Anna CCRI. "Our experiments show that Schwann cells are able to take up large amounts of material via phagocytosis."

As the first immune response to a nerve cut, Schwann cells secrete substances that attract T cells, macrophages and other immune cells. Now it turned out that not only a reaction between the classical immune cells takes place, but also between Schwann cells and T cells.

While Schwann cells initially fuel the inflammatory response by releasing interferon-gamma, they can later shut it down by up-regulating the T-cell inhibitory PD-L1 molecule.
"First activate, then shut down - that's the normal process of an inflammatory response. If this were also the case in cancer, then it could curb cancer growth," comments Sabine Taschner-Mandl. Whether and how these findings can be used for potential cancer therapies is now being researched.

**Picture:** Sabine Taschner-Mandl, PhD, Tamara Weiss, PhD and Jakob Berner, MSc
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**Figure:** Phagocytosis potential as part of the inflammatory response of human repair-related Schwann Cells.
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**Publikation**
Human repair-related Schwann cells adopt functions of antigen-presenting cells in vitro
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**About Sabine Taschner-Mandl (PhD)**
Sabine Taschner-Mandl, PhD has been head of the Tumor Biology group at St. Anna Children's Cancer Research Institute, CCRI, since 2018, where she has been working as a scientist since 2008. The aim of her research group is to tackle unresolved questions of neuroblastoma pathogenesis and develop new diagnostic and therapeutic approaches to facilitate precision medicine for children with malignant tumors. In addition, Sabine Taschner-Mandl is a lecturer at the Medical University of Vienna and Vienna University of Technology. She completed her studies of biology at the University of Vienna with a diploma thesis in vaccine development. This was followed by a dissertation and a postdoc position at the Institute of Immunology at the Medical University of Vienna. Besides her research work at CCRI, she was a visiting scientist at Significo and the University of Helsinki (EC-FP7 Marie Curie Program). She is leading and participating in several international and national projects (e.g. ERA-NET/ TRANSCAN LIQUIDHOPE, EC H2020 PRIMAGE) and initiatives. As member of the Executive Board and co-chair of the Biology Committee of

the European Society of Pediatric Oncology Neuroblastoma (SIOPEN) and in other international working groups (International Neuroblastoma Risk Group, INRG; Innovative Therapies for Children with Cancer, ITCC), she is fostering innovative research for the benefit of pediatric patients with cancer.

**About St. Anna Children's Cancer Research Institute, St. Anna CCRI**
St. Anna CCRI is an internationally renowned multidisciplinary research institution with the aim to develop and optimize diagnostic, prognostic, and therapeutic strategies for the treatment of children and adolescents with cancer. To achieve this goal, it combines basic research with translational and clinical research and focus on the specific characteristics of childhood tumor diseases in order to provide young patients with the best possible and most innovative therapies. Dedicated research groups in the fields of tumor genetics and epigenetics, immunology, molecular biology, cell biology, bioinformatics and clinical research are working together to harmonize scientific findings with the clinical needs of physicians to ultimately improve the wellbeing of our patients.
www.ccri.at www.kinderkrebsforschung.at

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