PRESS RELEASE

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GUT IMMUNE CELLS PROVIDE NEW INSIGHTS INTO COMPLICATIONS AFTER STEM CELL TRANSPLANTATION

After an allogeneic stem cell transplantation, the transferred immune cells are meant to fight remaining leukemia cells. However, they can also attack healthy tissue and trigger graft-versus-host disease (GvHD), most frequently in the gastrointestinal tract. A research team at Universitätsklinikum Regensburg, led by Elisabeth Meedt and Ernst Holler, has therefore examined IgA-producing plasma cells in the gut. The result: a loss of these cells was linked to severe GvHD and higher mortality, whereas high cell numbers were associated with an increased risk of relapse. The Wilhelm Sander-Stiftung funded the project with €194,000.

After a stem cell transplantation, the immune system is in a delicate balance: the transferred immune cells are meant to fight leukemia cells, but they can also attack the recipient's healthy tissue. The role played by the gut's local immune defense in this process is still poorly understood. The project at the Department of Internal Medicine III examined, in close cooperation with the Institute of Pathology, how IgA-producing plasma cells relate to GvHD, the defense against leukemia cells, and the gut microbiome. It was carried out by Sakhila Ghimire.

More than 400 gut biopsies examined

IgA-producing plasma cells form the antibody immunoglobulin A (IgA), which protects the mucous membranes and helps regulate the gut flora. Together with the pathology department, the team examined more than 400 gut biopsies. In addition, single-cell RNA sequencing and 10x Genomics analyses were carried out in cooperation with Dirk Busch of the Technical University of Munich, along with microarray analyses of 98 gut biopsies.

Fewer plasma cells in GvHD, more relapses with high cell numbers

The number of IgA-producing plasma cells initially declined after transplantation. In patients without acute GvHD, it recovered after about 100 days; in those with histologically confirmed GvHD, this recovery did not occur. In GvHD of the gastrointestinal tract, a reduced number of these cells was also associated with significantly higher mortality from this complication. Single-cell analyses independently confirmed that these cells are less common in intestinal GvHD. Surprisingly, an opposite association emerged: patients with persistently high numbers of these cells had a higher risk of leukemia relapse. Estimated relapse-

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related mortality was around 15 percent at both two and five years in patients with low cell numbers. In those with high cell numbers, it was 31 percent after two years and rose to more than 46 percent after five years.

Gut microbiome as a possible influencing factor

The researchers found a positive association between the amount of mucosa-associated bacteria and the local IgA response. This suggests that the composition and colonization of the gut may be linked to the activity of the local immune defense. Which role individual bacteria and changes in the microbiome play must be clarified in further studies.

A possible basis for more targeted monitoring

The study shows that IgA-producing plasma cells in the gut are closely linked to the immunological balance after allogeneic stem cell transplantation. Their loss could indicate a pronounced immune reaction in the gut, while their persistence in high numbers may be associated with a weaker defense against leukemia cells. In the long term, the findings could help to better assess risks after transplantation and to make monitoring and treatment more targeted. The aim is to limit harmful immune reactions against healthy tissue without impairing the vital defense against leukemia cells.

Wilhelm Sander-Stiftung: Research. Knowledge. Future.

The Wilhelm Sander-Stiftung has supported the research project with a total of around €194,000. The foundation's purpose is to promote medical research, in particular projects in the field of cancer research. Since its establishment, the foundation has approved more than €350 million in research funding in Germany and Switzerland. This makes the Wilhelm Sander-Stiftung one of the most significant private research foundations in the German-speaking region. It was established from the estate of the entrepreneur of the same name, who died in 1973.

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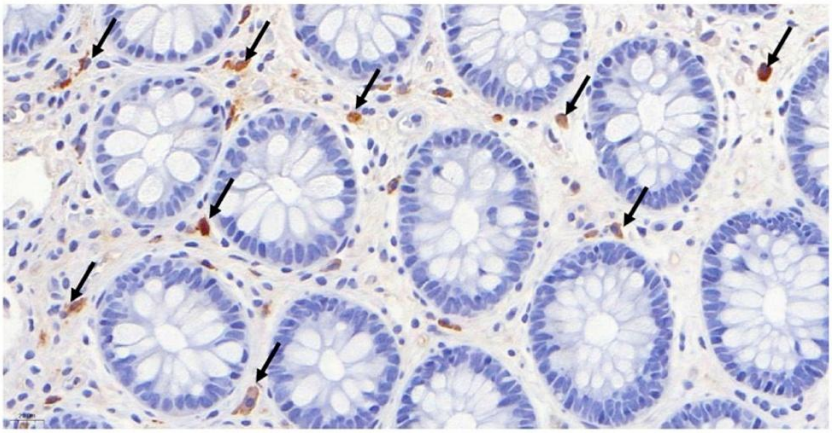
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Figure



Caption

Immunohistological staining of immunoglobulin A-positive plasma cells; positive cells (arrows) were detected in the lamina propria with close association to the epithelial line.

Image source

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