PRESS RELEASE

New way to prevent duodenal cancer

Bonn researchers link immune cells to higher risk of duodenal carcinoma in hereditary FAP

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Bonn, April 25 - People with the hereditary disease familial adenomatous polyposis (FAP) have a greatly increased risk of developing a malignant tumor of the duodenum. Researchers at the University Hospital Bonn (UKB) and the Cluster of Excellence ImmunoSensation² at the University of Bonn have now discovered a mechanism in the local immune system that can drive the development of cancer. They see this as a promising new approach to preventing duodenal carcinoma in people with FAP. The results have now been published in the journal "Nature Communications".

Familial adenomatous polyposis (FAP) is a hereditary disease which, in addition to a high risk of bowel cancer, also a greatly increased risk of duodenal cancer. At present, the only treatment available is close endoscopic monitoring with removal of the precursors, known as polyps, although this is also associated with an increased risk. "But there are no specific preventive therapies," says co-lead author Dr. Benjamin Krämer, Scientific Head of the Laboratory for Congenital Cellular Immunology at the UKB. "Since the severity of the disease varies greatly even among carriers of the same gene mutation, the search is on for other factors that influence the development of the disease - and the local immune system is becoming the focus of attention."

Neurotransmitter causes damage to the genetic material

The Bonn researchers have now discovered that certain cells of the innate immune system, known as type 3 innate lymphoid cells (ILC3), are present in significantly higher numbers in the duodenum of FAP patients. "We found an increased number of these cells in the mucosa, particularly in the vicinity of polyps and cancerous areas," says co-lead author Dr. Robert Hüneburg, senior physician at the Medical Clinic I and the National Center for Hereditary Tumor Diseases at the UKB.

The Bonn research findings provide clues as to how these immune cells could contribute to the development of cancer: they produce a Neurotransmitter called interleukin-17A (IL-17A). "This messenger appears to stimulate intestinal cells to produce more harmful molecules known as reactive oxygen species, or ROS for short. High concentrations of these ROS can damage the genetic material in the cells," says first author Dr. Kim Melanie Kaiser, who until recently conducted research as a doctoral student in the ImmunoSensation² Cluster of Excellence at the University of Bonn. Such damage to DNA, the carrier of genetic information, is a known factor that can drive the development of cancer.

"Our findings suggest that the increased number of interleukin-17A-producing ILC3 in the duodenum creates a local environment that favors the development of cancer in FAP patients," says co-lead author Prof. Dr. Jacob Nattermann from the Laboratory for Innate

Cellular Immunity, Deputy Director of Medical Clinic I and Senior Physician at the National Center for Hereditary Tumor Diseases at the UKB. He is also a member of the Cluster of Excellence ImmunoSensation² and the Transdisciplinary Research Area (TRA) "Life & Health" at the University of Bonn. "Targeting these immune cells or, in particular, blocking the messenger substance IL-17A directly in the duodenum could therefore represent a promising new approach to preventing duodenal cancer in people with FAP and offer an urgently needed therapeutic option in addition to pure endoscopic monitoring."

Participating institutions and funding:

These results are based on a collaboration between research institutions from all over Germany. The study was conducted under the leadership of researchers from Medical Clinic I at the University Hospital Bonn (UKB), with the ImmunoSensation² Cluster of Excellence at the University of Bonn also playing a key role. Also involved were the German Center for Neurodegenerative Diseases (DZNE) in Bonn, the German Rheumatism Research Center (DRFZ), which is affiliated with the Charité University Hospital in Berlin and cooperated as part of the DFG Priority Program SPP 1937 "Innate Lymphoid Cells", and the Ludwig-Maximilians-Universität (LMU) Munich, which participated in the context of the German Center for Infection Research (DZIF).

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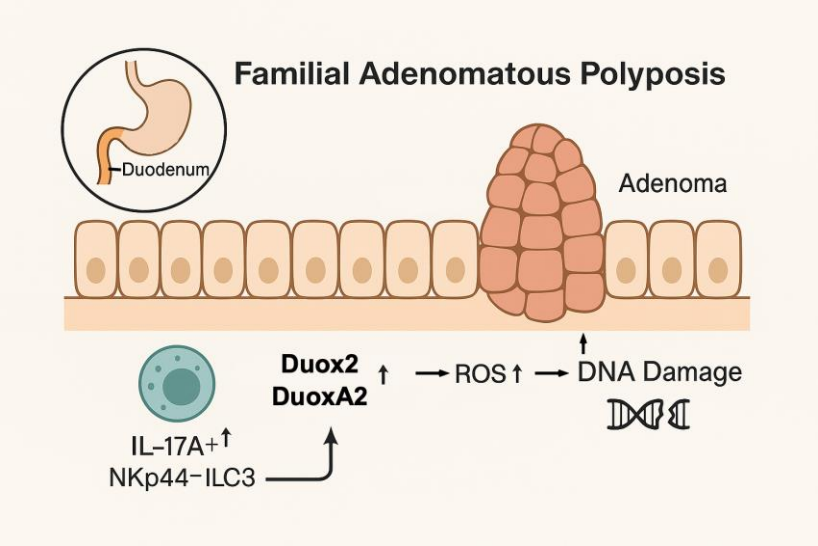

Caption: Process in the local immune system that can drive the development of cancer in hereditary FAP syndrome. Image was generated with ChatGPT4o.

Photo credits: University Hospital Bonn (UKB) / Dr. Benjamin Krämer

Caption: Dr. Kim Melanie Kaiser (bottom left), Dr. Benjamin Krämer (top left), Dr. Robert Hüneburg (bottom right) and Prof. Jacob Nattermann (top right) link immune cells with a higher risk of duodenal carcinoma in hereditary FAP.

Photo credits: University Hospital Bonn (UKB); (l. below) Dr. Kim M. Kaiser

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About Bonn University Hospital: The UKB treats around 500,000 patients per year, employs around 9,500 staff and has total assets of 1.8 billion euros. In addition to the 3,500 medical and dental students, 550 people are trained in numerous healthcare professions each year. The UKB is ranked first among university hospitals (UK) in NRW in the Focus Clinic List, had over 100 million third-party funds in research in 2023 and has the second highest case mix index (case severity) in Germany. The F.A.Z. Institute awarded the UKB first place among university hospitals in the category "Germany's Training Champions 2024"