

PRESS RELEASE

Rare genetic variants better assessed

Bonn researchers take the lead in developing classification criteria for gene variants that can lead to hereditary colorectal cancer

Bonn, December 07 - Genetic confirmation of the suspected diagnosis of "hereditary colorectal cancer" is of great importance for the medical care of affected families. However, many of the variants identified in the known genes cannot currently be classified with certainty with regard to their causative role in tumor formation. Under the leadership of the Institute of Human Genetics at the University Hospital Bonn (UKB), an international team of researchers has developed gene-specific classification criteria by which the medical relevance of a significant proportion of unclear variants can be reassessed. The results of the study will be published soon in the renowned journal "Genetics in Medicine". The article is already available online.

Families with hereditary tumor syndromes are at high risk for the occurrence of certain cancers, such as colorectal cancer or breast cancer. For many more common hereditary tumor syndromes, very effective, intensive, and early-onset surveillance programs and other preventive measures are available. Timely detection and reliable diagnosis of a hereditary predisposition is therefore extremely important for affected families.

Rare gene variants with unclear relevance for tumor formation

However, as a result of increasingly comprehensive genetic testing, more and more rare genetic variants are being found in the responsible genes, the causal significance of which for tumor development is currently still unclear. These are referred to as variants of uncertain significance (VUS). As a consequence, among the genetic variants listed in public international databases (especially ClinVar), in some genes more than 50 percent of variants are now VUS. "These variants cannot be used to make a diagnosis, nor can they be used to test healthy at-risk individuals; on the other hand, they often create a great deal of uncertainty, as carriers of a VUS may be at increased risk of tumors," says first author Dr. Isabel Spier of the Institute of Human Genetics. "Clarifying the causal role of VUS in cancer predisposition therefore directly contributes to better patient care."

Possible relief of carriers of rare gene variants

Medical Director and Chairman of the Board

Tel: +49 228 287-10900
Fax: +49 228 287-9010900
wolfgang.holzgreve@ukbonn.de

Communication and media

Viola Röser
Management

Tel: +49 228 287-10469
viola.roeser@ukbonn.de

Bonn University Hospital
Communication and media
Venusberg Campus 1
Geb. 02
53127 Bonn

At the Center for Hereditary Tumor Diseases of the UKB, researchers have been working for years to identify new genetic causes of hereditary tumor diseases. Under the leadership of the Institute of Human Genetics, a study to better characterize genetic variants has now been published in "*Genetics in Medicine*", an official journal of the American College of Medical Genetics and Genomics (ACMG). To this end, the research group led by Prof. Stefan Aretz collaborated with an international and multidisciplinary team of experts consisting of physicians and biologists. The group developed and validated specific classification criteria for assessing variants in the *APC* gene. Hereditary genetic alterations in *APC* are causative for familial adenomatous polyposis (FAP), one of the most common causes of hereditary colorectal cancer or hereditary polyp disease of the gastrointestinal tract. "The developed gene-specific classification criteria will allow a significant proportion of VUS of the *APC* gene to be reclassified into a medically relevant category" explains Spier. "We expect that a large proportion of VUS will be assessed as harmless, rare variants. This can then relieve all carriers of these variants worldwide."

"The study was only possible due to our excellent worldwide scientific networking and the establishment of an international committee for variant assessment, which we carried out in particular together with the *International Society for Gastrointestinal Hereditary Tumors* (InSiGHT), and the *Clinical Genome Resource* (ClinGen)," says Prof. Aretz. "I would like to highlight the close collaboration with Dr. Xiaoyu Yin from Melbourne, Australia, during her six-months stay as a visiting scientist at UKB." Subsequently, the Bonn researchers are planning an extensive reclassification study to re-evaluate, if possible, all previously known VUS in the *APC* gene with regard to their relevance. The work will also serve as a model project for similar approaches with other cancer genes.

Publication

Isabel Spier, Xiaoyu Yin, et al, Gene-specific ACMG/AMP classification criteria for germline *APC* variants: recommendations from the ClinGen InSiGHT Hereditary Colorectal Cancer / Polyposis Variant Curation Expert Panel, *Genetics in Medicine*, 2023, DOI: <https://doi.org/10.1016/j.gim.2023.100992>

Scientific contact:

Dr. Isabel Spier
Specialist in human genetics
Institute for Human Genetics
Center for hereditary tumor diseases
University Hospital Bonn
Tel.: +49 (0)228 287 51020
E-mail: isabel.spier@uni-bonn.de

Visuals:



Caption: Researchers from Bonn are leading the development of classification criteria for gene variants that can lead to hereditary colorectal cancer: (from left to right) Dr. Isabel Spier and Prof. Stefan Aretz from the Institute of Human Genetics at the University Hospital Bonn

Picture credits: University Hospital Bonn / Andreas Stein

Press contact:

Dr. Inka Väth

Deputy Press Officer at the University Hospital Bonn (UKB)

Communications and Media Office at Bonn University Hospital

Phone: +49 228 287-10596

E-mail: inka.vaeth@ukbonn.de

The **Centre for Integrated Oncology - CIO Bonn** is the interdisciplinary cancer centre of the University Hospital Bonn. All clinics and institutes at the University Hospital that deal with the diagnosis, treatment and research of all malignant diseases work together under its umbrella. The CIO Bonn is part of the nationwide network of selected oncological centres of excellence of German Cancer Aid. Recently, the "Centre for Integrated Oncology - CIO Aachen Bonn Cologne Düsseldorf" was founded together with the university cancer centres from Aachen, Cologne and Düsseldorf from the CIO Cologne Bonn, which has existed since 2007. Together, this network is shaping cancer medicine for around 11 million people.

About the University Hospital Bonn: The UKB cares for about 500,000 patients per year, employs about 9,000 people and has a balance sheet total of 1.6 billion euros. In addition to the more than 3,300 medical and dental students, a further 585 people are trained in numerous healthcare professions each year. The UKB is ranked number one among university hospitals (UK) in NRW in the Science Ranking as well as in the Focus Clinic List and has the third highest case mix index (case severity index) in Germany. The F.A.Z. Institute has named the UKB Germany's most sought-after employer and training champion among public hospitals in Germany in 2022 and 2023.