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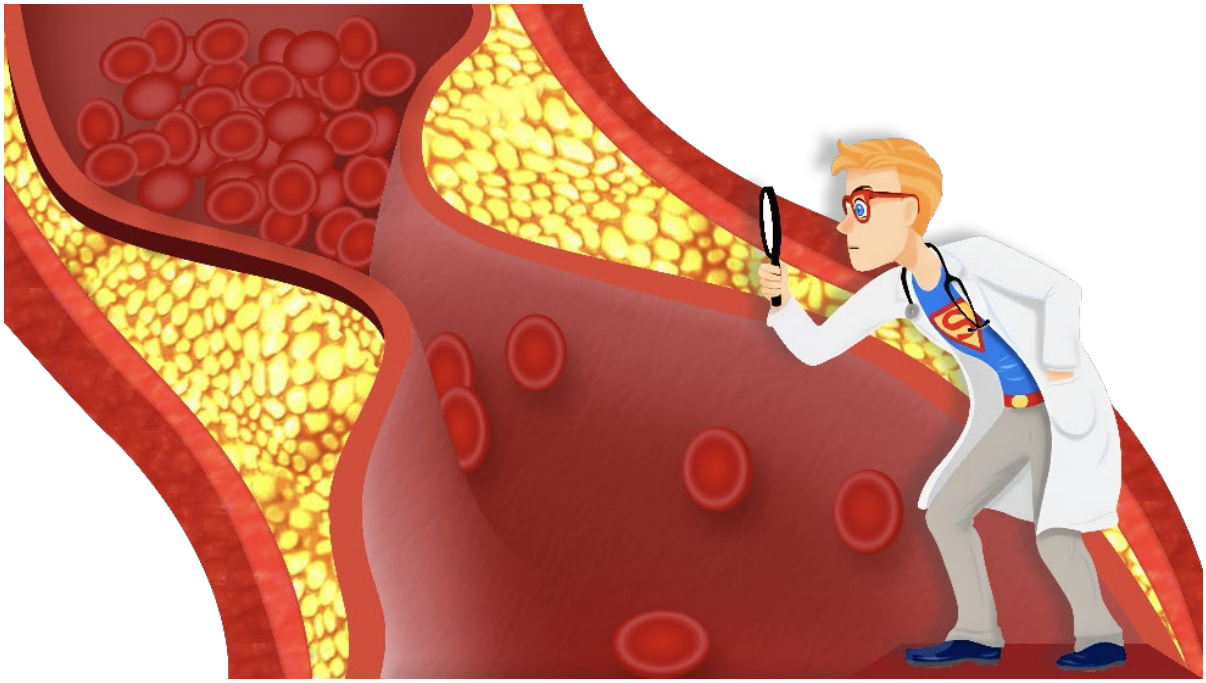
Research in Graubünden

Cholesterol in the Genome



At Cardio-CARE, researchers investigate the relationship between hereditary familial hypercholesterol-emia and elevated cholesterol levels. Graphic: © sameermusa / commissioned by Cardio-CARE

Links between genetic findings and elevated levels

A study by Cardio-CARE and the University Heart and Vascular Center Hamburg shows that, in familial hypercholesterolemia (FH), genetic findings and blood values often do not match. Only half of those affected genetically have markedly elevated cholesterol levels, while many people with high cholesterol values do not show a hereditary alteration. The study illustrates how complex the disease is and highlights the challenges involved in identifying FH patients for prevention programmes.

When the German government adopted a draft law in 2024 introducing nationwide screening of children for the early detection of familial hypercholesterolemia (FH), two key questions arose: How common is FH in Germany? And how effective would such an approach be? Data for children are unfortunately not yet available. For the Cardio-CARE team, however, this meant that existing data from a representative sample of adults in Hamburg could provide valuable indications. Dr Cristian Riccio of Cardio-CARE and Dr Natalie Arnold from Hamburg led the investigation.

Familial hypercholesterolemia – explanation and results

FH is an inherited disorder that makes it difficult for the body to remove cholesterol from the blood, thereby increasing the risk of heart attacks. Mutations in specific genes involved in cholesterol

metabolism are considered the main cause. In Hamburg, the analysis of more than 7,300 individuals showed that 0.31% carry a disease-causing genetic variant. Surprisingly, only half of them had markedly elevated cholesterol levels, while conversely most people with high cholesterol values did not carry such a mutation.

Implications for practice

"A single genetic variant does not necessarily lead to severely elevated cholesterol levels," explains Dr Riccio. For screening programmes, this means that not every high cholesterol value is genetically determined, and not every change in FH-related genes inevitably results in strongly elevated cholesterol levels.

"Identifying people with FH early—before a first heart attack or stroke occurs—is a major challenge in everyday clinical practice," emphasises Dr Arnold. "Our results show that the wide range between genetic findings and measured cholesterol levels makes targeted and efficient FH screening considerably more difficult."

The study looking ahead

The study makes clear that diagnosing FH is more complex than previously assumed and at the same time highlights the urgent need for better, more targeted screening strategies in order to identify affected individuals at an early stage. It also demonstrates how crucial international collaboration is for progress in modern research.

"In the end, our goal is to detect and prevent cardiovascular diseases earlier," says Dr Riccio. The results were published in September in *Deutsches Ärzteblatt International*.

Author: Dr Cristian Riccio

Cardio-CARE AG

At the Medizincampus Davos, Cardio-CARE is working on what is currently the largest genome project in the German-speaking world. The project is made possible through funding from the Kühne Foundation. Its aim is to better understand the genetic foundations of cardiovascular diseases, improve diagnosis, and identify new starting points for therapies. The project benefits from close collaboration with the University Hospital Zurich and the University Medical Center Hamburg-Eppendorf. The vision is to prevent diseases more precisely and treat them more effectively in the future by understanding their development in each individual person in greater detail.

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