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Pressemitteilung

Berlin Institute of Health in der Charité (BIH)
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How genes and small molecules influence our personal disease risk

Every person has an individual chemical fingerprint. The composition of small molecules in the blood, such as fats or sugars, determines how our body reacts to external influences, which diseases we are susceptible to and how severe an illness will be. In an international collaboration with partners from Cambridge (UK), scientists from the Berlin Institute of Health at the Charité (BIH) have now discovered more than 300 regions in the genome that contribute to this individual chemical fingerprint. They have now published their results in Nature Medicine.

Our body continuously processes thousands of small molecules to maintain our metabolism, and thus our health. Even small changes can cause illness and metabolism is as individual as the person. Scientists at BIH have now discovered rare and common changes in the genetic code that influence the personal chemical fingerprint and the individual disease profile. "With our study, we are finally illuminating the genetic control of our metabolism based on many hundreds of small metabolites, which has never been shown in such detail," says Professor Claudia Langenberg, Head of the Computational Medicine Department, adding: "This means we now better understand how and why genetic differences contribute to the development of diseases."

Blood samples from 20,000 participants

The scientists measured the amount of small molecules, such as sugars, fats or hormones, from blood samples of about 20,000 participants in two large population studies to investigate the influence of the genome. They identified regions in the genome that are linked to many, often very different, metabolites. "These metabolic 'hotspots' in the genome have helped us to better understand which genes are relevant to the changing amounts of molecules in the blood," explains Professor Claudia Langenberg. "With these new findings, we were then able to show which changes in metabolism contribute to the development of individual diseases, such as breast cancer," she adds.

Metabolism also determines drug effects

The results show that metabolism not only contributes to maintaining health or allowing diseases to develop, but also significantly determines how effective or sometimes harmful drugs work. For example, the scientists found common variation in the genetic code close to the DPYD gene in about one fifth of the study participants. DPYD encodes for product, called enzyme, that is responsible to break down certain cancer drugs and people harboring those genetic variants are at an increased risk to accumulate toxic levels in the blood. This means that genetic testing can tailor treatment decisions. "Variations near genes that are also the target of drugs can give us clues about possible unwanted side effects. For example, we were able to show that drugs that reduce the conversion of steroid hormones in the body and thus counteract male hair loss and prostate enlargement may increase the risk of depression, which is consistent with reports from drug studies," she explains.

The scientists have also identified many examples of the influence of metabolites on various diseases, including an increased blood concentration of homoarginine that increases the risk of chronic renal failure. This is relevant because

the administration of homoarginine is currently being tested for the prevention of cardiovascular disease. In these people, special attention should therefore be paid to maintaining kidney function.

International cooperation makes research possible

The study is the result of many years of cooperation between BIH scientists and colleagues from all over the world, especially from the Medical Research Council (MRC) Epidemiology Unit at the University of Cambridge. Many experts have worked together to better understand and assign the biological relevance and causal genes of the results, including from the Helmholtz Centre in Munich, Qatar and the pharmaceutical company Pfizer.

Already, Claudia Langenberg is leading a new initiative. "We need larger studies that better map the genetic diversity of different populations to understand the biological and clinical effect of genetic variations that differ between certain populations."

Original publication: "Rare and common genetic determinants of metabolic individuality and their effects on human health", Nature Medicine on 10 November 2022; DOI: 10.1038/s41591-022-02046-0;
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Über das Berlin Institute of Health in der Charité (BIH)
Die Mission des Berlin Institute of Health in der Charité (BIH) ist die medizinische Translation: Erkenntnisse aus der biomedizinischen Forschung werden in neue Ansätze zur personalisierten Vorhersage, Prävention, Diagnostik und Therapie u□bertragen, umgekehrt führen Beobachtungen im klinischen Alltag zu neuen Forschungsideen. Ziel ist es, einen relevanten medizinischen Nutzen fu□r Patient*innen und Bu□rger*innen zu erreichen. Dazu etabliert das BIH als Translationsforschungsbereich in der Charité ein umfassendes translationales Ökosystem, setzt auf ein organu□bergreifendes Verständnis von Gesundheit und Krankheit und fördert einen translationalen Kulturwandel in der biomedizinischen Forschung. Das BIH wurde 2013 gegründet und wird zu 90 Prozent vom Bundesministerium für Bildung und Forschung (BMBF) und zu zehn Prozent vom Land Berlin gefördert. Die Gründungsinstitutionen Charité – Universitätsmedizin Berlin und Max-Delbrück-Centrum für Molekulare Medizin in der Helmholtz-Gemeinschaft (MDC) waren bis 2020 eigenständige Gliedkörperschaften im BIH. Seit 2021 ist das BIH als so genannte dritte Säule in die Charité integriert, das MDC ist Privilegierter Partner des BIH.

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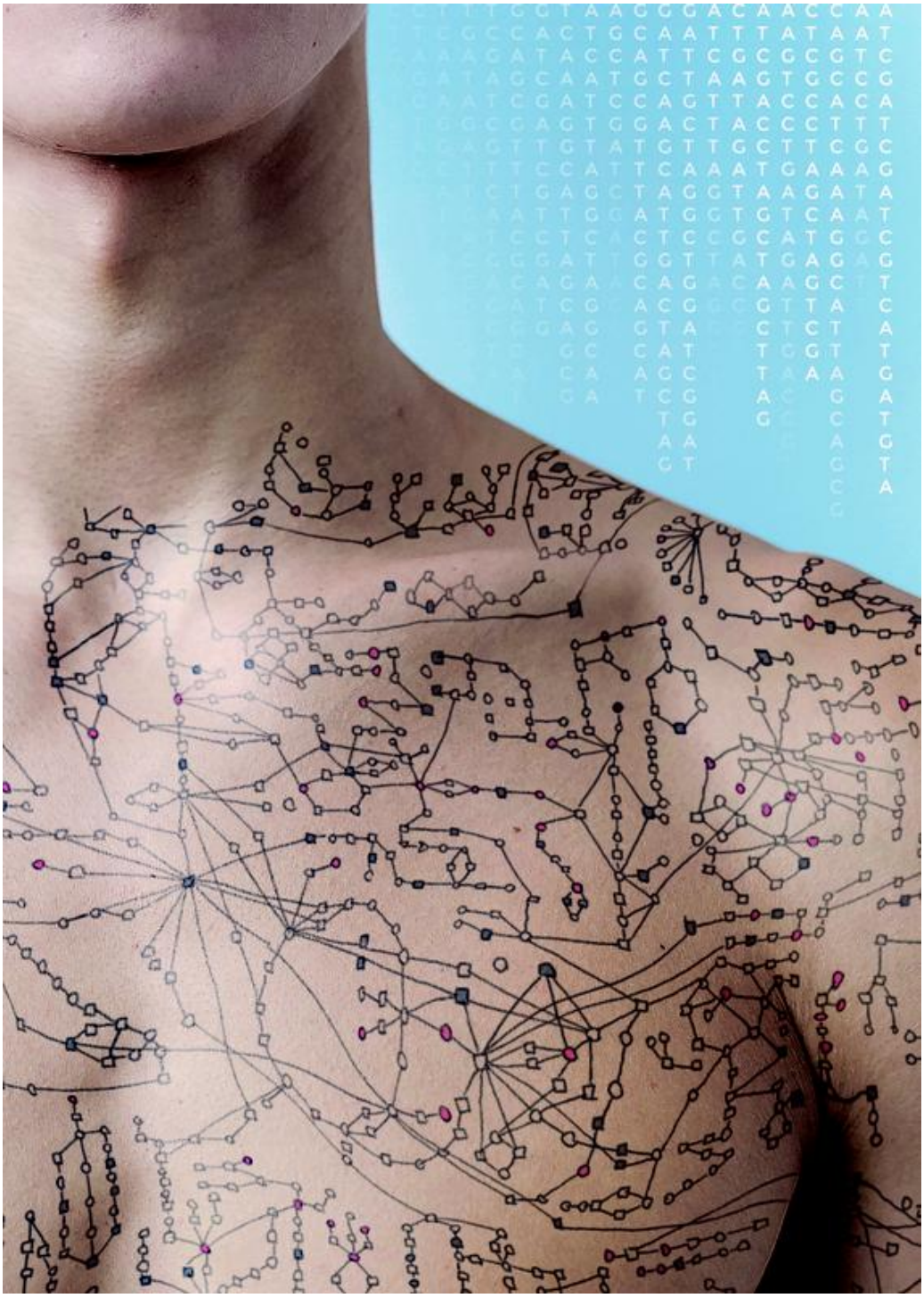

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