Computer-aided facial analysis helps diagnosis

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In rare diseases, the computer-aided image analysis of patient portraits can facilitate and significantly improve diagnosis. This is demonstrated by an international team of scientists under the leadership of the University Hospital Bonn and the Charité – Universitätsmedizin Berlin on the basis of so-called GPI anchor deficiencies. Using data on genetic material, cell surface texture and typical facial features, researchers utilized artificial intelligence methods to simulate disease models. The results may also be groundbreaking for other diseases and are now being presented in the journal *Genome Medicine*.

Mabry syndrome is a rare disease that causes mental retardation. It is triggered by a change in a single gene. "This disease belongs to a group that we describe as GPI anchor deficiencies and which includes more than 30 genes," explains physician and physicist Prof. Dr. Peter Krawitz from the Institute for Genome Statistics and Bioinformatics of the University Hospital Bonn. GPI is the abbreviation for glycosylphosphatidylinositol. GPI anchors attach specific proteins to the cell membrane. If this does not work properly due to a gene mutation, signal transmission and further steps in the cell-cell communication are impaired.

The spectrum of the external appearance of GPI anchor deficiencies is very broad: The clinical impact of a mutation in a particular gene can range from mild to profound. This also applies to distinctive facial features. In Mabry syndrome for example, a narrow, sometimes tent-shaped upper lip, broad bridge of the nose and wide-set eyes with long

palpebral fissures are among the classic features, but these may be more or less pronounced. This often complicates the diagnosis of this rare disease. The elevated alkaline phosphatase (AP) levels in the blood which are also considered characteristic for the syndrome cannot be detected in every patient. "The result is that many patients and their relatives often suffer many years of uncertainty until the correct diagnosis is made," says Krawitz.

An international research team led by Dr. Alexej Knaus and Prof. Krawitz from the Institute for Genome Statistics and Bioinformatics of the University Hospital Bonn and Prof. Dr. Denise Horn from the Institute of Medical Genetics and Human Genetics of the Charité investigated how the diagnosis of GPI anchor deficiencies can be improved with the help of modern, particularly fast DNA sequencing methods, cell surface analysis and computer-aided image recognition (next-generation phenotyping).

In the large-scale overview study, the scientists used photographs of the faces of a total of 91 patients. Cell surface changes characteristic for GPI anchor deficiencies were detected in some of the participants. Genetic analysis also revealed gene mutations that are typical for this rare group of diseases. "The artificial modeling of gene-typical faces that we achieved with these datasets clearly shows that the computer-aided evaluation of patients' portraits can facilitate and improve the diagnosis of GPI anchor deficiencies, which is significant progress," says lead author Dr. Knaus.

With the assistance of combined data from the laboratory and the computer, the authors hope to gain better understanding of the molecular processes involved in such diseases. For example, it was shown that increased blood alkaline phosphatase levels and conspicuous image analysis results provide a reliable indication of a new mutation in a GPI anchor deficiency. Because of the shared molecular causes shown during

the research and the similarity of the patients that has now been quantified, Krawitz also advocates using the term GPI anchor deficiency for this group of diseases.

The researchers now want to further refine the innovative combination of cell and genetic material analysis and computer-aided image analysis. Krawitz already considers the results a breakthrough: "It is foreseeable that these methods can also be applied to other diseases. This would be a big leap forward in terms of diagnosis."

More information: Alexej Knaus et al. Characterization of glycosylphosphatidylinositol biosynthesis defects by clinical features, flow cytometry, and automated image analysis, *Genome Medicine* (2018). DOI: 10.1186/s13073-017-0510-5

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