Quantifying acute-phase inflammation proteins by nuclear magnetic resonance spectrometry

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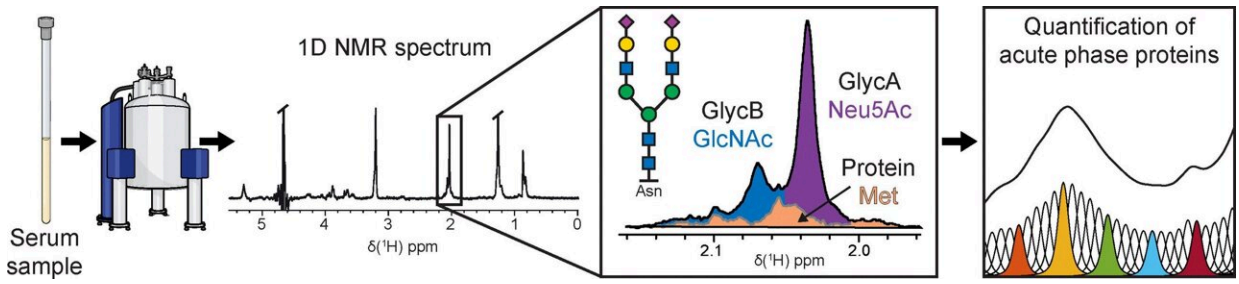

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The analysis of all small molecules in an organism (the metabolome) has huge potential for medical diagnostics. A German research team is investigating this with nuclear magnetic resonance spectrometry (NMR).

In a study recently published in *Angewandte Chemie International Edition*, they quantified acute-phase proteins from serum samples that act as markers for inflammatory diseases. They successfully obtained several diagnostic parameters from a single, short, NMR experiment.

In addition to genomics and proteomics, metabolomics is becoming established as another mainstay of medical research and diagnosis. Bodily fluids like blood are highly complex mixtures of only partially

known compounds. Metabolomic analysis is thus correspondingly difficult and complex. A team led by Ulrich L. Günther and Alvaro Mallagaray uses advanced NMR techniques to link the metabolomes of cells and organisms to diseases.

NMR spectroscopy is based on the behavior—which varies depending on the chemical environment—of magnetically active atomic nuclei, primarily hydrogen (^{1}H) and carbon (^{13}C) under the influence of a strong external magnetic field. Using this phenomenon, it is possible to obtain measurements and characteristic spectra. In medical diagnosis, this principle is also used in the form of MRI (magnetic resonance imaging) to image tissue.

In prior studies, NMR measurements of blood serum produced signals for special carbohydrate building blocks (acetyl resonances of N-acetylated carbohydrates) that are linked to acute-phase glycoproteins. These carbohydrate-containing proteins arise in cases of strong immune responses to acute inflammation. As well as changes in their concentration, their glycosylation pattern—meaning the type, number, and arrangement of their carbohydrate building blocks—can vary in a specific way depending on the disease in question.

The team employed a series of different NMR processes to fully assign the NMR signals from human serum. This led them to the conclusion that the two strongest signals, designated as glycoproteins A and B, result from N-acetylneuraminic acid and N-acetylglucosamine building blocks, respectively, which contradicts a hypothesis proposed in a prior study. By using diffusion-edited NMR experiments, they were able to prove that the components of these signals can be tied to specific, acute-phase proteins.

"NMR spectra allow for the simultaneous quantification of several acute-phase inflammation proteins," according to Ulrich L. Günther. "A proteo-

metabolomic NMR signature of significant diagnostic potential is obtained within 10–20 minutes."

Working at the Universities of Lübeck and Oldenburg, the University Hospitals of Greifswald and Lübeck, the University Heart Center in Lübeck, and the German Center for Cardiogenic Vascular Research (Greifswald and Lübeck), the team was able to use serum samples from patients with COVID-19 or cardiogenic shock, a dangerous side effect of heart attacks.

In comparison to samples from healthy individuals, they found significant changes in various specific acute-phase proteins in the serum. "In the case of Parkinson's disease, our method provides a yes-no diagnosis, as Parkinson's patients have a very specific glycosylation in their blood that does not occur in healthy people," Günther adds.

More information: Alvaro Mallagaray et al, Towards a Precise NMR Quantification of Acute Phase Inflammation Proteins from Human Serum, *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202306154

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