Researchers mapped interactions of key group of human proteins, the protein phosphatases

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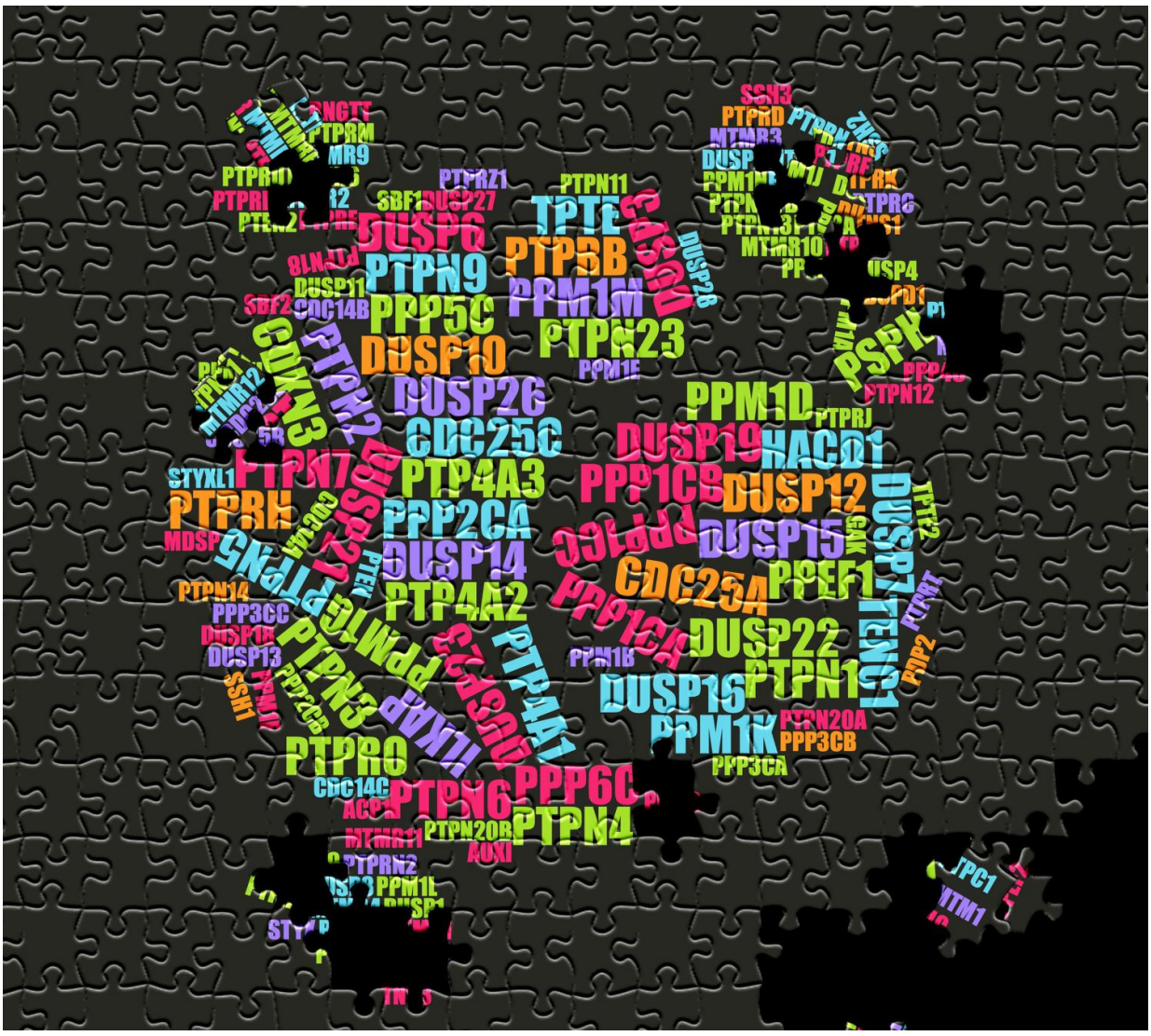

Building the human protein phosphatase interaction puzzle. The human protein

phosphatases are illustrated in the form of the most well studied phosphatase, the protein phosphatase 2A (PP2A). PP2A is composed of the structural A and catalytic C subunits, and a regulatory B subunit. When the PP2A catalytic C subunit associates with the A and B subunits several protein isoforms, namely holoenzymes, are produced with distinct activity and substrate specificity. Credit: Markku Varjosalo

Coordinated activities of protein kinases and protein phosphatases ensure phosphorylation homeostasis and amplitude of signaling response, and understandably its imbalance is linked to diseases, such as cancer. Unlike with protein kinases, the current knowledge of protein phosphatase functions and especially on their formed interactions and complexes remains fragmentary.

In a study published in the 26th of April issue of *Cell Systems* (advanced online 15th March), a Finnish-Swiss research team led by Dr. Markku Varjosalo from the Institute of biotechnology and University of Helsinki, report global quantitative interactomics analysis covering half of the human protein phosphatome. They further derive and characterize the molecular functions and pathways that the protein phosphatases connect via their stable or transient interactors. Furthermore, their study reveals novel physical as well as functional links to phosphatase-based regulation of human cancer.

"This study is a continuum of our almost a decade long efforts to systematically dissect the molecular mechanisms behind the protein phosphorylation. After our extensive analyses on protein kinases, the protein phosphatases were naturally to follow. The protein phosphatases were too long thought to just be the negative counterpart of protein kinases, with promiscuous activity and low intrinsic substrate specificity. Recent studies such as ours, however, establish protein phosphatases as

positive and essential regulators of signal transduction, with remarkable substrate specificity and coordinated activities. The phosphatases are also promising targets for therapeutic intervention in the treatment of various cancers", Dr. Varjosalo states.

More information: Leena Yadav, Fitsum Tamene, Helka Göös, Audrey van Drogen, Riku Katainen, Ruedi Aebersold, Matthias Gstaiger, and Markku Varjosalo: Systematic Analysis of Human Protein Phosphatase Interactions and Dynamics. *Cell Systems* 4, 1-15, April 26, 2017 (online 15th March, 2017)

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