

Details of protein evolution investigated

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Celestine Chi in the NMR lab at Uppsala Biomedical Centre. Credit: Uppsala University

Proteins govern the biology of the cell. Through random mutation the sequences of our proteins slowly change over time, usually without affecting function. But sometimes new functions will be invented in this process. Scientists at Uppsala University have studied such a case in molecular detas. The results show how several factors conspire to shape a plastic protein-protein interaction.

In a previous study the team reconstructed two interacting proteins from extinct organisms. One of these organisms was the ancestor of most of present day animals that lived sometime around 600 million years ago. The other one was an ancestor to present day fishes present 440 million years ago. Proteins from these animals were resurrected in the laboratory



and analysed using different methods. Now the team has used nuclear magnetic resonance (NMR) to study in molecular detail the interaction of these ancient proteins and compared it to that of the corresponding modern human proteins.

"We observe how the oldest proteins interact weaker and that this is due to a combination of differences in structure (what the protein looks like) and dynamics (how they move) compared to younger variants," says Celestine Chi who lead the study together with Per Jemth, both at the department of Medical Biochemistry and Microbiology, Uppsala University.

The two proteins, denoted CBP/p300 and NCOA, are so-called transcriptional coactivators, which means that they facilitate the cellular process of transcription where DNA is used as template to make a messenger RNA which in turn is used by the ribosome to make proteins. The scientists speculate that mutations in one of the two proteins resulted in a weak interaction some 600 million years ago that slightly improved transcription. Subsequent mutations further shaped structure and dynamics to optimise the interaction and consolidate their <u>function</u>.

"We are interested in how evolution shapes proteins and how new functions arise. There are still many unanswered questions regarding protein evolution on a molecular level," says Per Jemth. "We will investigate the evolution of other protein-protein interactions and look for general patterns.

More information: Per Jemth et al. Structure and dynamics conspire in the evolution of affinity between intrinsically disordered proteins, *Science Advances* (2018). <u>DOI: 10.1126/sciadv.aau4130</u>



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