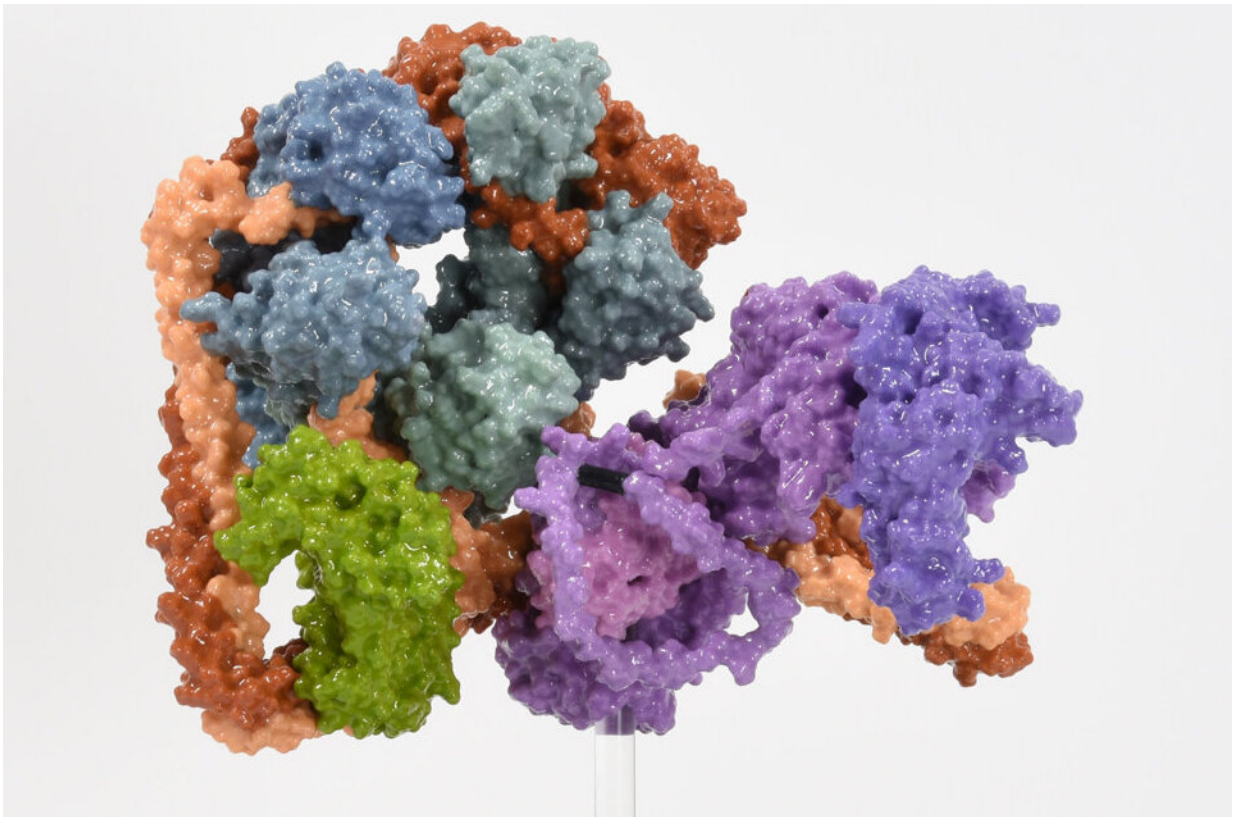


New biology unveiled for fundamental cellular machinery

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3D printed version of the endogenous Human Commander complex. Credit: Markku Varjosalo & Esa-Pekka Kumpula

Cellular communication relies on receptor molecules on the cell surface. The periodic uptake and sorting of these receptors, critical for their degradation or recycling, are governed by an elaborate machinery prominently featuring the Commander complex.

Research teams at the Institute of Biotechnology, University of Helsinki, led by Dr. Markku Varjosalo and Prof. Juha Huiskonen dissected the molecular interactions and atomic structure of this supercomplex, in its purest native form present in human cells.

The study is [published](#) in *Nature Structural & Molecular Biology*.

New avenues for potential therapeutic interventions in diseases

The Commander complex's three-dimensional arrangement and the extent of its interaction landscape have remained a mystery until now. The research team employed cryogenic electron microscopy to capture the structure, complemented by [mass spectrometry](#) to analyze complex interactions within cells.

The analysis revealed mutations within the complex associated with [developmental disorders](#). This research opens avenues for potential therapeutic interventions in diseases such as the Ritscher-Schinzel syndrome, Alzheimer's Disease, and [viral infections](#) like COVID-19 linked to the Commander complex.

"With the combination of our techniques, we can truly start building a large-scale mechanistic picture of how these fundamental cellular machinery function in our bodies and what happens when things go

wrong in them," Dr. Esa-Pekka Kumpula, one of the study's lead authors, emphasizes.

"We saw first-hand that despite the advent of excellent predictive models, experimental evidence is still critical for determining the correct, biologically relevant structure," he concludes.

More information: Saara Laulumaa et al, Structure and interactions of the endogenous human Commander complex, *Nature Structural & Molecular Biology* (2024). [DOI: 10.1038/s41594-024-01246-1](https://doi.org/10.1038/s41594-024-01246-1)

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