

[PRESS RELEASE]

Protein communities: protein "villages" serving cells

Publication in Nature [1]: by combining approaches of protein localization in the cell and inter-protein interactions, the team of Denis Lafontaine, RNA Molecular Biology, Faculty of Science, Université libre de Bruxelles, has determined how protein communities are organized in a cell and identified new proteins with an important role in ribosome production. The work was carried out in collaboration with Profs Trey Ideker (University of California San Diego, La Jolla, U.S.A.) and Emma Lundberg (KTH Royal Institute of Technology, Stockholm, Sweden).

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If cells were "countries", the proteins would be their citizens organized into inter-connected towns and villages. Thousands of proteins would populate each of these towns and villages and perform tasks essential to their functioning. Knowing the roles of each protein in the cell is essential for major advances in the fight against certain diseases such as cancer.

To date, two important experimental approaches have co-existed:

- intracellular localization: like countries, cells are composed of distinct "geographical areas" with specific characteristics. Determining the area in which a protein is found allows us to guess its function, up to a certain point.
- interactomics is the study of the interactions of a protein with other proteins in a cell. Identifying the "friends" of a protein also enables us to guess its role.

"1 + 1 = 3"

By combining these two sources of information, Denis Lafontaine's team, RNA Molecular Biology, Faculty of Science, has contributed to the discovery of a third layer of information, i.e. the detection of new protein communities and the prediction of their functions. Today, their research has been published in **Nature**.

"Our objective was to systematically establish the different levels of organization of the cell: towns, villages, hamlets, localities, etc. and their modes of interaction," explains Denis Lafontaine.

"We were able to show that certain proteins were close or not close. This allowed us to predict and then verify their functions within the cell," explains Denis Lafontaine.

Among other things, the study identified new protein communities involved in the production of ribosomes, which are nanomachines essential to the survival of the cells at the heart of Prof. Lafontaine's research for the past 20 years. When ribosomes are made in excess, we get cancers, and when not enough are produced, ribosomopathies, which are developmental diseases mainly affecting the blood and brain.

Insert: "A drop of oil in water"

In a recent article published in **Nature Reviews Molecular and Cellular Biology** [2], Denis Lafontaine developed his vision of intracellular organization, which does not only depend on stable membrane-bounded structures, but also on dynamic biomolecular condensates governed by the physics of immiscible liquids. "Some compartments are formed in the cells and maintained simply because they are made up of liquids that do not mix," explains Denis Lafontaine, "It's a bit like putting balsamic vinegar in olive oil."

Additional information:

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References:

1. Qin Y, Huttlin EL, Winsnes CF, Gosztyla ML, Wacheul W, Kelly MR, et al. Mapping cell structure across scales by fusing protein images and interactions Nature. 2021.
2. Lafontaine DLJ, Riback JA, Bascetin R, Brangwynne C. The nucleolus as a multiphase liquid condensate. Nature Reviews in Molecular and Cellular Biology. 2020;22(3):165-82. Epub 2020 Sep 1. doi: 10.1038/s41580-020-0272-6. PubMed Central PMCID: PMC32873929.