# Interview with Prof. Denis L.J. LAFONTAINE

**Director of Research at Fonds de la Recherche Scientifique (F.R.S./FNRS), Professor at Université libre de Bruxelles (ULB), Head of the RNA Molecular Biology laboratory**

## What are the key figures and area of expertise of your laboratory?

Created twenty years ago, my laboratory employs a dozen researchers. It has to its credit >90 scientific publications in internationally peer-reviewed journals accounting for more than 9,000 citations (h-index 49), as well as the training of fifty researchers from 15 nationalities. The broad area of expertise of my laboratory is RNA biology. Ribonucleic acids (RNAs) play fundamental roles in our cells, being at the core of gene expression. The recent Covid19 pandemic has illustrated more than we could have ever anticipated the biotechnological power of RNA molecules (new generation of vaccines) and the importance to conduct research on this molecule.



## Could you tell us about your main areas of interest and give us some examples of current research

## projects?

My team is studying how we make ribosomes, the nanomachines inside our cells responsible for the production of proteins (a process called Translation), and how the structure of the nucleolus (the cell's ribosome factory) is organized and maintained. We are studying the diseases associated with defective ribosomal assembly. If ribosomes are in excess, they cause cancers because the excess protein stimulates the proliferation of cells. If they are in deficit or not working well, they induce ribosome-related pathologies, the so-called ribosomopathies, affecting primarily the blood (haematopoiesis) and the brain (neurodevelopmental disorders).

We are notably studying Diamond-Blackfan anemia (DBA), a congenital disease that affects the production of red blood cells and makes patients dependent on weekly blood transfusions. In a collaborative effort, the study of the mutations underlying this pathology has enabled us to develop and test therapeutic vectors based on gene correction to restore normal ribosome production. We have also characterized the impact of ribosome biogenesis dysfunction in Labrune syndrome, a terrible disease in which patients develop cysts in their brain.

## What research partnerships have you developed?

The laboratory is a member of several European academic consortia including: RiboEurope and DBAGeneCure, funded by the European Commission within the framework of the European Joint Programme on Rare Diseases (EJP-RD), and of two COST actions: Epitran and Translacore. It also offers its expertise in the form of services or scientific collaborations to Belgian companies (GSK, Progenus, …).

## Could you tell us about your spin-off project?

Our spin-off project, RIBOGENESIS, developed by Pr Christiane ZORBAS, is based on the biosensor properties of the nucleolus whose morphology varies greatly in disease such as cancer, viral infection, and neurodegeneration. We have developed a powerful patented algorithm to characterize nucleolar morphology with unprecedented statistical power. We plan to use nucleolar morphology as a proxy to screen novel molecules with anticancer properties. So far, we have benefited from two funds from the Walloon Region (FIRST Spin-off and PoC – proof of concept).

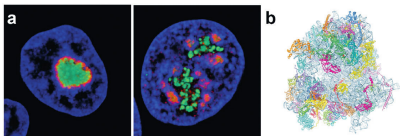
## What do you see as the main challenges ahead for

## molecular and cell biology research?

The main challenge for us will be to integrate the concepts of soft matter and biophysics in biology. There is an urgent need to decompartmentalize research. We have recently developed our vision of the nucleolus as a multiphase liquid condensate (see Nature Reviews Molecular Cell Biology, Sept. 2020 issues). Put simply, the nucleolus behaves like a liquid droplet inside our cells sharing many of the biophysical properties of immiscible liquids like “when oil and vinegar are mixed”. In fact, each cell comprises many such compartments or “droplets” that do not mix. The biophysics underlying the behavior of cell condensates will be essential to understand how cells are organized and functionally compartmentalized.

## For more information:

- Lab website: www.LafontaineLab.Com
- Lab Twitter: @LafontaineLab
- Denis L.J. Lafontaine, Joshua A. Riback, Rumeyza Bascetin, Clifford P. Brangwynne (2020) “The nucleolus as a multiphase liquid condensate” Nature Reviews Molecular Cell Biology DOI: 10.1038/s41580-020-0272-6




© LafontaineLab – ULB - a, The nucleolus (the cell’s ribosome factory) in a healthy (left) and disease (right) cell (size range: microns); b, The ribosome is the nanomachine inside our cells responsible for protein production (size range: nanometers)