DEPARTEMENT DES RELATIONS EXTERIEURES
Communication Recherche

Aéropole de Charleroi
Rue des Professeurs Jeener et Brachet, 12 – 6041 Charleroi
Nathalie Gobbe, T +32 (0)71 60 02 06, +32 (0)474 84 23 02,
M ngobbe@ulb.ac.be
Nancy Dath, T +32 (0)71 60 02 03**, M** ndath@ulb.ac.be

PRESS RELEASE

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The RNA Metabolism Laboratory, Université libre de Bruxelles reveals decisive characteristics of human ribosome biogenesis. Ribosomes are sophisticated molecular machines that are essential to decoding the genetic information and translating it into functional proteins.

Proteins are major cellular constituents, contributing either a structural or functional role, and ribosomes are key players in protein synthesis. Ribosomes are sophisticated molecular machines that are essential to decoding the genetic information and translating it into functional proteins.

The genetic information, transmitted from parent to child, from mother to daughter cells, lies in a very stable and quite inert repository molecule, DNA. With some exceptions, DNA-encoded genes are first transcribed into messenger RNAs (mRNAs), which in turn are translated by ribosomes into active proteins. Each ribosome, containing around 85 core pieces (4 RNAs and around 80 proteins), is made of two specialized subunits: one "reads" the message, and the other puts cognate protein building blocks, the amino acids, together. Despite its relatively limited number of components, it takes an exceptionally complex "assembly line" to synthesize ribosomes.

…"*For a cell, assembling a functional ribosome is like solving an immensely challenging 3-D jigsaw puzzle: each piece has to find its correct partners, at the right time, at the right place. There is no room for mistakes in ribosome assembly because in the mature ribosome, many pieces are so intimately intertwined that it would be difficult to tear them apart without breaking them altogether"…*

Because ribosomes are absolutely essential for gene expression, disruption of their synthesis irreparably leads to severe diseases. In fact, a new class of human diseases has recently been discovered and designated as "ribosome diseases" or "ribosomopathies".

Ribosomopathies was the focus of the "9th International Conference On Ribosome Synthesis", co-organized by **Prof Denis Lafontaine – RNA Metabolism Laboratory, Université libre de Bruxelles (IBMM, Faculty of Sciences)** -, which took place in Banff, AB, Canada, last summer. At the meeting, researchers discussed that ribosomopathies provoke impaired hematopoiesis and increased cancer susceptibility and that the etiology of ribosomopathies is mutation in ribosomal components or disruption of the ribosomal assembly machinery. A stunning example of ribosomopathies is the recently discovered T-cell acute lymphoblastic

leukemia identified by Prof Lafontaine's Belgian colleague Dr Kim De Keersmaecker (KU Leuven) [1].

Historically, ribosome biogenesis has been best studied in budding yeast. This model organism shares many characteristics with human cells, making it an extremely powerful experimental tool. It took more than 15 years and the considerable research effort of several dozens of teams around the world, including that of Prof Lafontaine in Belgium, to identify the approximately 200 factors now known to be required to assemble ribosomes in yeasts.

Now, in the 22nd August issue of *Molecular Cell* [2], the team led by Prof Lafontaine has tested directly in human cells the involvement in ribosome biogenesis of 625 nucleolar proteins, identifying for the first time in a single work 286 novel ribosome assembly factors, including 74 without yeast counterparts. The study reveals that 38% of the ribosome assembly factors identified by Prof Lafontaine's team have been connected to severe human diseases, mainly cancer and genetic disorders. The study also showed that nearly one third of the human factors identified perform additional or even entirely different functions than their yeast homologs. This conclusion is very important as it poses fundamental implications for understanding ribosomopathies at the molecular level and for developing effective therapeutic agents.

This work provides a key reference dataset and fundamental resource to the scientific community, including multi-disciplinary teams and clinicians, providing useful insights into human disease research. It provides powerful evidence that shows ribosome biogenesis is far more complex in humans than previously assumed and creates a valuable resource for those investigating ribosomopathies by identifying potentially important novel biomarkers for malfunctions in ribosome synthesis. An on-line, fully searchable, information-rich database summarizing this work is available at www.ribogenesis.com.

*Prof Denis Lafontaine is the lead organizer of the 10th anniversary edition of the triennial "**International Conference On Ribosome Synthesis**", which will be held in Brussels in the summer of **2015**.*

Contact :
Denis Lafontaine
Métabolisme de l'ARN, Université libre de Bruxelles
+ 32 (0)2 650 97 71 – Denis.Lafontaine@ulb.ac.be

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