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Press release

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The RNA Molecular Biology Laboratory headed by Professor Denis Lafontaine (www.LafontaineLab.com) at the Université libre de Bruxelles (www.ulb.com) has just published a study in *Nature Communications* revealing essential aspects of the regulation of the anti-tumor protein p53.

Because p53 protects us by killing cancer cells, it is considered a “good” protein. In normal cells, which of course don’t need to be killed, p53 is scarce, because it is degraded all the time. Its stabilization in cancer cells leads to cell death. The level of p53 is regulated in many different ways. Some important up-regulators of p53 are to be found in the ribosome, an essential cell nanomachine responsible for the synthesis of all the proteins in all living cells. Certain ribosomal proteins can capture and sequester a p53-degrading protein, thus preventing p53 degradation.

At the heart of our cells lies an important factory called the nucleolus. This is where ribosomes are synthesized. For decades, the aspect of the nucleolus has been acknowledged as a good indicator of the health status of a cell. The shape, size, and number of nucleoli can vary greatly when a cell is stressed or diseased. Nucleolar abnormalities notably appear in cancer cells and virus-infected ones. Currently, cancer pathologists are not exploiting the full potential of the nucleolus as a biomarker, for lack of reliable quantitative tools that are robust enough for implementation in routine clinical protocols.

Professor Denis Lafontaine says “Our aim was twofold. On the one hand, we wanted to answer a fundamental biological question: what are the principles governing nucleolar integrity? We notably wondered which cell components are important in maintaining nucleolar architecture.”

Although the nucleolus was discovered by the Italian scientist Fontana in 1774, these basic questions have not yet been answered. To address them, the Lafontaine Lab built a high-throughput screening platform: a robot microscope that can look into thousands of cells in a very short time, checking the morphology of their most intimate details and reporting it to a tailor-made computer algorithm.

As proof of concept, the Lafontaine Lab focused on what happens to the nucleolus in cells lacking a ribosomal protein. *“It was like playing Mikado”*, says Denis Lafontaine, *“We removed each ribosomal protein, one at a time, and asked our robot and software: is the nucleolar structure impacted or not?*”

Professor Lafontaine carries on: *"On the other hand, we wanted to develop a powerful computer code to distinguish normal from abnormal nucleoli both qualitatively and quantitatively. In other words, we wanted to be able to tell unequivocally what a nucleolus looks like in a healthy or a diseased cell. Why? Because we aimed to provide clinicians with the tool they lack."*

In collaboration with Professor Christophe De Vleeschouwer of the Université catholique de Louvain (ICTEAM-ELEN), the Lafontaine Lab developed an innovative index, coined the "index of nucleolar disruption", in short the "iNo score". This score provides statistically validated information about whether the nucleolar structure is damaged or not, and if it is damaged, how severe the damage is.

Professor Lafontaine concludes "*A major conclusion of our work is that only a few among the eighty ribosomal proteins are required to maintain nucleolar structure. And the really astounding result is that the ribosomal proteins most essential to the structure of the nucleolus are precisely those which are important in regulating the p53 level. This was totally unexpected, and far more than we had hoped for. Basic research will always keep surprising us.*"

This work has important biomedical research applications, as the iNo score has great potential for use in clinical biology.

The study entitled "**Involvement of human ribosomal proteins in nucleolar structure and p53-dependent nucleolar stress**", published in *Nature Communications* DOI: 10.1038/ncomms11390, is available on-line at http://www.nature.com/ncomms/index.html

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