PRESS RELEASE

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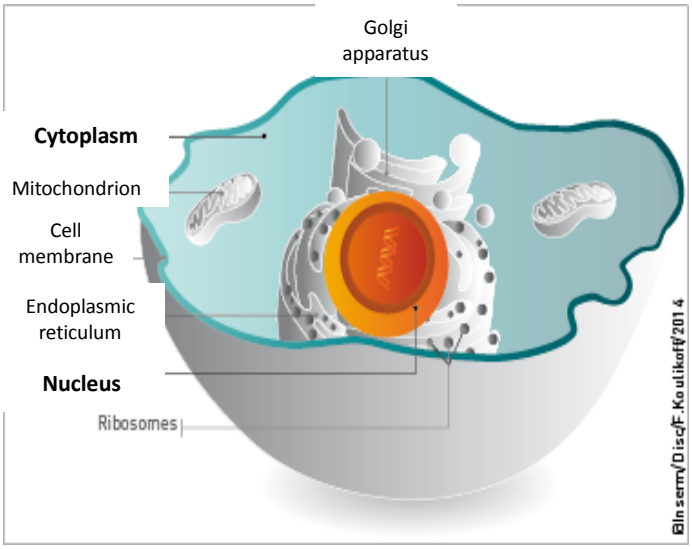
A mechanism for eliminating proteins accidentally localised to the cell nucleus.

An international collaboration coordinated by the German Cancer Research Center (DKFZ) (University of Heidelberg), including French researchers from the Institute of Genetics and Development of Rennes (IGDR) (CNRS/University of Rennes 1) under the leadership of Gwenaël Rabut, Inserm Researcher, and teams from Sweden and Canada, has just demonstrated a new molecular mechanism that may allow cells to destroy proteins accidentally localised to the nucleus.
This research is published in the journal Nature.

Biological processes are far from perfect. Despite millions of years of refinement, the molecular mechanisms that help living beings to function make many errors, which can have serious consequences unless they are detected and corrected. For example, many cancers are caused by errors that occur while our genetic material is being copied. Similarly, incorrect folding of some neuronal proteins leads to the formation of toxic aggregates that disrupt nervous system function and cause neurodegenerative diseases, such as Alzheimer's disease or Parkinson's disease.

To prevent this happening, cells have established complex molecular mechanisms that control the quality of proteins and eliminate those that are defective. These mechanisms are localised and implemented mainly in the cytoplasm (the cellular compartment where the proteins are synthesised).



While working on several factors involved in protein quality control, researchers discovered that some of them are also localised in the cell nucleus (the compartment that contains the genetic material), and that they enable the degradation of proteins that are abnormally present in this compartment.

During this study, researchers from the Institute of Genetics and Development of Rennes (including Gwenaël Rabut, Inserm Researcher, project coordinator and manager in Rennes, and Ewa Blaszczak, doctoral student, joint first author of the article) were able to observe that these factors involved in protein quality control interact with each other in the nucleus and bring about the ubiquitination (the step preceding degradation) of a protein accidentally localised to the nucleus.

By using an observation method developed at the University of Heidelberg, based on fluorescence timing in the proteins of interest, the researchers were able to identify some twenty proteins the degradation of which depended on quality control factors localised in the nucleus. Since several of these proteins are normally localised to the cytoplasm, and accumulate in the nucleus when they are no longer degraded, the researchers propose that this quality control system serves to eliminate not only defective proteins, but also proteins accidentally localised to the nucleus.

These discoveries were made using a model organism, baker's yeast, but it is likely that similar mechanisms also exist in humans.

A. Khmelinskii, Ewa Blaszczak *et al.*, Protein quality control at the inner membrane – DOI: 10.1038/NATURE14096

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