Peering deep into the cell to reveal essential components in cell division

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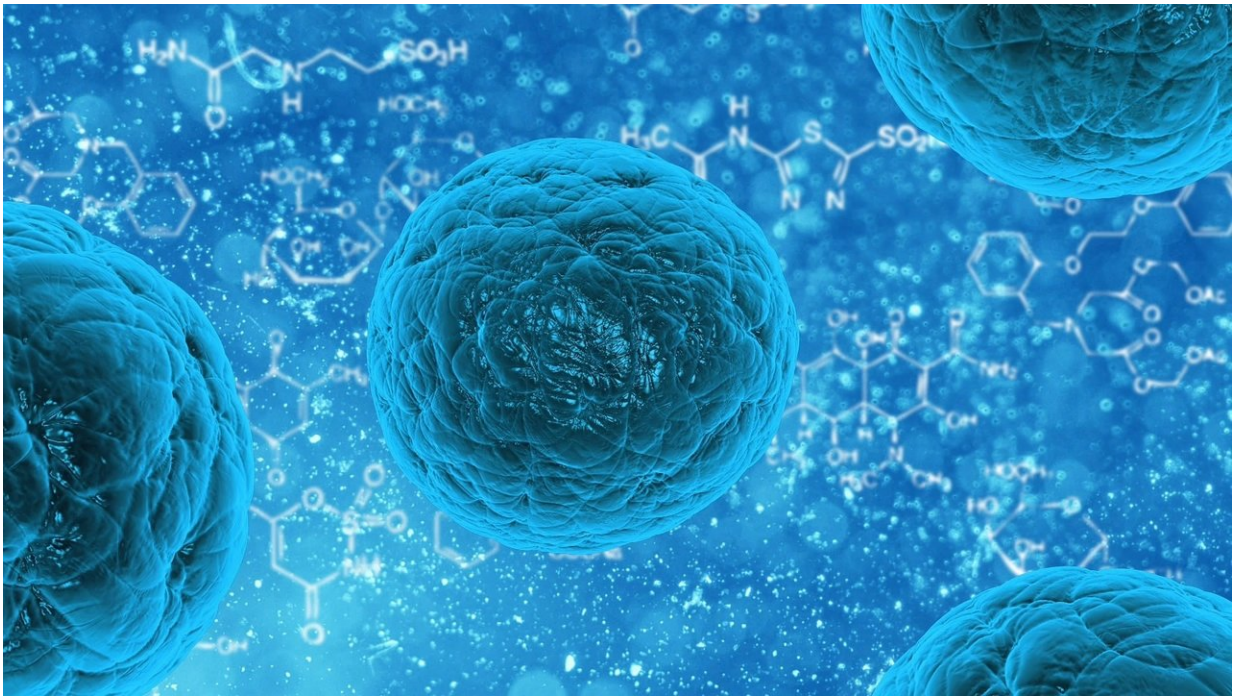

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The cell is the basic biological unit of all known living organisms, and the core of the cell is the nucleus, which contains the majority of the cell's genetic material. The largest structure in the nucleus of eukaryotic cells is the nucleolus. It is best known as the site of production of ribosome—the "factory" for protein production. The nucleolus also plays a role in the cell's response to stress and is tightly connected to cell cycle

progression.

In spite of this great deal of knowledge about the nucleolus, the relationship between cell cycle progression and nucleolar integrity remains poorly understood. Gaining a deeper understanding of the nucleolus is valuable, as malfunction of nucleoli can be the cause of several human conditions called nucleolopathies. Furthermore, the nucleolus has been investigated as a target for cancer diagnosis.

Recently, a team of University of Tsukuba-centered researchers made a breakthrough in the study of the nucleolus, and published their findings in *Science Advances*.

"We examined the role of nucleolar proteins in mitosis (cell division) in human cell lines by performing a global analysis using small interfering RNAs specific to nucleolar proteins; we focused on the protein NOL11, with currently unknown mitotic functions," first author of the study Yuki Hayashi explains. "NOL11 depletion reduced ribosomal RNA levels and caused nucleolar disruption during interphase."

Nucleolar disassembly during mitosis appears to be a programmed event in line with the activation of the protein kinase Cdk1 that is tightly regulated during the cell cycle. In contrast to the physiological mitotic nucleolar disassembly, "untimely" interphase nucleolar disruption is induced when rRNA transcription is suppressed by a variety of stressors. Notably, when interphase nucleolar disruption is induced following depletion of several rRNA transcription factors, Wee1, a kinase that phosphorylates and inhibits Cdk1, accumulates. At the same time, Cdk1 activity decreases. All these lead to delayed mitotic entry.

"Our findings therefore suggest that maintenance of nucleolar integrity during interphase is essential for proper cell cycle progression to mitosis via the regulation of Cdk1 and Wee1," senior author Keiji Kimura says.

"This is the first study, to our knowledge, to provide evidence that the maintenance of nucleolar structure is essential for proper timing of mitotic entry."

More information: Yuki Hayashi et al, Nucleolar integrity during interphase supports faithful Cdk1 activation and mitotic entry, *Science Advances* (2018). DOI: 10.1126/sciadv.aap7777

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