Protein kinase R and dsRNAs, new regulators of mammalian cell division

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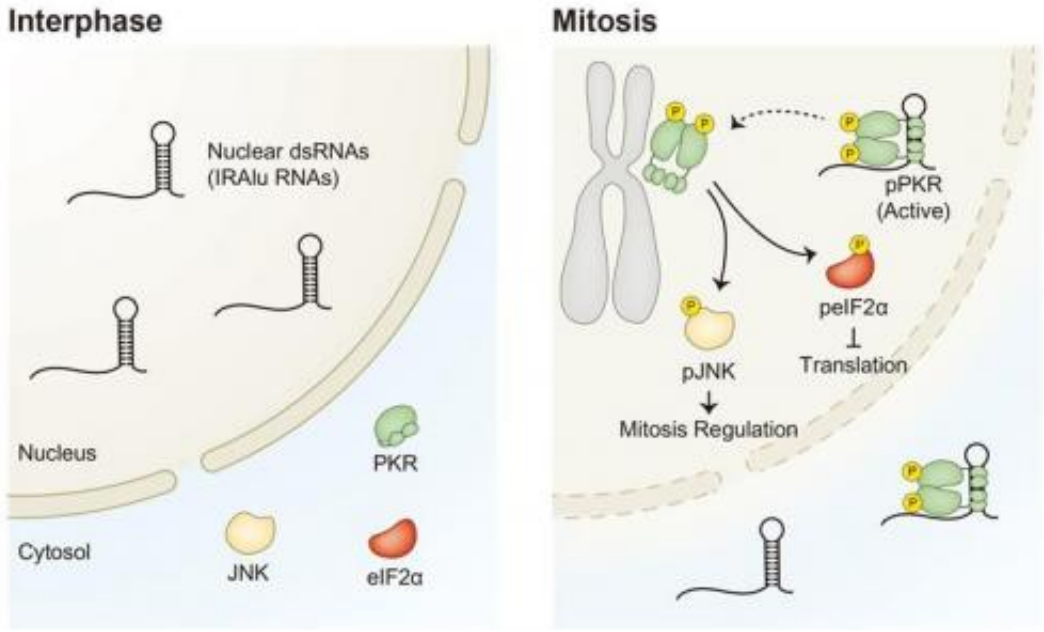


When cells are undergoing division, intermixing of cellular compartments allow dsRNAs and PKR to interact, leading to activation of PKR. When activated, PKR regulates protein synthesis and mitotic processes.

The research team of the Center for RNA Research at IBS has succeeded in revealing that the dsRNAs and Protein Kinase R (PKR) regulate division of mammalian cells.

This finding will provide important clues to understanding the process of tumor formation and the mechanism for suppressing cancer since the

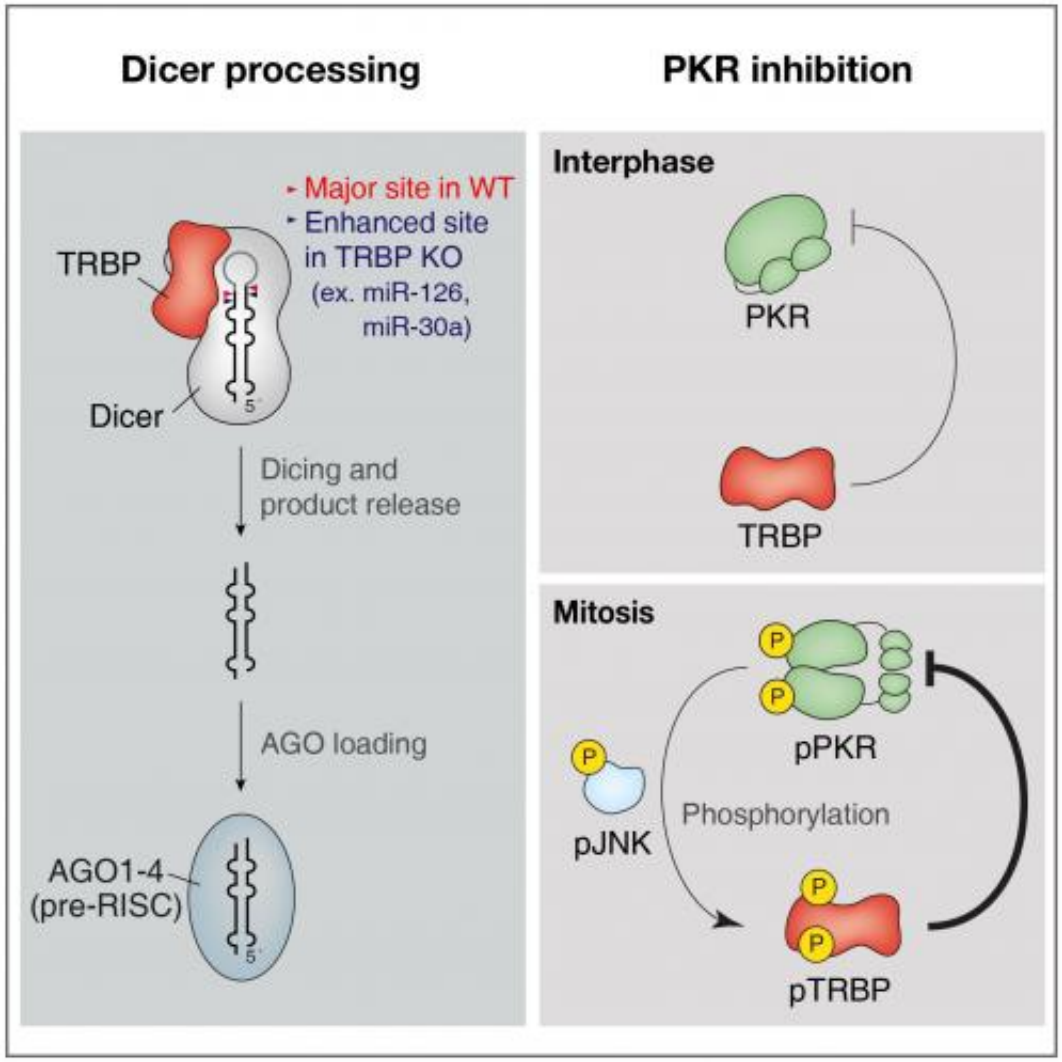
abnormal cell division marks the early events of cancer development.

For the first time, the IBS research team has found that during mitosis, the cellular dsRNAs activate PKR, an enzyme previously known as a trigger of immune response during virus infection. Activated PKR then regulates protein synthesis and orchestrates mitotic processes. Disruption of PKR activation resulted in misexpression of mitotic factors, delay in mitotic progression, and ultimately defects in cell division.

Overall, the research team has demonstrated a novel function of PKR in regulating cell cycle and dsRNA as a signal transmitter that delivers information via PKR during mitosis.

In their follow-up research, they also found that PKR activation during mitosis is tightly regulated by TAR RNA Binding Protein (TRBP), an inhibitor of PKR activation. This work demonstrates that TRBP, apart from its known function in microRNA biogenesis, also controls the cell cycle by regulating PKR activation.

"This achievement will introduce a new research direction in understanding the functions of various genes implicated in immune reaction as well as the cellular roles of dsRNAs that were previously considered as junk" says V. Narry Kim, both the director of the Center for RNA Research at IBS and the professor of the School of Biological Sciences at the Seoul National University.



By analyzing cells with genetic deletion of TRBP, the research team revealed cell cycle dependent regulation of PKR by TRBP and evaluated the function of TRBP in microRNA biogenesis.

More information: Yoosik Kim, Jung Hyun Lee, Jong-Eun Park, Jun Cho, Hyerim Yi, and V. Narry Kim (2014). PKR is activated by cellular dsRNAs during mitosis and acts as a mitotic regulator. *Genes & Development* 28: 1310-1322. DOI: 10.1101/gad.242644.114 Genes & Dev. 2014. 28: 1310-1322

Yoosik Kim, Jinah Yeo, Jung Hyun Lee, Jun Cho, Daekwan Seo, Jong-Seo Kim, and V. Narry Kim (2014). Deletion of Human tarbp2 Reveals Cellular MicroRNA Targets and Cell-Cycle Function of TRBP. *Cell Reports* 9:1061-1074. DOI: 10.1016/j.celrep.2014.09.039