

# Overexpression of proteins 14-3-3 related to chemotherapy resistance

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Certain proteins, such as 14-3-3, conserve their basic functions of cell cycle control in diverse organisms, from worms to humans. In a study led by Julián Cerón and Simó Schwartz Jr, researchers from the Bellvitge Biomedical Research Institute (IDIBELL) and the Research Institute of Vall d'Hebron (VHIR) respectively, have described germ line functions of par-5, which is one of the two 14-3-3 proteins existing in *Caenorhabditis elegans*, worms used as experimental model in genetic studies. The overexpression of the 14-3-3 proteins is related to the resistance of tumors to chemotherapy, which could have implications for clinical practice.

Researchers found that par-5 gene, as its human homologs, is required for DNA damage response in *C. elegans* validating the model to investigate chemotherapies and genetic modifications since 14-3-3 proteins are therapeutic targets in cancer. The results of this research have been published in the latest issue of *Journal of Cell Science*.

The powerful genetic tools of *C. elegans* have allowed a precise functional dissection of the single 14-3-3 [protein](#) present in their germline. The researchers have discovered that par-5 is not only necessary for proper [cell cycle](#) regulation, but also to prevent the accumulation of endogenous DNA damage and genomic instability.

Moreover, this study reveals that par-5 is required for DNA repair response when it is damaged by chemicals or ionizing radiation. In such response, the researchers propose a model where PAR-5 regulates

CDK-1 phosphorylation to stop the cell cycle and repair the damage induced by chemotherapeutic agents.

The overexpression of the 14-3-3 protein has been related to chemotherapy resistance in cancer cell lines while its downregulation sensitizes cells to therapy-induced cell death. Therefore, this study in *C. elegans* provides the basis for a model to study chemotherapy response in the context of a whole living organism.

Regulators proteins 14-3-3, evolutionarily conserved, bind to signaling proteins and affect their stability, activity or cellular localization. So, they are involved in the regulation of various cellular processes, including apoptosis, the cell cycle and stress response.

In addition, the researchers found that par-5 is required for cell cycle arrest in response to replicative stress and ionizing radiation.

**More information:** The 14-3-3 gene par-5 is required for germline development and DNA damage response in *Caenorhabditis elegans*. David Aristizábal-Corrales, Laura Fontrodona, Montserrat Porta-de-la-Riva, Angel Guerra-Moreno, Julián Cerón and Simo Schwartz. *J Cell Sci* 2012 125:1716-1726

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