# Discovering why chemotherapy only works for some cancer patients

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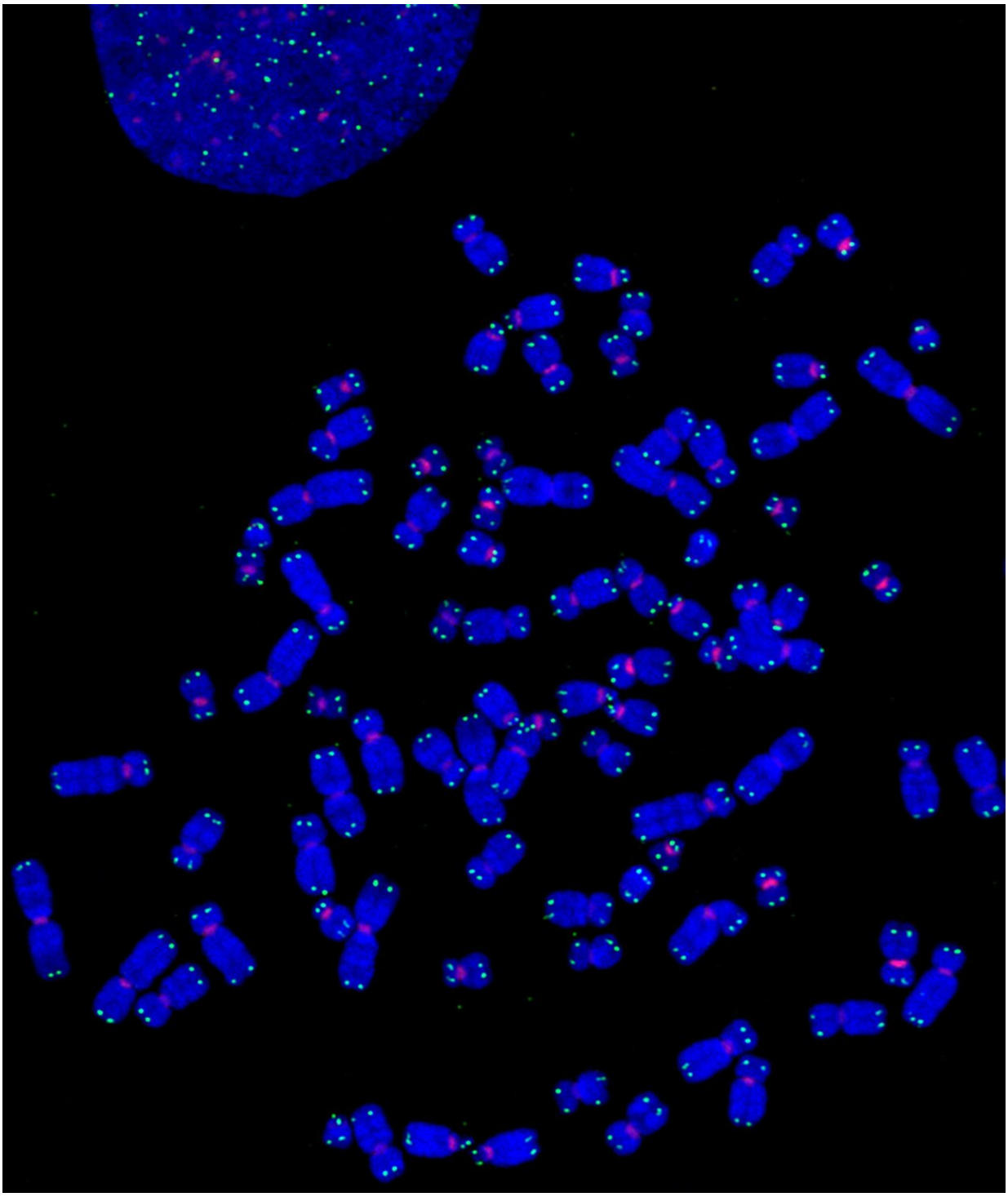

Credit: Children's Medical Research Institute (CMRI)

Researchers at Children's Medical Research Institute have demonstrated why chemotherapy drugs work better with some types of cancers than with others.

Dr. Pragathi Masamsetti, the lead author of a new paper published in *Nature Communications*, has been studying the pathways of cell death caused by chemotherapy drugs for the past five years after a surprise initial discovery piqued her interest. Now that her Ph.D. is finished, she is optimistic that her research will form the groundwork for other scientific or clinical developments in cancer treatment.

"This research could influence which class of chemotherapy is used for each cancer by giving doctors and scientists a better understanding of how the mutations in each type of cancer respond to various chemotherapy drugs."

Chemotherapy drugs work by causing a lethal level of stress on the processes occurring when cells are rapidly dividing, a hallmark of cancerous tissue. But these drugs, which attempt to stop rapid cell division, are a blunt solution and are not always effective.

"Chemotherapy can be very powerful in the right situation, but we are only beginning to understand the mechanism behind why some cancer cells die and why some proliferate when targeted by chemotherapy.

"Depending on the type of mutation in a patient, the cancer cells can avoid dying. These cells may go on to proliferate and actually promote the cancer."

Dr. Masamsetti's research revealed that cancers avoid cell death via a range of cellular pathways. The exact pathway the cancer cell uses depends on the particular mutations and other factors present in the cell. Cells with certain cancer mutations, such as the common p53 mutation,

are adept at avoiding their own death and go on to create further instability in the genome, making the cancer even more diverse and hard to eradicate.

Her research paints a picture of what must be present or absent in the cancer cell in order for a cell to avoid its own death via one pathway or another.

"I feel like this will give a lot of scope for future study into what is happening when chemotherapy is effective and when it's not. Building on previous knowledge with new techniques has allowed a new level of detail, so now hopefully other labs can better understand the relationship between cancer cells, chemotherapy and genetic mutations. This will be a big bridge to connect all the stories."'

The research made extensive use of live cell imaging, adding chemotherapy drugs to cells in real time in the ATAC facility at Children's Medical Research Institute. While this study was fundamental scientific research, Dr. Masamsetti sees her work as assisting clinics on the path toward personalized medicine.

"By knowing the ways in which cancer cells avoid cell death, it will help us to identify cancer treatments in the future. Once we can identify the mutations involved in each cancer then we can tailor our treatment approach as specifically to the instance of cancer as possible.

"Ultimately this is a step towards more personalized medicine, but we have to do more fundamental scientific research in order to understand how cancer works."

**More information:** V. Pragathi Masamsetti et al. Replication stress induces mitotic death through parallel pathways regulated by WAPL and telomere deprotection, *Nature Communications* (2019). DOI:

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