Scientists offer insight into adaptive ability of cells

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The Stowers Institute's Rong Li Lab has published findings that shed light on the ability of cells to adapt to disruptions to their basic division machineries – findings that may help explain how cancer cells elude the body's natural defense mechanisms or chemotherapy treatment. The work was published in the November 26 issue of *Cell*.

Working with yeast cells, the team disabled a motor protein, type II myosin — which normally powers cell division — and observed the cellular response. As predicted, blocking division initially resulted in severe growth and cytokinesis defects. But after several selection passages, some cells were able to solve the problems. Unexpectedly, these cells ended up with more than the normal number of chromosomes. The abnormal chromosome numbers led to changes in the patterns of gene expression, which correlated with the cells' ability to evolve new ways to complete division and resume growth.

"The ability of cellular systems to evolve is linked to their component and network complexity, which allows the cell to develop 'workarounds' to salvage normal functions, even in times of crisis," said Giulia Rancati, Ph.D., Postdoctoral Research Associate and co-equal lead author on the paper. "Surprisingly, the adaptation was accomplished not by changes in DNA sequences but largely by modifying the number of chromosomes in the cell (known as aneuploidy), which were passed on to future generations."

"Another process that contributed to the successful adaptation involved

polyploidization, in which yeast cells multiplied their entire set of chromosomes," said Norman Pavelka, Ph.D., Postdoctoral Research Associate and co-equal lead author on the paper. "Aneuploidy and polyploidy are hallmarks of cancer, and these findings suggest that they may contribute directly to the ability of cancer cells to evolve, allowing them to multiply, even as the body's natural mechanisms for cellular regulation or chemotherapeutic drug treatment work to limit their growth."

The work establishes an exciting new path for the Rong Li Lab.

"These findings validated our view that evolvability is a trackable and important subject for study," said Rong Li, Ph.D., Investigator and senior author on the paper. "We are now working to determine whether there are many distinct mechanisms of evolvability correlating with varying types and degrees of cellular disruptions. Additionally, we would like to explore the possibility of predicting the likely evolutionary paths and outcomes based on the architecture of molecular networks present in the cell; and in extending our research into mammalian cell systems to directly study the role of aneuploidy in the evolution of cancer."

Source: Stowers Institute for Medical Research