# Similarities between the two gap phases of the cell cycle indicate a default biochemical program in living cells

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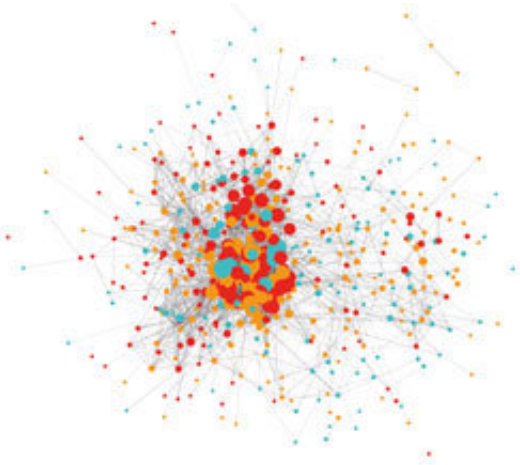

A protein interaction network in a biological system, where gold stands for changes only in cellular thermal shift assay stability (NC), cyan for changes only in expression level (CN) and red for changes in both (CC). Credit: Elsevier

The two 'gap' phases of the cell cycle were long thought to be under different regulatory control circuits, but a new study from A*STAR overturns this idea.

Pär Nordlund from the A*STAR Institute of Molecular and Cell Biology and colleagues found that the protein complexes formed during the gap 1 (G1) and gap 2 (G2) phases of the cell cycle are remarkably

similar—suggesting that the cell is hardwired for a default biochemical mode of operation when it's not actively replicating genetic material or dividing itself.

"This observation of similar biochemical programs in G1 and G2 cells is new, exciting, and unexpected," Nordlund says.

Cells in our bodies multiply through a four-stage process: cells first increase their mass and prepare for DNA replication during G1; they then copy DNA during the synthesis stage; next, they check the fidelity of duplicated DNA and assemble the materials needed for division during G2; and finally they align replicated chromosomes and divide during mitosis.

Transition from each stage is a tightly regulated event, requiring the assembly and disassembly of various protein complexes to execute many different functions—including to provide molecular checkpoints on cell-cycle progression.

Researchers had previously shown that the expression levels of some of these proteins, and their corresponding RNA molecules, rise and fall at certain points of the cell cycle. However, those analyses overlooked of the dynamic interactions between proteins and their binding partners that underpin how the cell moves through the phases of its cycle.

Nordlund and his colleagues profiled the dynamics of interaction states between all the proteins found in human blood cells during the transition of cell cycle's four stages. They used a technique previously developed by Nordlund's team—the Cellular Thermal Shift Assay (CETSA), which enabled them to discern which proteins stood alone and which were linked in protein complexes.

They identified more than 750 proteins that formed complexes or broke

them apart at some point in the cell cycle. However, most of these altered protein interaction states occurred during the synthesis and mitosis stages of the cell cycle—not during the gap phases.

Differences between G1 and G2 were comparatively minor, despite the unique roles played by gap stages in readying the cell for the next phase of the cycle. "This implies a well-working constant program that the cell reverts to," says Nordlund. "It extends our basic understanding of the biochemical programs in one of the fundamental processes in living cells."

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