Discovery of cellular counting mechanism used for size control in algae with links to cancer genetics

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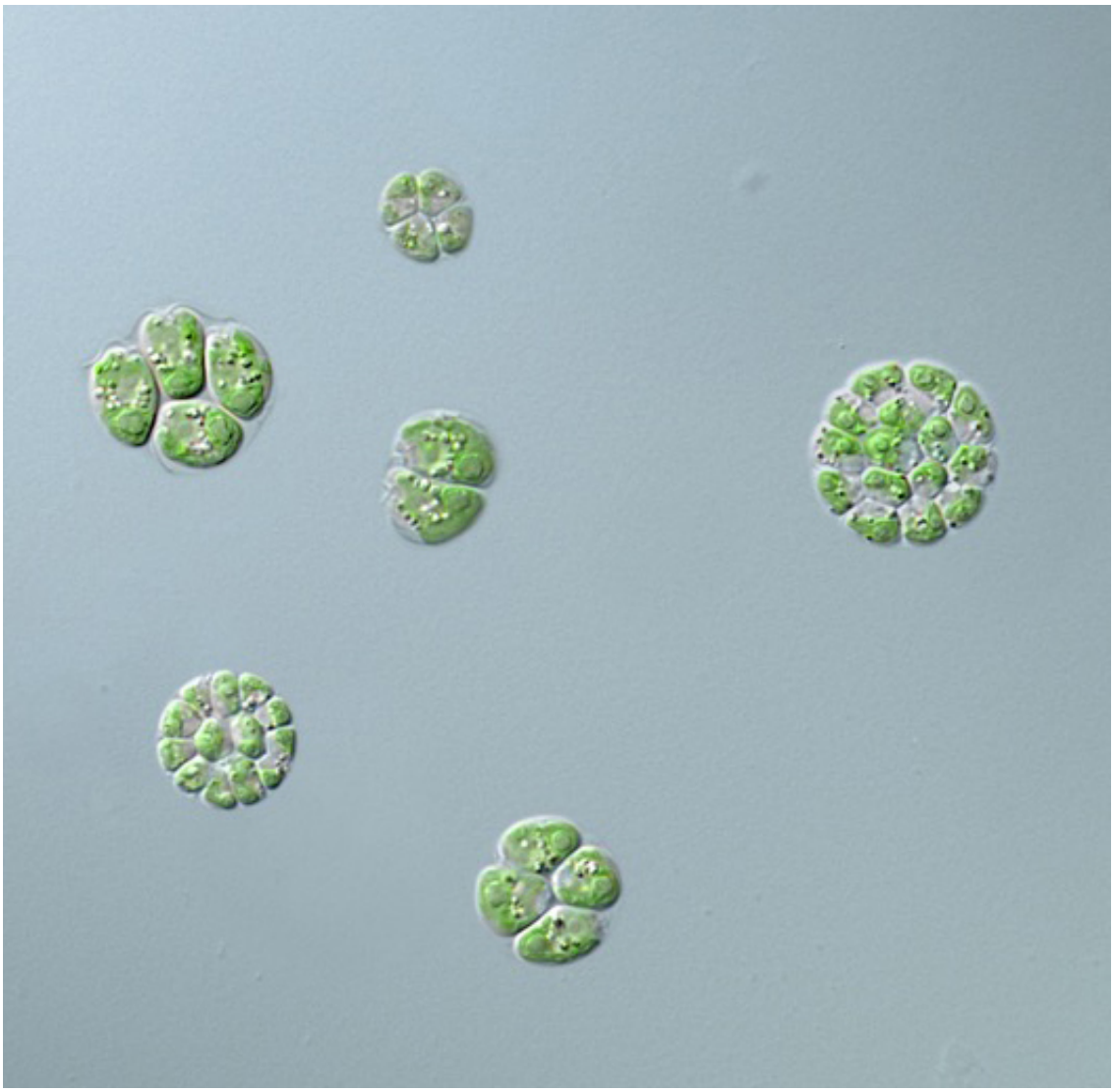
This image shows the numbers of divisions for *Chlamydomonas* cells scale with mother cell size. Left to right are cells of increasing size with the first cell too small to divide and next four undergoing one, two, three or four divisions to produce 2, 4, 8 or 16 daughters. Credit: Dianyi Liu and James Umen.

James Umen, Ph.D., associate member at Donald Danforth Plant Science Center, and colleagues have discovered a protein that enables the single-celled green alga *Chlamydomonas* to count cell divisions, a process that is critically important for its cells to maintain optimal size. The findings were published March 25, in a paper titled, "A new class of cyclin dependent kinase in *Chlamydomonas* is required for coupling cell size to cell division," in the open access journal *eLife*. Umen and his team including lead authors postdoctoral scientist Yubing Li and graduate student Dianyi Liu, identified a "sizer" protein called CDKG1 that helps *Chlamydomonas* count cell divisions.

Unlike the textbook paradigm of cell proliferation where cells double in size and then immediately split into two new daughters, cells of *Chlamydomonas* and many of its green algal relatives can enlarge more than ten times in size before they start dividing.

"If they were to only divide once after growing so large they would continue to get bigger and eventually would outgrow themselves and die," said Umen. "*Chlamydomonas* solves this size-control problem by rapidly dividing several times in succession until its daughter cells have been reduced to an appropriate size and are then ready to start growing again. The puzzle is how *Chlamydomonas* mother cells determine their size and count out the appropriate number of divisions."

The paper describes a process where cells produce a limited amount of CDKG1 just before they are about to start dividing. Initially, there is a high concentration of CDKG1, but with each round of division some of it gets broken down and the rest is parceled into daughters, each of which receives less than half the CDKG1 that its mother had. By the last round of division, the amount of CKDG1 per cell has dropped to almost undetectable levels.



These are clusters of wild-type *Chlamydomonas* cells and mutants in the division counting pathway that divided too many or too few times. Credit: Su-chiung Fang, Jamie Simon and James Umen.

The team found that the larger a cell had grown prior to the division the more CDKG1 it produced and the more times it could divide. Based on these observations Umen and coworkers hypothesized that CDKG1 might act like a gauge or ruler that enables cells to count out the appropriate number of divisions by coupling the amount of CDKG1

made to mother cell size. Accordingly, the authors found that when cells could not produce CDKG1 they stopped dividing prematurely and ended up too large, and when cells were forced to produce excess CDKG1 they underwent extra divisions and became too small.

Cell division and size control underlie biomass traits in algae whose manipulation could be critical for improving yields in next-generation algal biofuel crops; but the discovery of CDKG1 and how it helps cells count divisions has implications far outside of green algae where it was discovered. The authors found that CDKG1 is analogous to a human protein called CDK4/6 that stimulates cell proliferation and whose activity is frequently misregulated in cancers. Until recently, it was thought that CDK4/6-like proteins were limited to complex multicellular organisms like animals. Finding a similar protein to CDK4/6 in a unicellular alga not only forces a rethinking about when and how such proteins arose during evolution but opens up new opportunities to investigate genetic mechanisms of cell division control that have deeper roots than previously imagined.

Provided by Donald Danforth Plant Science Center

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