A cell cycle cue triggers cell growth resumption after division

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Abstract

The decoupling of the fundamental processes of cell division and growth is important for maintaining cell integrity. Through a chemical approach, we delayed the clock that controls when cells separate, uncoupling cell division and cell growth. This led to polarized cell growth before the cells completed separation. Using fluorescent markers to denote the cell’s stage in the cell cycle, we observed that only cells that were in mitosis exhibited this uncoupling. Previously it was thought that growth resumption occurred after completion of cell division, but this observation suggests that growth is triggered earlier, from a mitotic cue. This mitotic cue allows the tips to become better equipped to compete with the septum, causing the septum not to separate. Cdc42, a conserved GTPase that is a master regulator of cell division and polarity, appears at the septum and remains there until the cells separate then oscillates between the cell tips. However, in the uncoupled cells, Cdc42 leaves during septum formation, before the cells separate and is found at the tips. Further investigations into the specific cues could lead to a better understanding of what this cell cycle trigger is and how this cue affects Cdc42 at the tips.

Introduction and Background

Before mitosis, wild type S. pombe cells must stop their growth in order to ensure proper cell division. Then growth is restored once the cells divide. This is fundamental in ensuring that cells maintain proper size. The cue that causes cell growth to resume is largely not understood.

How does growth resume after cell division?

Cdc42, a highly conserved GTPase, is a master regulator of cell division and polarity. Cdc42 is controlled by GEFs that activate Cdc42 and GAPs that inactivate Cdc42. Active Cdc42 has been found to oscillate between the ends, demonstrating a competition between the two ends.

Methods

Latrunculin A (LatA)

The cells are treated with 10µM of LatA for 30 minutes and then rinsed, and then the cells are allowed to recover. The LatA depolymerizes all of the actin in the cell. Leading to the disruption of both actin cables, the actomyosin ring and actin patches.

Lectin

Lectin was used to stick the cells to the plate, this allows the same cells to be imaged before during and after the treatment of the cells. This technique was adapted to our lab in order to observe the effects of LatA on the cells.

Results

Mitotic cue triggers growth

Press (Prematurely Elongating Sans Separation) Phenotype

Figure 3: When cells are treated with LatA a portion of the cells resume growth either during or after septum formation, but these cells fail to separate. The LatA disrupts the actomyosin ring and therefore delays cell separation, but the cells continue to grow. Therefore they become long and end up becoming multi-septated.

Conclusion

Only the cells that were in mitosis when the actin was disrupted, showed the PRESS phenotype leading to the conclusion that there must be a mitotic cue that triggers the resumption of growth after cell division. The cells must pass this certain cue before the cells can resume growth, and this is not dependent on the physical separation of the cells. Also, it was shown that in the uncoupled cells, Cdc42 leaves the middle of the cells while septum was still forming and went to the tips. This could show that there is a link between this mitotic cue and the localization of Cdc42 at the tips of the cells following cell separation. This mitotic cue allows the tips to become better equipped to compete for resources with the middle. Future work in finding this cell cycle trigger could lead to a better understanding of the cell cycle and a better understanding of how this cue affects the localization of Cdc42 at the tips.

References