Received: 4 October 2022 | Accepted: 6 October 2022

DOI: 10.1002/bies.202200193

BioEssays

IDEA TO WATCH

Thoughts & Opinion

What can asymmetrical cell snakes do?

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CTP synthase (CTPS), the rate-limiting enzyme of de novo CTP synthesis, forms the cytoophidium (meaning 'cell snake' in Greek; cytoophidia as plural) in many types of cells.[1] These cell snakes are dynamic, reversible, and consist of correctly folded proteins. Dozens of cytoophidium-forming proteins have been identified in several organisms across prokaryotes and eukaryotes.[2] Cytoophidium assembly is controlled by ligand binding, post-translational modifications, pH value and molecular crowding.[3] Therefore, the formation of cytoophidia may reflect the cell status and also influence cell behaviours.

A cell can have many small cytoophidia and/or have only few major large ones. We have previously shown that a fission yeast cell normally has only one large cytoplasmic cytoophidium and one small nuclear cytoophidium. When the mother cell divides into two daughter cells, there are four different inheritance combinations of cytoophidia in the cytoplasm and nucleus.[4]

Darekar and Laín have hypothesized that asymmetric inheritance of cytoophidia may contribute to the determination of distinct cell fate of daughter cells. They clearly reasoned by potential effects of the cytoophidium on nucleotide metabolism and so on cell fate determination.[5] Given the size of the cytoophidium reflects the amount of its protein components, the cell inheriting the large CTPS cytoophidium is presumably having more CTPS than its sibling at the beginning of the cell cycle. However, will this difference lead to distinct fate of the two cells?

To answer this question, it is important to understand whether such alteration in protein levels is sufficient to change metabolic equilibrium of the cell and how long can this effect last for? The complicated coordination between all participant molecules could make metabolic influences of these cytoophidia quite unpredictable. Of course, this does not rule out the possibility that asymmetric cytoophidium inheritance may alter the cell fate. In addition to modulating nucleotide synthesis, the cytoophidium may have many other biological functions depending on its component proteins. In addition, having such a large protein aggregate may trigger specific signaling pathways, and the cytoophidium may interact with other classic and nonclassic organelles. Therefore, we should also consider the advantage (or disadvantage) of cytoophidia inherited from different ways.

Are cytoophidia inherited asymmetrically in multicellular organisms? Under physiological conditions, some types of cytoophidia are observed in different tissues in fruitflies and vertebrates. Fruitfly carrying fluorescent labelled cytoophidium proteins is an excellent model for real-time observation of cytoophidium dynamics. However, tracking cytoophidium dynamics in living tissues is a challenge, especially in mammalian models.

Or, perhaps we can start with another question: what would happen if there is no cytoophidium? If we think that the behaviour of cells that inherit cytoplasmic or nuclear cytoophidia are different from that of other cells just because the distribution of cytoophidium proteins or bulky protein aggregates in the two daughter cells is uneven, then the prohibition of cytoophidium assembly is supposedly to eliminate this prejudice against the two daughter cells.

In some cases, point mutations at specific sites that disrupt the polymerisation of individual cytoophidium-forming proteins have been reported, and it is possible to introduce genes into cultured cells and model organisms. Theoretically, the determination of cell fate may be messed up in specific cell populations due to mutations. Finally, before really testing this hypothesis, the most important thing may be to find the right cytoophidium in the right type of cells.

This article comments on the hypothesis paper by Suhas Darekar and Sonia Laín, https://doi.org/10.1002/bies.202200128

CONFLICT OF INTEREST

The authors declare no conflict of interests.

DATA AVAILABILITY STATEMENT

None.

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How to cite this article: Chang, C. C., & Liu, J. L. (2022). What can asymmetrical cell snakes do? *BioEssays*, *44*, e2200193. https://doi.org/10.1002/bies.202200193