Modeling the Coordination of Growth and Inheritance to Achieve Vacuole Size Scaling

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Short Abstract **— Organelle size impacts function and is therefore regulated by the cell. To study this regulation, we apply a novel image analysis method to quantitatively measure the size of the yeast vacuole. Mutants with inheritance defects show increasingly altered vacuole-to-cell size scaling as mothers undergo replicative aging. Modeling demonstrates that vacuole-to-cell size scaling can arise naturally from constant cell and organelle growth rates without the explicit need for feedback, but this is sensitive to proper inheritance which distributes vacuole between mother and bud. These results illustrate how vacuole biogenesis and inheritance are coordinated during the cell division cycle.**

Keywords **— organelle, scaling, growth, inheritance**

I. Background

ORGANELLES allow the cell to achieve greater complexity by providing isolated environments which can then be optimized to carry out biochemical reactions. As the cell grows, organelles also grow or scale with the cell, presumably to increase their capacity to meet the cell's functional needs. Such scaling trends have been observed for a variety of organelles [1,2,3,4], but it is less well known how the cell regulates the size of its organelles.

The yeast vacuole is functionally analogous to the mammalian lysosome, and is responsible for much of the degradative catabolism of the cell. It is comprised of a set of membrane-bound lobes which undergo fusion and fission dynamics. We have developed a novel image analysis method to extract measurements of vacuole volume and surface area [5] in order to study whether and how vacuole size scaling is established in yeast.

II. Results

Measurements of vacuole size reveal that the vacuole indeed scales in size with the cell. Wild-type strains show characteristic patterns of volume and surface area scaling [6]. These patterns are altered in various mutants, with a striking change in strains with defects in inheritance—the segregation of vacuole from mother to bud during asymmetric cell division.

A. Ageing effects in inheritance mutants

Population measurements of vacuole size scaling in the *vac8Δ* inheritance mutant [7] reveal that overall, cells have larger vacuoles when compared to wild-type. Controlling for replicative age shows that *vac8Δ* cells accumulate vacuole during successive budding cycles. Vacuole growth rates do not change in response to the inheritance defect.

B. Modeling of vacuole growth rates

These experimental observations have led to the development of a model of vacuole size scaling with parameters for cell and vacuole growth rates as well as inheritance. Interestingly, setting constant vacuole and cell growth rates results in vacuole size scaling trends without requiring a feedback term, and scaling is robust to variance in the growth terms. However, these trends depend on proper inheritance of the vacuole, without which scaling diverges with increasing replicative age as observed experimentally.

III. Conclusion

Quantitative microscopy and modeling reveal that constant vacuole and cell growth are sufficient to give rise size scaling. Growth is coordinated with inheritance to ensure proper distribution of the vacuole between mother and bud during cell division, resulting in vacuole-to-cell size scaling.

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