

Department of Biological Sciences Faculty of Science

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Cell size determines proteome composition in mammalian, yeast, and bacterial cells

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Cell size is tightly controlled in single-celled organisms and the cells of healthy mammalian tissues, but it remains unclear how changes in cell size impact cell physiology. To address this, we measured how changes in cell size affect proteome composition. We found that size-dependent changes to the proteome are widespread, predicted by subcellular localization, and occur in organisms across the tree of life. In eukaryotes, size-dependent proteome changes are highly conserved. In both yeast and humans, the dilution of the genome elicits a starvation-like proteome phenotype, suggesting that growth in large cells is limited by genome concentration in a manner analogous to a limiting nutrient. Interestingly, we find that large cell size is likely the primary determinant of proteome content for both replicatively-aged yeast cells and senescent mammalian cells. Taken together, our data indicate that the cell size-to-ploidy ratio is a universal determinant of proteome content and that polyploidization therefore represents an elegant mechanism to increase cell size without altering cellular composition.