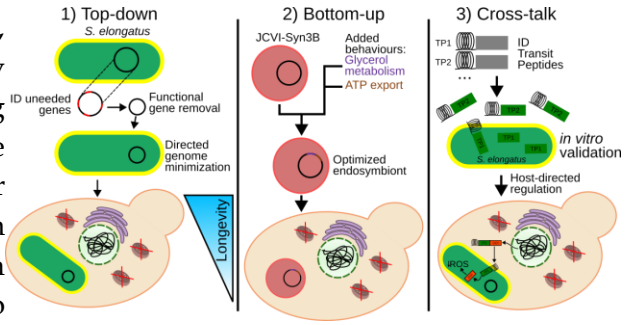
Development of improved synthetic endosymbiosis from the top-down and bottom-up

Jordan Quenneville, Bidhan C. De, Angela Thomas , Yang-le Gao, Angad P. Mehta



Over the course of evolutionary history, one of the greatest changes were the primary endosymbiotic events. These biosphere-altering events culminated in the evolution of the chloroplast and mitochondrion, allowing for eukaryotic carbon fixation and massive gains in cellular energy production. Through cell fusion protocols established in our lab, we are able to recreate primary endosymbiosis using OXPHOS-defective yeast and prokaryotes for up to 24 generations. Here, we expand on this work by improving synthetic endosymbiosis via three approaches: 1) A top-down approach by minimizing the *Synechococcus elongatus* genome, removing essential genes which become non-essential in an endosymbiotic context to enhance endosymbiotic longevity. 2) A bottom-up approach through adding metabolic capabilities to minimal cells. By optimizing glycerol metabolism and ATP export in minimal cells, we can build up minimal cells into ideal endosymbionts. 3) Enabling host to endosymbiont regulation via specialized transit peptides. By harnessing *Paullinella chromatophora* transit peptides, we envision functional protein delivery to photosynthetic endosymbionts allowing for host-directed endosymbiont regulation. Once optimized, synthetic endosymbiosis holds significant potential for both industry and health.

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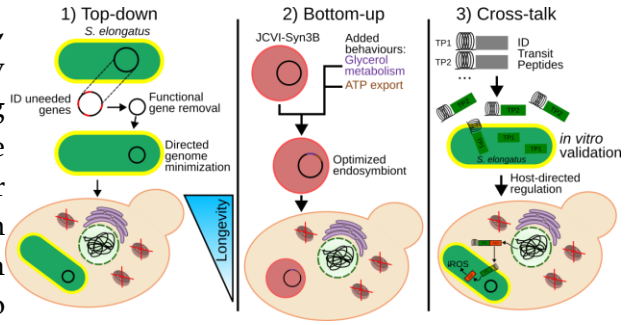

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