Supplementary Note:

We observed an acute response to the addition of the magnetic streptavidin coated beads that included an upregulation of the biotin biosynthesis pathway in *S. cerevisiae,* which includes enzymes and transporters involved in the synthesis and uptake of biotin and biotin precursors, respectively. We looked for and found this response in our data as well as in data from previous work reliant on the biotin/streptavidin interaction (Janssens et al. 2015) (Figure SN 1). We reasoned that the streptavidin beads were, in addition to binding the covalently linked biotin on the cell wall of labeled mothers, leaching biotin from the media and causing the upregulation of the biotin genes. Given that biotin is essential for yeast growth, we sought to test our aging protocol in manner that would not perturb biotin levels by taking advantage of the fact that although *S. cerevisiae* cannot synthesize biotin *de novo*, it can make biotin from the precursor 7,8-diaminopelargonic acid (DAPA), which does not bind streptavidin ((Yang, Tani, and Ogata 1971) (Phalip et al. 1999), Figure SN1). Furthermore, using DAPA would also enable beading in growth media.

We first determined that *S. cerevisiae* could grow on DAPA media without any biotin at a rate comparable to wild type (Figure SN1). We next aged yeast mothers on DAPA media in the ministats and compared their age (in bud scars) as well as age-dependent transcriptome to those mother cells grown in standard biotin-containing media (Figure SN2). The strength of the correlation between wild type cells grown in biotin versus DAPA led us to conclude that the aging process in both conditions is extremely similar (Figure SN2). To ensure however that we were not placing undue stress on the aging cells we switched to using DAPA for the remainder of our experiments. Additionally, growth in DAPA media allowed for beading of cells in actual growth media. In initial MAD iterations, binding of magnetic beads was done in PBS (Figures 1 and 2).

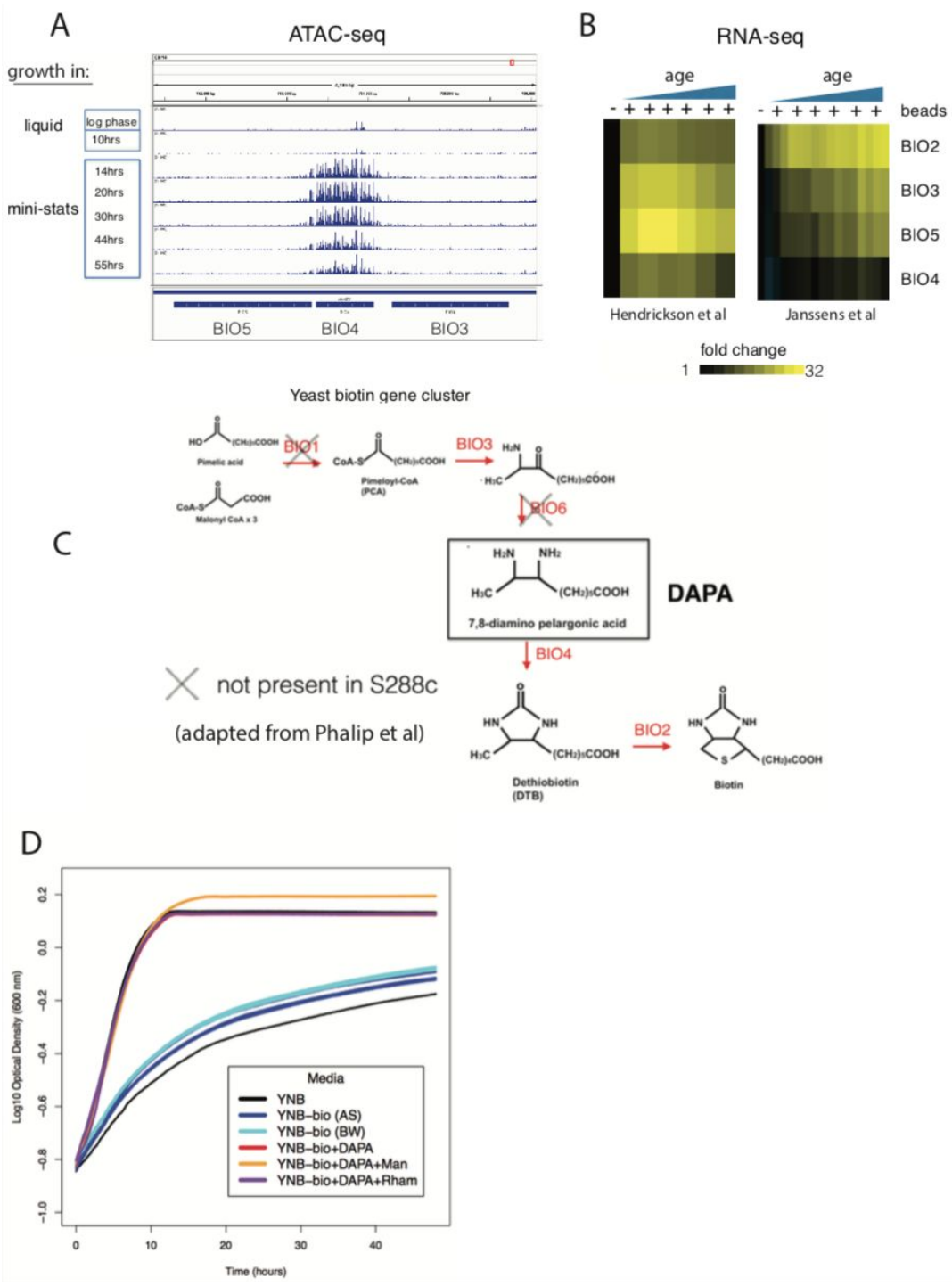

Figure SN1: (A) ATAC-Seq insertional density at the biotin gene locus of ministat-aged cultures. (B) RNA-Seq analysis of biotin genes at increasing ages from this manuscript and Janssens *et al.* (C) Biotin pathway in yeast. (D) Growth curves of DBY12000 in different media. AS and BW are two separate minus biotin preparations.

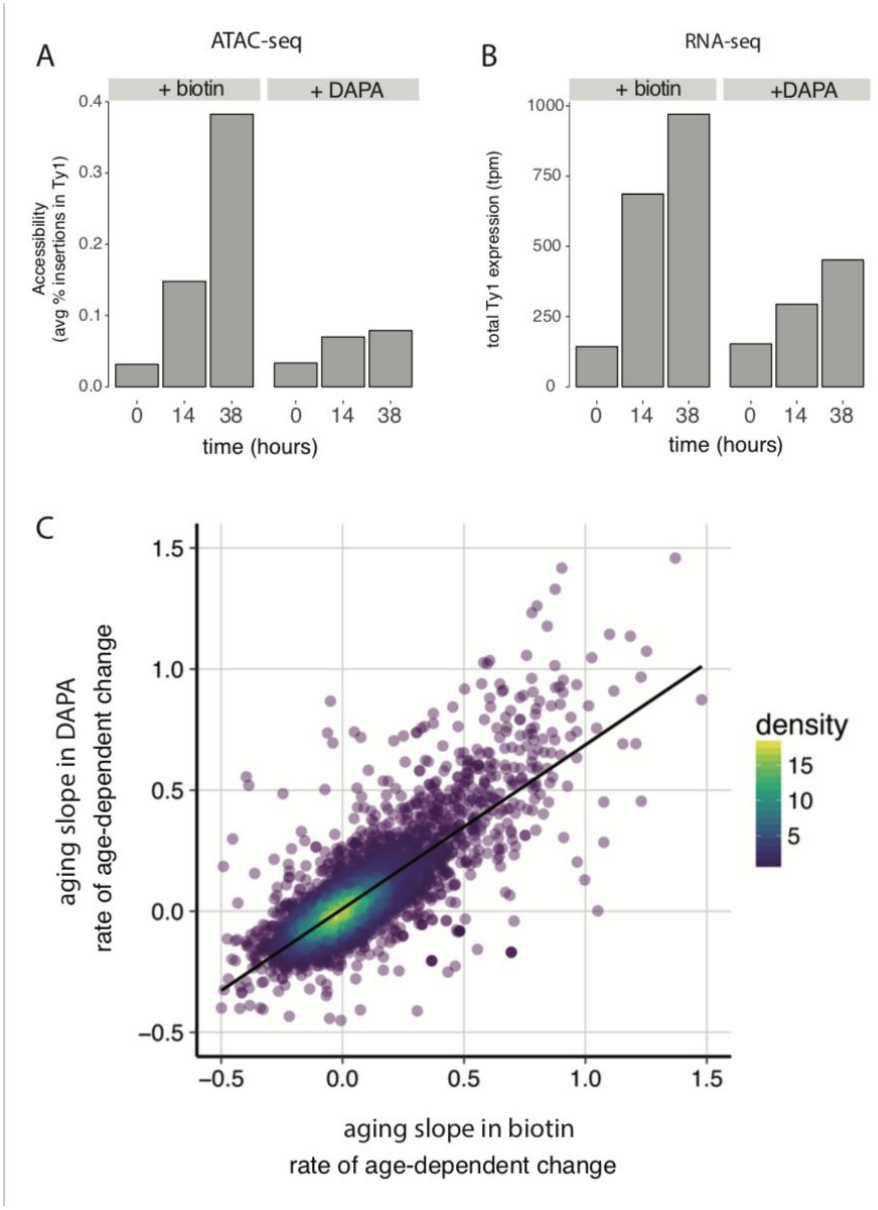

Figure SN2: (A) ATAC-Seq insertional density increases with age at Ty1 loci in both biotin and DAPA (B) Ty1 expression increases with old age in both biotin and DAPA. (C) Age-related gene expression changes are similar in media containing biotin or DAPA.

Janssens, Georges E., Anne C. Meinema, Javier González, Justina C. Wolters, Alexander Schmidt, Victor Guryev, Rainer Bischoff, Ernst C. Wit, Liesbeth M. Veenhoff, and Matthias Heinemann. 2015. “Protein Biogenesis Machinery Is a Driver of Replicative Aging in Yeast.” *eLife* 4 (December): e08527.

Phalip, V., I. Kuhn, Y. Lemoine, and J. M. Jeltsch. 1999. “Characterization of the Biotin Biosynthesis Pathway in Saccharomyces Cerevisiae and Evidence for a Cluster Containing BIO5, a Novel Gene Involved in Vitamer Uptake.” *Gene* 232 (1): 43–51.

Yang, Han-Chul, Yoshiki Tani, and Koichi Ogata. 1971. “Studies on the Metabolism of Biotin Vitamers by Microorganisms.” *Agricultural and Biological Chemistry* 35 (6). Taylor & Francis: 870–84.