Background:

The budding yeast has served as a useful model organism in aging studies, leading to the identification of genetic determinants of longevity, many of which are conserved in higher eukaryotes. However, factors that promote longevity in a laboratory setting often have severe fitness disadvantages in the wild.

Aims and Methods:

To obtain an unbiased view on longevity regulation, we analyzed how a replicative lifespan is shaped by transcriptional, translational, metabolic, and morphological factors across 22 wild-type *Saccharomyces cerevisiae* isolates.

Results:

We observed significant differences in lifespan across these strains and found that their longevity is strongly associated with up-regulation of oxidative phosphorylation and respiration and down-regulation of amino- acid and nitrogen compound biosynthesis.

Conclusions:

As calorie restriction and TOR signaling also extend the lifespan by adjusting many of the identified pathways, the data suggest that the natural plasticity of yeast lifespan is shaped by the processes that not only do not impose cost on fitness, but also are amenable to dietary intervention