

## Editorial comments:

1. Protocol to be filmed should have detailed, step-by-step directions highlighted, which is not necessarily the case; e.g.:

-Section 2: This section is fairly vague (and is perhaps not necessary to film; note that we can show the point that the strains should have a growth defect in another section of the video).

We agree. We don't need to film this section, but we need to be clear that having a growth defect in liquid culture (mutation or drug) is a pre-requirement for the screen.

-Section 6: You have indicated that bioinformatic analysis should be filmed, but not highlighted any of the steps; also the last step highlighted is fairly vague. Please

We won't film the bioinformatics analysis. We will only film the content in Figure 3, and the highlighted portion of step 6.10.

2. 6.6-6.8: It looks like this is geared to the analysis you did for the results (including in the provided scripts); how might it be altered for the protocol as presented, with all sequencing done in triplicate?

Thank you for this important point. We have revised the script in the protocol to better align with the protocol and to analyze triplicates.

3. Results: '...when backcrossing all yfm S with yfm P...' (first paragraph)-the use of the generic 'yfm' seems out of place in this section, which should be focused on specific results. Could this be '...suppressors with parentals' (or similar)? See also later in the paragraph.

We agree that it seems out of place. We have revised the text to "When grown on the same plate for the same amount of time, we confirmed the 2:2 segregation when back-crossing all suppressed strains (S strains) with their parental strains (P strains), which resulted in 2 small (growth defect) and 2 large (suppressor phenotype) colonies. Individual examples for suppressed *elf1Δ*, *clr6-1* and *fal1Δ* cells are shown in Figure 2B. We have confirmed that all isolated S strains carry a monogenic, genetic element that suppresses the slow-growing phenotype of their P strains (data not shown)".

4. Table 1: There should be one sheet per uploaded table; either split into 4 tables or upload as supplemental material. Note also that a 650+ row table will be tricky to include within the final manuscript.

We have split the table into 4 tables and uploaded the tables as supplementary material. We have modified the text to reflect the changes.