

SGD Variant Viewer

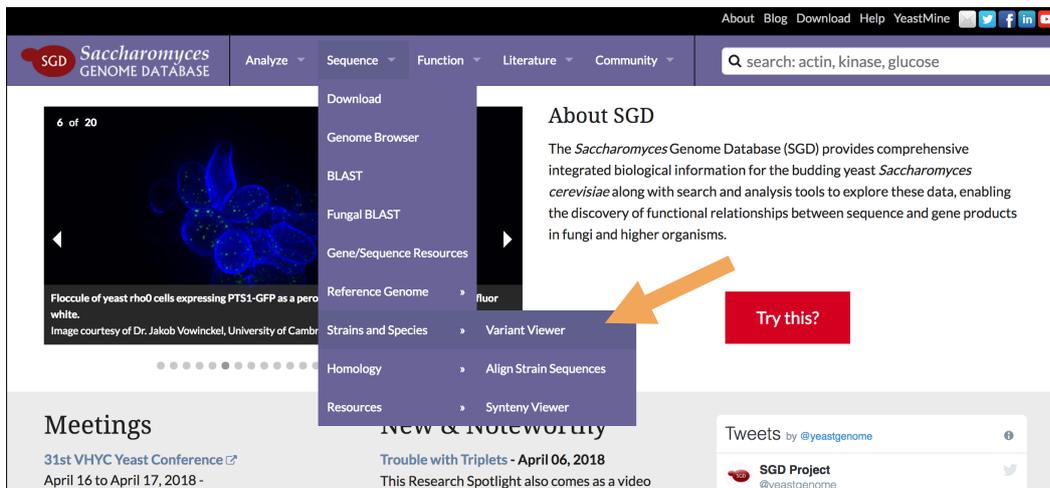
SGD's Variant Viewer (<https://yeastgenome.org/variant-viewer>) is an open-source web application that compares nucleotide and amino acid sequence differences between 12 common *S. cerevisiae* laboratory strains. For a given open reading frame, Variant Viewer breaks down the position and nature of any strain-specific sequence differences relative to the reference strain S288C. When used at a multi-gene level, it also provides a matrix of alignment scores that enables quick identification of genes with higher or lower variation.

Variant Viewer can be used to probe the genetic differences between *S. cerevisiae* strains that give rise to their unique phenotypes. For example, while strain Sigma1278b readily undergoes pseudohyphal growth, the reference genome strain S288C does not.

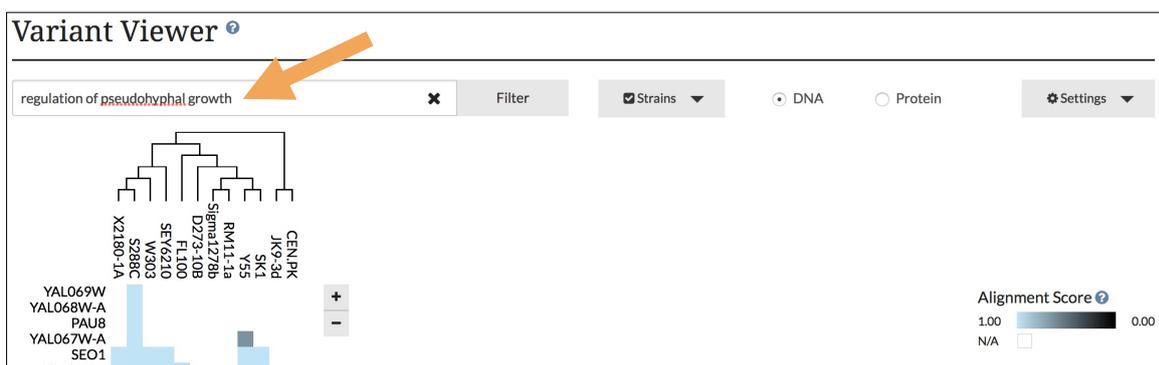
In this exercise, we will use Variant Viewer to find out what genetic differences between Sigma1278b and S288C explain why they differ in their ability to form pseudohyphae.

S288C vs. Sigma1278b: Pseudohyphal Growth

- Open the SGD home page (www.yeastgenome.org), open the Sequence tab on top of the page, then select Strains and Species followed by Variant Viewer from the pull-down menus. Or just type in the URL: yeastgenome.org/variant-viewer



- The **Filter** box accepts one or more genes, as well as Gene Ontology (GO) terms. Because we are interested in genes involved in pseudohyphal growth, search for the GO term “**regulation of pseudohyphal growth**” and click Filter.



- The **matrix**, shown on the left, will have changed to only include genes annotated with the Gene Ontology term “regulation of pseudohyphal growth”.
 - This matrix enables you to visualize high-level differences in multiple genes relative to strain S288C. Each square in the matrix corresponds to one of the twelve strains in Variant Viewer, shown at the top, and to an open reading frame, shown on the left.
 - The color of each square indicates how similar the sequence is relative to strain S288C. As indicated on the Alignment Score figure on the right, lighter shades of blue indicate high sequence similarity whereas darker shades indicate more dissimilarity. Note that if the square is white, it means a comparison could not be made.
- Next, we will want to make the matrix display only info for the strains we are interested in (S288C and Sigma1278b). Open the **Strains** pull-down menu, press Deselect All, then re-select Sigma1278b.
- To focus on the strain gene sequences with the most dissimilarity to S288C, sort the matrix by variation. To do so, open the **Settings** menu and select Variation; this will sort the genes by their level of variation and put the genes with most differences on top.

The screenshot shows the Variant Viewer interface for the gene 'regulation of pseudohyphal growth'. The 'Strains' menu is open, showing 'S288C (reference)' and 'Sigma1278b' selected. The 'Settings' menu is also open, showing 'Sort By' set to 'Variation'. An Alignment Score legend is visible on the right, ranging from 1.00 (light blue) to 0.00 (dark blue).

- Click on the top gene, **FLO8**, and select **Protein**. Scroll with your mouse along the sequence. Find a stop codon (*) in the S288C sequence that replaces tryptophan (W) in Sigma1278b, thus causing premature termination of translation of FLO8 in S288C.

The screenshot shows the protein sequence viewer for FLO8 / YER109C. The sequence is shown for S288C, X2180-1A, SEY6210, W303, JK9-3d, FL100, CEN.PK, D273-10B, Sigma1278b, RM11-1a, SK1, and Y55. An orange arrow points to a stop codon (*) in the S288C sequence at position 206, which replaces tryptophan (W) in Sigma1278b.

- Now that we have identified that a premature stop affects S288C FLO8, click the FLO8 / YER109C link to examine the FLO8 locus summary page. From the FLO8 Locus Summary page, you will learn that this is a transcription factor required for flocculation, diploid filamentous growth, and haploid invasive growth. The nonsense mutation at codon 142 is indeed responsible for the inability of S288C to form pseudohyphae!

S288C vs. W303: Budding Pattern

Another example strain difference in yeast is between S288C and W303. Haploid S288C cells exhibit an axial budding pattern, whereas diploid cells exhibit a bipolar budding pattern. On the other hand, strain W303 shows bipolar bud site selection in both haploid and diploid cells. Using Variant Viewer, examine the axial budding gene **BUD4** and see if you can locate any genetic differences between S288C and W303 that would explain the difference in budding phenotypes.