SGD Variant Viewer

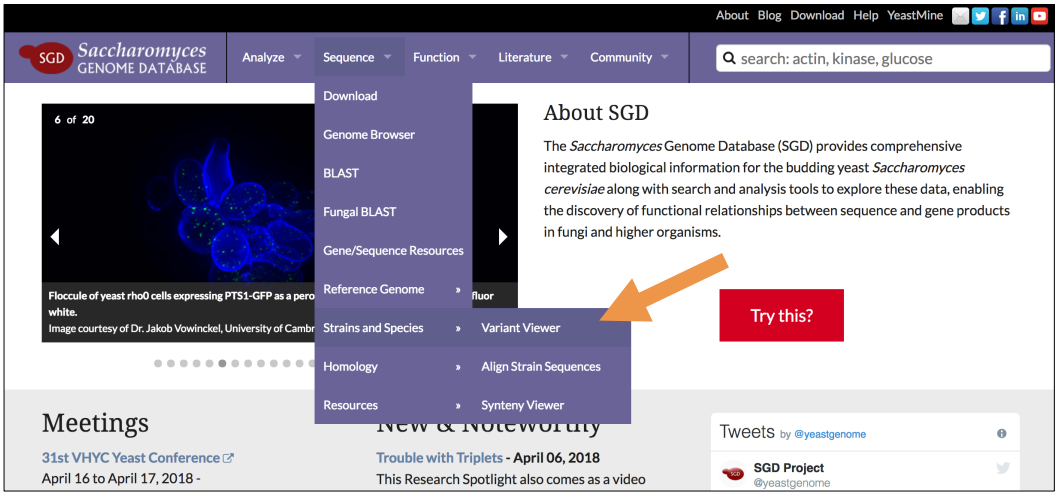
SGD's Variant Viewer (**https://yeastgenome.org/variant-viewer**) is an open-source web application that compares nucleotide and amino acid sequence differences between 12 common *S. cerevisiae* laboratory strains. For a given open reading frame, Variant Viewer breaks down the position and nature of 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 haploid S288C cells exhibit an axial budding pattern, diploid cells exhibit a bipolar budding pattern. On the other hand, strain W303 shows bipolar bud site selection in both haploid and diploid cells.

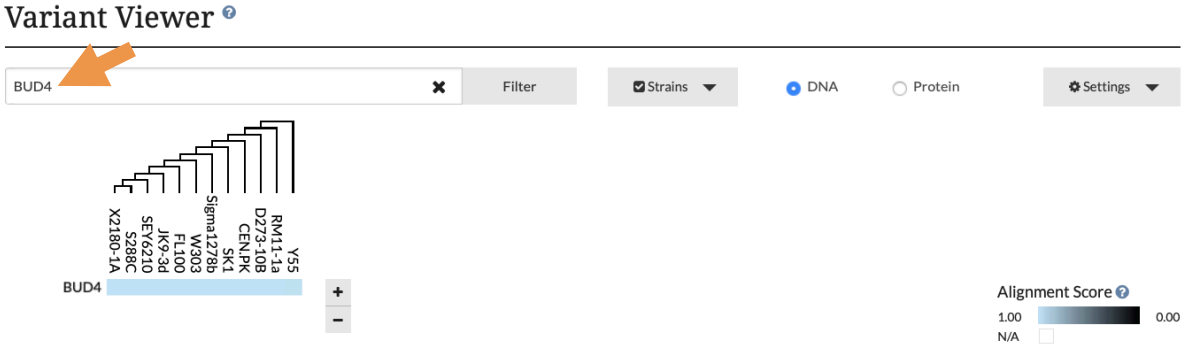
In this exercise, we will use Variant Viewer to find out what genetic differences are present between W303 and S288C strains of axial budding gene **BUD4** and explain why they exhibit different budding phenotypes.

S288C vs. W303: Budding Phenotype

- 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



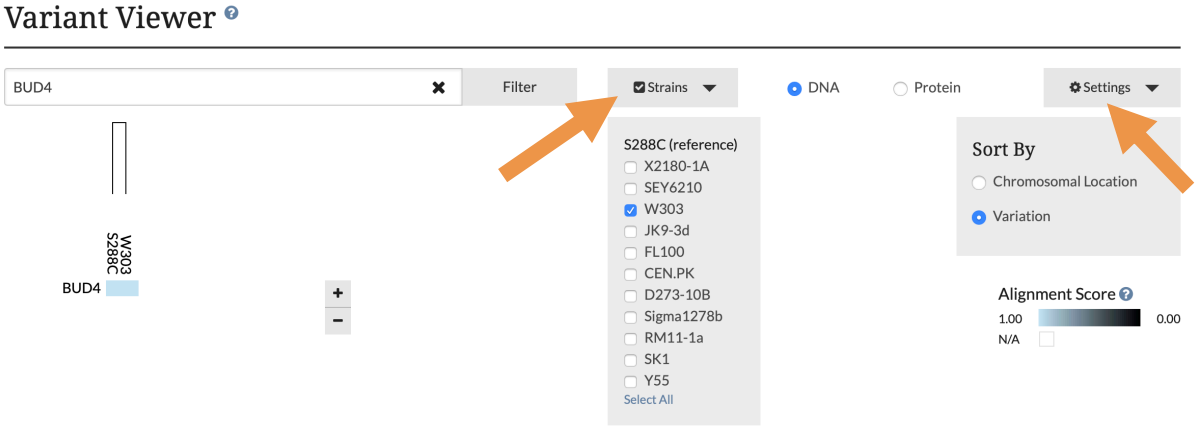
- The **Filter** box accepts a gene name or a list of gene names. Because we are interested in axial budding gene BUD4, search for BUD4 and click Filter.



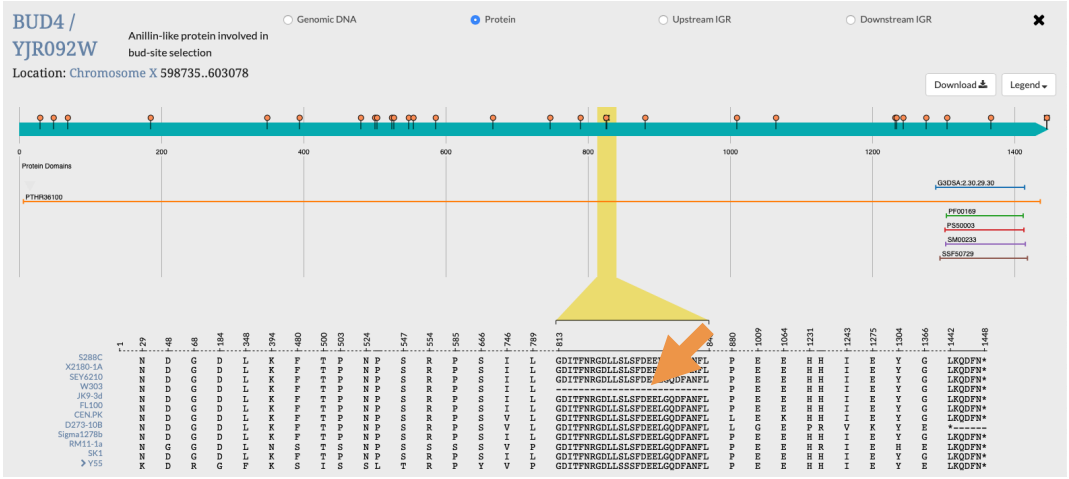
- The **matrix**, shown on the left, will have changed to only include the searched gene(s).
    - This matrix enables you to visualize high-level differences in multiple genes relative to strain S288C. Each square in the matrix corresponds to one of the twelve strains in Variant Viewer, shown at the 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 W303). Open the **Strains** pull-down menu, press Deselect All, then re-select W303.

- 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.



- Click on **BUD4**, and select **Protein**. Scroll with your mouse along the sequence. Find the nucleotide sequence from position 813-840 in the S288C sequence that replaces the in frame deletion in the W303 strain, thus causing the difference in budding phenotypes.



- Now that we have identified that an in-frame deletion affects W303 BUD4, click the BUD4 / YJR092W link to examine the BUD4 locus summary page. From the BUD4 Locus Summary page, you will learn that this is a protein involved in bud-site selection and is required for the axial budding pattern. The deletion from nucleotide position 813-840 is indeed responsible for the inability of W303 to exhibit an axial budding pattern!

Variant Viewer: Sequence Tab

- Variant Viewer is also embedded in the Sequence tab of every gene page, with the data for the gene already pre-loaded from the results of the Variant Viewer search. This allows you to look at the variant information for a gene without starting from the tool's entry page.