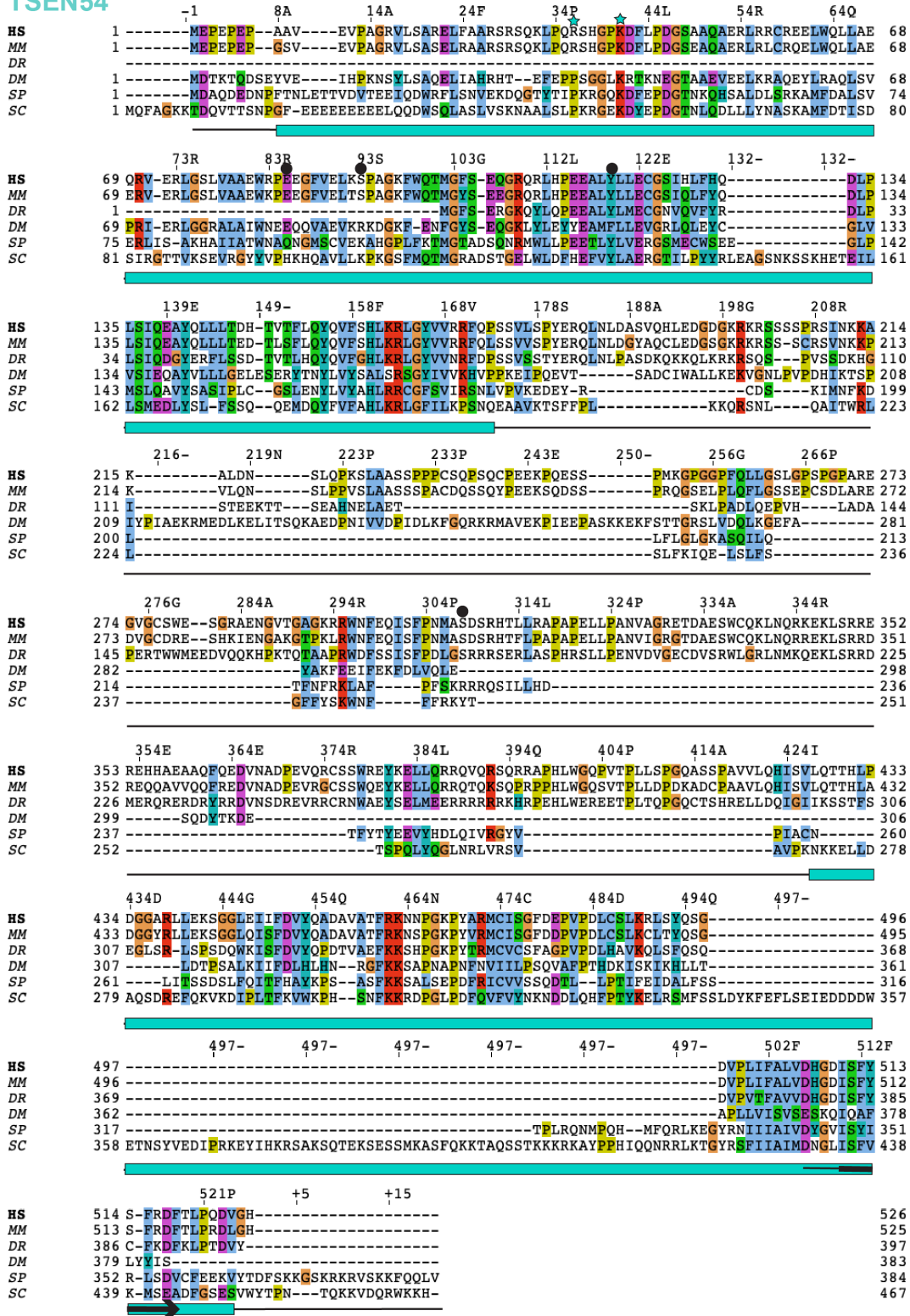
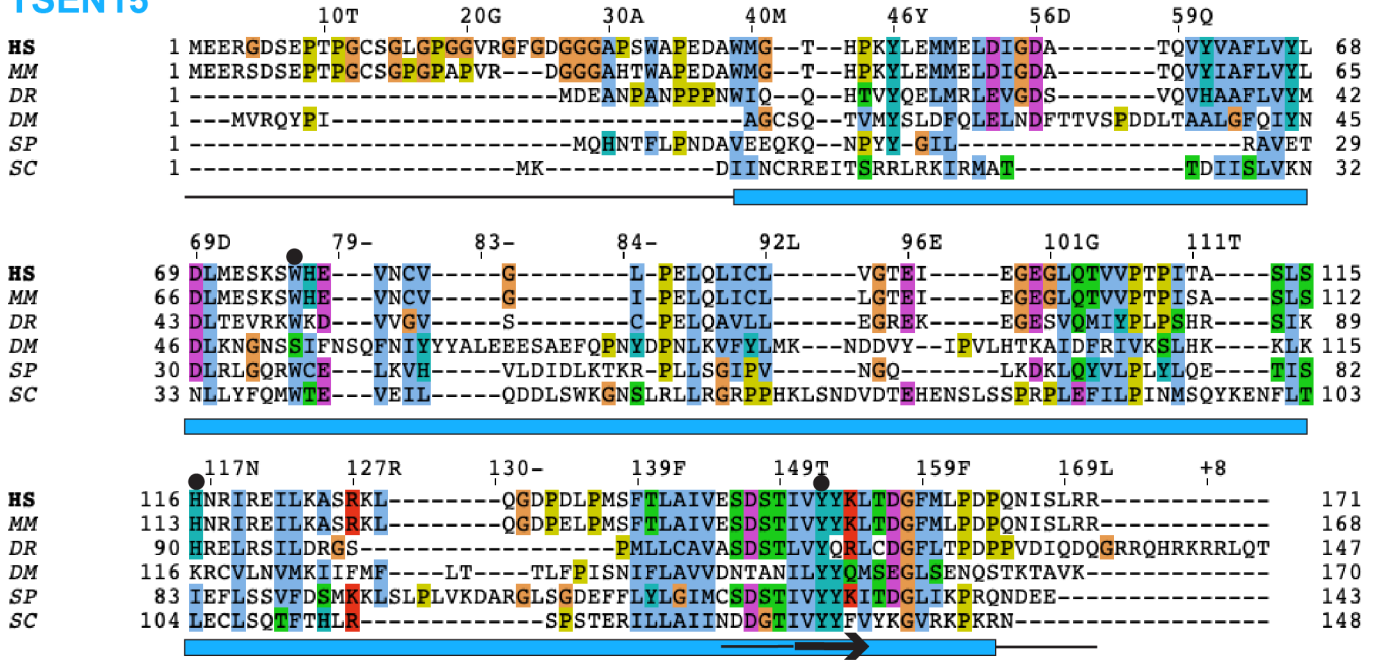


TSEN54



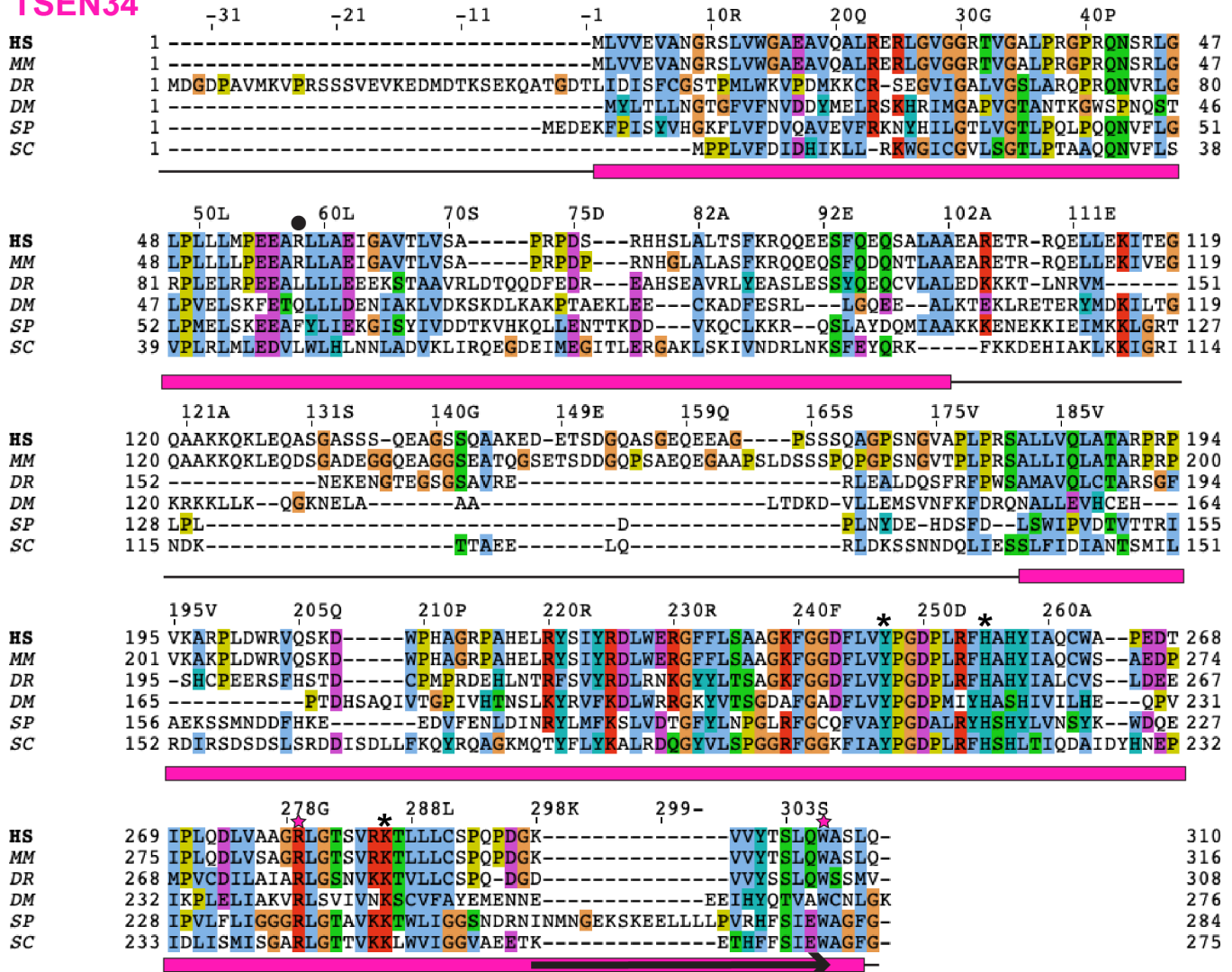
Supplementary Data 1: Eukaryotic TSEN54 alignment. Alignment of TSEN54 protein from *Homo sapiens* (HS), *Mus musculus* (MM), *Danio rerio* (DR), *Drosophila melanogaster* (DM), *Schizosaccharomyces pombe* (SP), and *Saccharomyces cerevisiae* (SC). Under the alignment, the structured regions (teal box) and not observed in the structure (black solid line) are noted. Key features important for the structural integrity of the complex are the conserved β -sheet (509-517, a thick black arrow) and the buried L10 like loop (506-509, thin black line in the structured region). PCH mutations (black circle) and some key residues (R36 and K41, teal star) are also annotated.

TSEN15



Supplementary Data 2: Eukaryotic TSEN15 alignment. Alignment of the TSEN15 proteins from *Homo sapiens* (HS), *Mus musculus* (MM), *Danio rerio* (DR), *Drosophila melanogaster* (DM), *Schizosaccharomyces pombe* (SP), and *Saccharomyces cerevisiae* (SC). Under the alignment is a blue box showing the regions mapped in the structure. Labelled features include the conserved β -sheet (150-155), annotated with a thick black arrow, and the buried L10 like loop (144-150) annotated with a thin line. PCH mutations are indicated by a black circle.

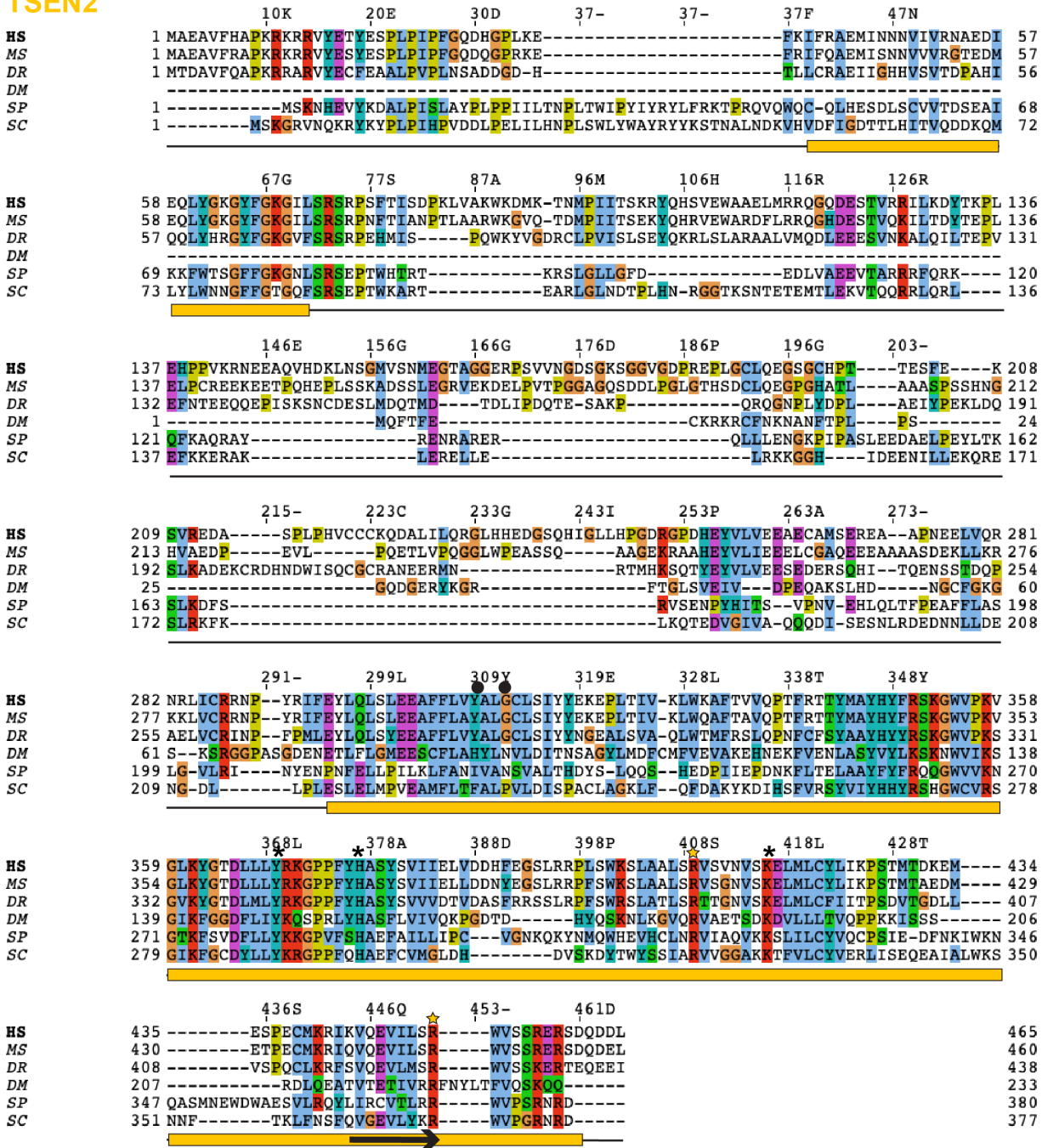
TSEN34



Supplementary Data 3: Eukaryotic TSEN34 alignment.

Alignment of the TSEN34 (3' endonuclease) proteins from *Homo sapiens* (HS), *Mus musculus* (MM), *Danio rerio* (DR), *Drosophila melanogaster* (DM), *Schizosaccharomyces pombe* (SP), and *Saccharomyces cerevisiae* (SC). Labelled conserved features are the β -sheet (298-306) (thick black arrow), and catalytic residues Y247, H255, and K286 (*). The well-established PCH-linked mutation site R58 is annotated (solid black circle) as are the cation- π residues R279 and W306 (pink stars).

TSEN2



Supplementary Data 4: Eukaryotic TSEN2 alignment.

Alignment of the TSEN2 (5' endonuclease) proteins from *Homo sapiens* (HS), *Mus musculus* (MM), *Danio rerio* (DR), *Drosophila melanogaster* (DM), *Schizosaccharomyces pombe* (SP), and *Saccharomyces cerevisiae* (SC). The conserved β -sheet (444-452) (thick black arrow), catalytic residues Y369, H377, and K414 (*), cation- π residues 409 and 452 (orange stars), and two residues known to be mutated in some cases of PCH, Y309 and G312 (black solid circles) are all annotated.