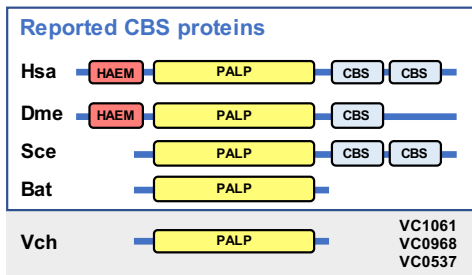
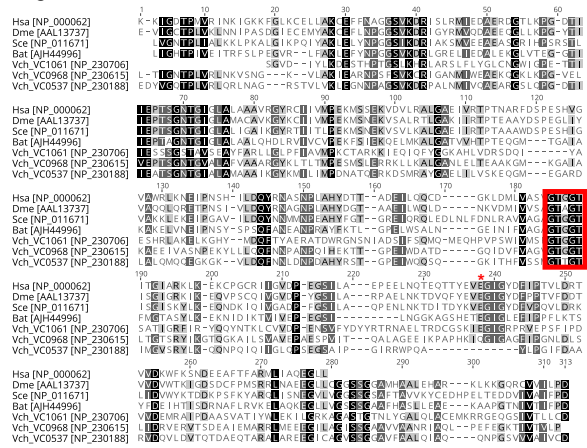


## A. *cbs* candidates

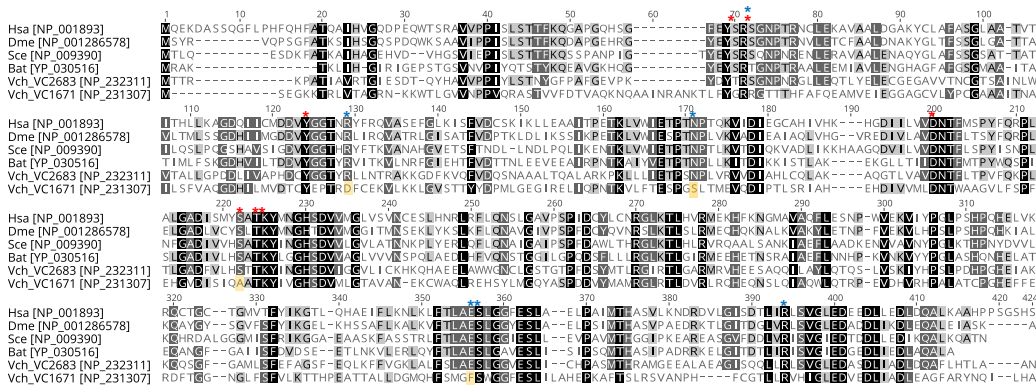


- Hsa: *Homo sapiens*
- Dme: *Drosophila melanogaster*
- Sce: *Saccharomyces cerevisiae* S288C
- Bat: *Bacillus anthracis* str. Sterne
- Vch: *Vibrio cholerae*

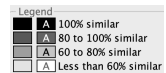
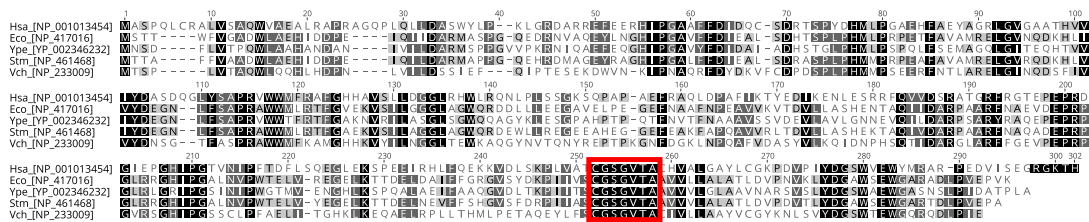
### Alignment for PALP:



## B. *cse* candidates



## C. *3mst* candidates



S1 Fig. Identification of orthologs for H<sub>2</sub>S-producing enzymes in *V. cholerae*.

(A) CBS orthologs. Left panel, domain architectures of CBS proteins are presented. In

CBS proteins, the catalytic core domain PALP (pfam00291) is highly conserved

across phyla [1]. There are three PALP-containing proteins in *V. cholerae*, encoding

by *vc1061*, *vc0968*, and *vc0537*, respectively. Right panel, multiple sequence alignment (MSA) of PALP regions, showing that all the three CBS candidate proteins in *V. cholerae* have the active-site loop residues of CBS (outlined with red) <sup>[1-4]</sup>. However, only VC1061 processes the key site for the function of H<sub>2</sub>S biogenesis reported by Devi et al. 2017 <sup>[1]</sup> (red asterisk).

(B) CSE orthologs. Cys/Met metabolism PLP-dependent domain (Cys\_Met\_Meta\_PP, pfam01053) is the conserved domain in CSE proteins. *V. cholerae* encodes two Cys\_Met\_Meta\_PP enzymes VC2683 and VC1671. Red and blue asterisks indicate key active-site residues in binding with co-factor pyridoxal-5'-phosphate (PLP) and inhibitor DL-propargylglycine (PAG), respectively <sup>[5]</sup>. VC1671 is not a CSE homolog, since it lacks four key active-site residues (shaded with yellow).

(C) 3MST orthologs. Active-site loop residues of 3MST are shown in red <sup>[6]</sup>. Hsa, *Homo sapiens*; Dme, *Drosophila melanogaster*; Sce, *Saccharomyces cerevisiae* S288C; Bat, *Bacillus anthracis* str. Sterne; Eco, *Escherichia coli*; Ype, *Yersinia pestis* CO92; Stm, *Salmonella typhimurium* LT2; Vch, *V. cholerae*.

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