Comparative genomics of prokaryotic succinate:quinone oxidoreductases

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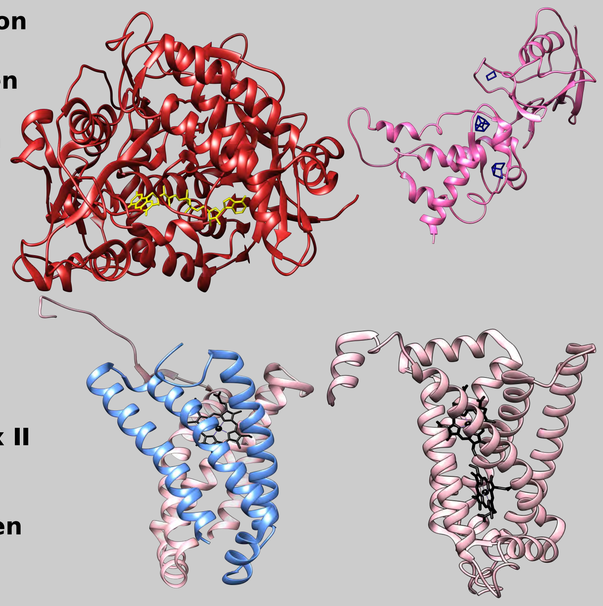
Introduction

Succinate dehydrogenases and fumarate reductases (Complex II, here abbreviated as SDH) catalyze the conversion of succinate to fumarate and vice versa. Complex II has been a focus of research for many years because this conversion is highly conserved in all domains of life, the catalytic subunits of this complex are homologous to a variety of other proteins, and the enzymes are a part of aerobic and anaerobic electron transport chains and the TCA cycle (Hägerhäll 1997). However, research on complex II has been mostly focused on model organisms and mitochondria, and has not been widely analyzed in context of evolution (Jardim-Messeder, et al. 2017). Studying the evolution of this complex's subunits provides insights into the evolution of energy metabolism per se.

Structural characterization of SDH subunits

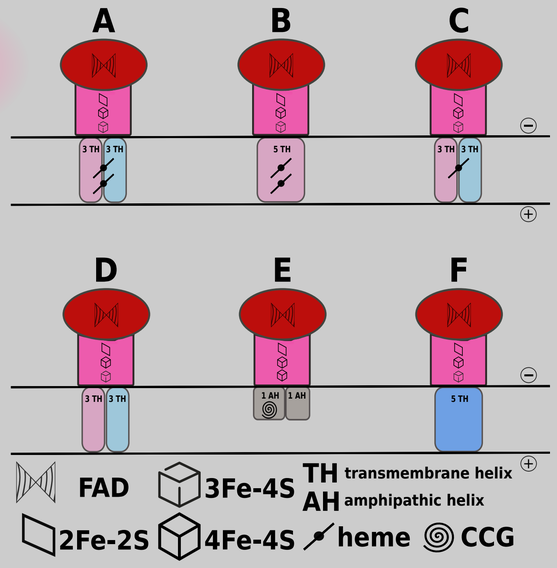


**From top left to bottom right:
subunit A (red, FAD in yellow),
subunit B (hot pink, FeS clusters in dark blue),
subunits C+D of type C and subunit C of type B
(C in light pink, D in light blue, heme in black).
Last figure is type B (W.succinogenes, PDB:2BS2).
Other figures depict type C (E.coli, PDB:1NEK).**

Complex II

Succinate Dehydrogenase | **Fumarate Reductase**

SDH type classification



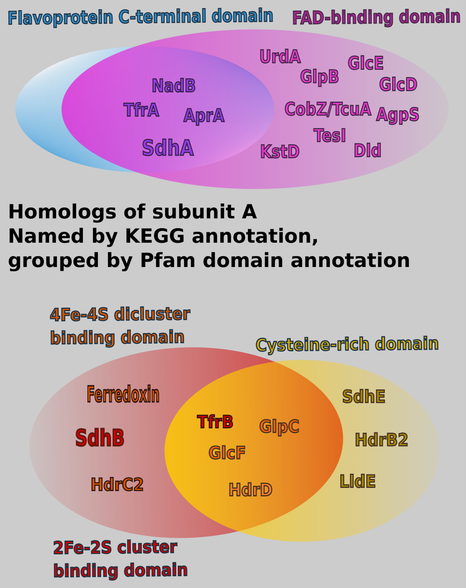
**Each type is shown with its cofactor.
The schemes of membrane subunits include the number and type of helices.
Horizontal lines represent the cytoplasmic membrane.
"-" is cytoplasm, "+" is periplasm.**

**Overall, complex II has an FAD-binding subunit, an iron-sulfur (FeS) cluster subunit, and 1 or 2 membrane anchor subunits that may contain hemes (Lancaster 2002).
These enzymes are currently classified into types A to F (Schäfer et al. 2002; Hägerhäll 1997; Lemos et al. 2001; Hards et al. 2019), based on the structure and cofactor content of anchor subunits.
Using comparative genomics on a large dataset of 35017 genomes, we aim to elucidate the evolution of each subunit of this complex.**

Methods

Results

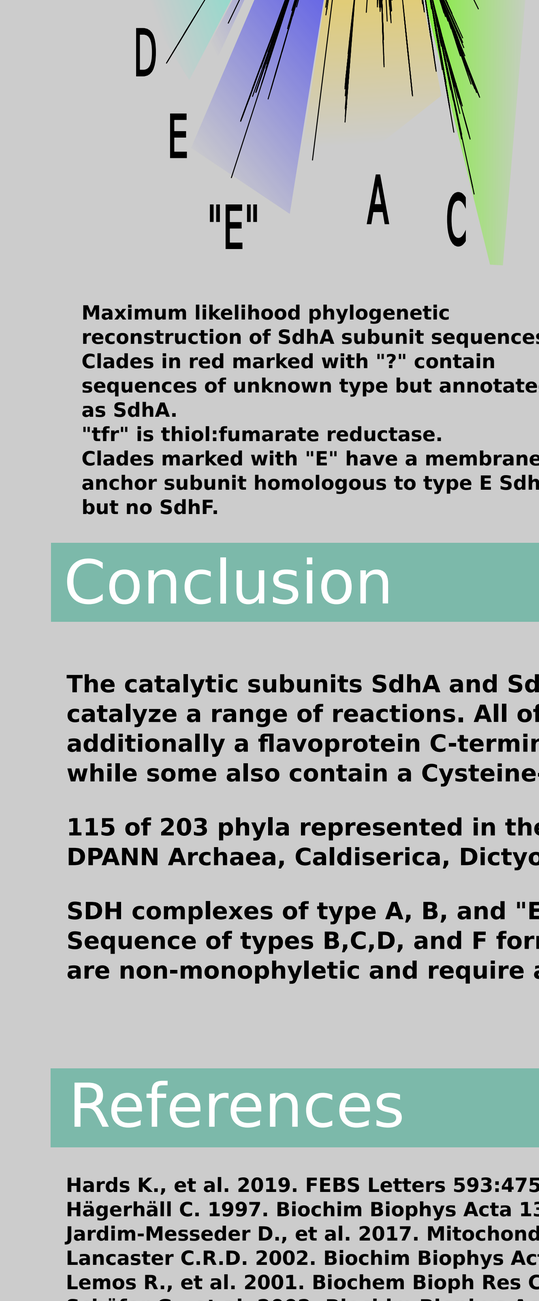
Homology search of SDH



**Homologs of subunit A
Named by KEGG annotation,
grouped by Pfam domain annotation**

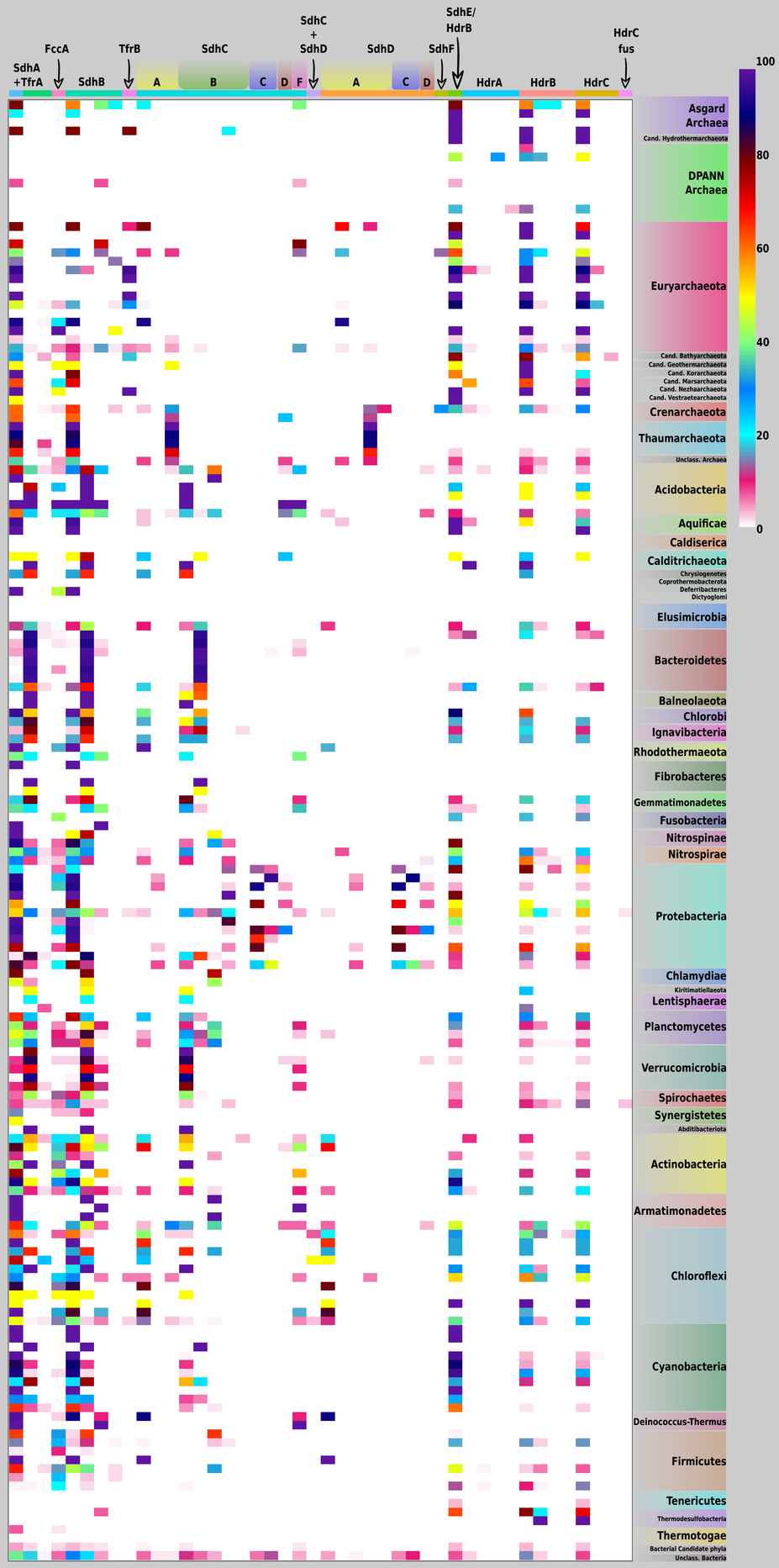
**Homologs of subunit B (and SdhE)
Named by KEGG annotation,
grouped by Pfam domain annotation**

Phylogenetic analysis of SDH



**Maximum likelihood phylogenetic reconstruction of SdhA subunit sequences.
Clades in red marked with "?" contain sequences of unknown type but annotated as SdhA.
"tfr" is thiol:fumarate reductase.
Clades marked with "E" have a membrane anchor subunit homologous to type E SdhE but no SdhF.**

Taxonomic distribution of SDH



**Taxonomic distribution of MCL clusters that contain SDH sequences.
Calculated in percent of genomes from class (order if class unknown, phylum if both unknown) per cluster.
Each cluster is annotated with the subunit and SDH type where applicable.
HdrABC (Heterodisulfide reductase) clusters were kept for SdhE - HdrB differentiation.**

Conclusion

The catalytic subunits SdhA and SdhB have homologous relationships to a diverse group of enzymes that catalyze a range of reactions. All of the SdhA homologs contain an FAD-binding domain, and some additionally a flavoprotein C-terminal domain, similar to SdhA. SdhB homologs contain FeS clusters, while some also contain a Cysteine-rich domain, similarly to the type E membrane subunit.

115 of 203 phyla represented in the dataset contain SDH sequences. No SDH subunits were found in DPANN Archaea, Caldiserica, Dictyoglomi, Tenericutes, and a variety of bacterial Candidate phyla.

SDH complexes of type A, B, and "E" are more widely distributed than complexes of type C, D, E, F. Sequence of types B,C,D, and F form distinct phylogenetic clades, while the ones from types A and "E" are non-monophyletic and require additional analysis.

References

**Hards K., et al. 2019. FEBS Letters 593:475-486
Hägerhäll C. 1997. Biochim Biophys Acta 1320:107-141
Jardim-Messeder D., et al. 2017. Mitochondrion 34:56-66
Lancaster C.R.D. 2002. Biochim Biophys Acta 1553:1-6
Lemos R., et al. 2001. Biochem Bioph Res Comm 281:141-150
Schäfer G., et al. 2002. Biochim Biophys Acta 1552:57-73**

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