

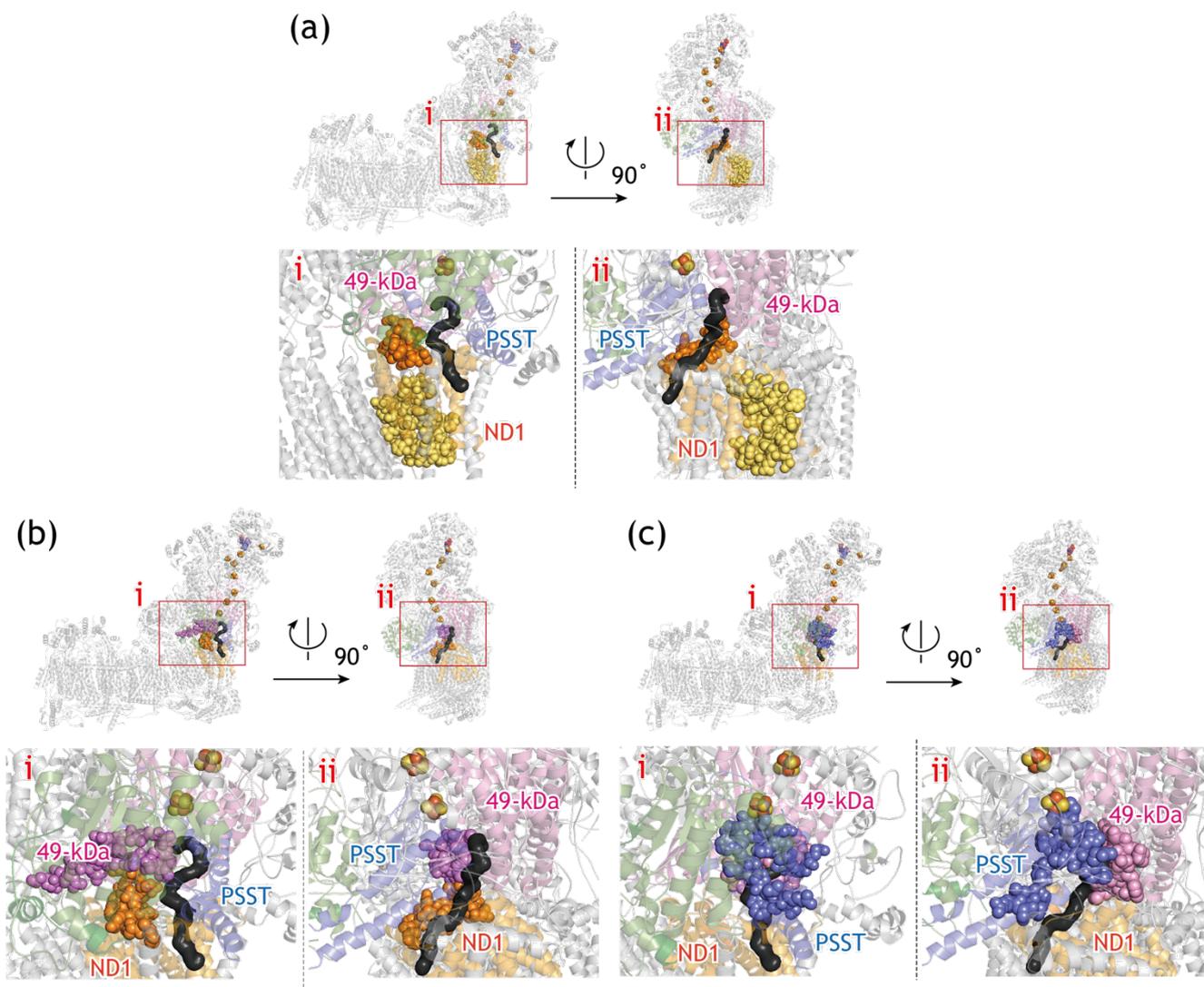
## **SUPPORTING INFORMATION**

### **Exploring the binding pocket of quinone/inhibitors in mitochondrial respiratory complex I by chemical biology approaches**

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Figure S1. Summary of photoaffinity labeling using different quinone-site inhibitors. P. S1

Table S1. Nomenclature of the 14 core subunits of respiratory complex I. P. S2



**Figure S1. Summary of photoaffinity labeling studies using various quinone-site inhibitors.**

The regions labeled by photoreactive inhibitors are shown by spheres in ovine complex I (PDB entry 5LNK). The quinone/inhibitor-access channel is shown in black. (a) The region labeled by photoreactive acetogenins ( $[^{125}\text{I}]\text{TDA}$  and  $[^{125}\text{I}]\text{DANA}$ ): the loop connecting the TMH5-6 and the region spanning TMH4-5 (Val144–Glu192) are shown in orange and yellow spheres, respectively. (b) The region labeled by a photoreactive quinazoline ( $[^{125}\text{I}]\text{AzQ}$ ): the interface between the N-terminal region (Val44–Arg63) in 49 kDa and the matrix side loop connecting the TMH5-6 (Thr201–Ala217) in ND1 are shown in pink and orange spheres, respectively. (c) The region labeled by photoreactive fenpyroximates ( $[^{125}\text{I}]\text{APF}$  and  $[^{125}\text{I}]\text{AIF}$ ): the interface between the PSST (Ser43–Arg66) and 49 kDa (Asp160–Arg174) are shown in blue and pink spheres, respectively.

**Table S1. Nomenclature of the 14 core subunits of respiratory complex I**

Domain	<i>Bos taurus</i> (bovine)	<i>Homo sapiens</i> (human)	<i>Escherichia coli</i>	<i>Thermus thermophilus</i>	Cofactors, transmembrane helices (TMHs), and other comments <sup>a</sup>
<b>Hydrophilic domain</b>	75-kDa	NDUFS1	NuoG	Nqo3	[2Fe-2S], 2 x [4Fe-4S]
	51-kDa	NDUFV1	NuoF	Nqo1	FMN, [4Fe-4S]
	24-kDa	NDUFV2	NuoE	Nqo2	[2Fe-2S]
	49-kDa	NDUFS2	NuoCD	Nqo4	
	30-kDa	NDUFS3		Nqo5	
	TYKY	NDUFS8	NuoI	Nqo9	2 x [4Fe-4S]
	PSST	NDUFS7	NuoB	Nqo6	[4Fe-4S] (N2)
<b>Membrane domain</b>	ND1	ND1	NuoH	Nqo8	8 TMHs <sup>b</sup>
	ND2	ND2	NuoN	Nqo14	11 TMHs <sup>b</sup> , homologous to MrpD <sup>c</sup>
	ND3	ND3	NuoA	Nqo7	3 TMHs
	ND4	ND4	NuoM	Nqo13	14 TMHs, homologous to MrpD <sup>c</sup>
	ND4L	ND4L	NuoK	Nqo11	3 TMHs
	ND5	ND5	NuoL	Nqo12	16 TMHs, homologous to MrpA <sup>c</sup>
	ND6	ND6	NuoJ	Nqo10	5 TMHs

<sup>a</sup> Assignments of cofactors and TMHs are based on the structure of bovine complex I.

<sup>b</sup> One C-terminal TMH in Nqo8 and three N-terminal TMHs in Nqo14 in *T. thermophilus* complex I are missing in mammalian enzyme.

<sup>c</sup> They are evolutionary linked with the subunits of bacterial Mrp-type antiporter.

