Complete Structure of a Bifunctional 11-subunit Membrane Protein Complex from Bovine Heart Mitochondria, the Cytochrome bc1 Complex

Joong W. Lee, J. K. Lee, N. Chan, B. K. Jap
Lawrence Berkeley National Laboratory (LBNL), Berkeley, California, USA

S. Iwata, K. Okada, M. Iwata, and S. Ramaswamy
Uppsala University

The complete structure of the bifunctional membrane protein complex, the 11-subunit bc1 complex (cytochrome c reductase) from bovine heart mitochondria, will be presented for two different space groups which reveal different conformational states.[1] The structure was solved using two different crystal forms: $P6_522$ (a = b = 211 Å, c = 339 Å; asym. unit = bc1 monomer, 11 subunits, 240 kD), and $P6_5$ (a = b = 130 Å, c = 721 Å; asym. unit = bc1 dimer, 22 subunits, 480 kD); these crystals diffract up to 3.0 and 2.8 Å respectively at high-brilliance/low-divergence synchrotron sources which are required to resolve the closely spaced diffraction spots, especially for the long 721 Å axis. The initial MIR phases were determined for the $P6_522$ crystal form at 4-Å resolution; this was followed by multi-crystal averaging to extend the phases out to the current resolution of 3.0 Å. This provided clear, easily fittable densities which afforded a good working model of the complex. The R-factors for the final refined models are 28.5% and 32.0% for the $P6_522$ and $P6_5$ forms respectively. Atomic details for the arrangement of the four redox centers and the two quinone binding sites are well determined for both native and inhibitor-bound crystals, and reveal two different positional states for the Rieske [2Fe-2S] redox active center. These structural details, together with other reported structural work on bc1 complexes,[2,3] suggest an intricate three-state mechanism by which ubiquinol and cytochrome c are oxidized/reduced. Furthermore, the bifunctional nature of this protein complex was revealed by the specific binding of the Rieske mitochondrial targeting presequence to the core protein subunits. This also disclosed the structure-specific recognition requirements for mitochondrial processing peptidases.

———

[1]S. Iwata, J. W. Lee, K. Okada, J. K. Lee, M. Iwata, B. Rasmussen, T. A. Link, S. Ramaswamy, and B. K. Jap. Science, (1998) in press.
[2]D. Xia, C. A. Yu, H. Kim, J. Z. Xian, A. M. Kachurin, L. Zhang, L. Yu, and J. Deisenhofer, Science, 277, 60 (1997).
[3]Z. Zhang, L. S. Huang, V. M. Shulmeister, Y. I. Chi, K. K. Kim, L. W. Hung, A. R. Crofts, E. A. Berry, and S. H. Kim. Nature 392, 677 (1998).