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Preface

Biogenesis/assembly of respiratory enzyme complexes

Recent decades have seen remarkable advances in our understanding of the mechanisms of the major protein complexes of oxidative phosphorylation. Information has poured in from the development of microbial models amenable to site-directed mutagenesis, from a large number of high resolution structures, from established and novel spectroscopic methods and from ever more sophisticated computational tools. An excellent example of the diversity of such information can be found in a recent Special Issue of BBA Bioenergetics on Respiratory Oxidases, edited by Bernd Ludwig. Running in parallel to studies of respiratory complex function is the expanding area of research into how these multi-subunit, integral membrane complexes are assembled. Certainly, the ordered assembly of these multi-subunit complexes, each containing a catalytic core with a variety of redox centers, presents a considerable challenge for the cell. Challenges for the cell are always challenges for researchers seeking to unravel the details of the process. Research of the assembly of the respiratory complexes is younger than that of their function, but it has moved quickly by taking advantage of emerging techniques in molecular and cell biology, protein chemistry and spectroscopy. Moreover, mistakes in assembly can lead to human disease and the analysis of various disease-causing mutant forms of assembly proteins has been instrumental. In the 1980s the Tzagoloff and Poyton groups, and others, found that the assembly of the respiratory complexes in yeast required large numbers of complex-specific gene products. Currently, the specific roles of many of the assembly proteins in mitochondria and in bacteria have been identified or deduced. As expected, they cover a wide range of functions, acting as protein chaperones and translocases, as copper chaperones, as heme synthesis and delivery proteins, as Fe/S center chaperones, as translational activators and more. Three dimensional structures are available for some of the assembly proteins and mechanistic details are beginning to emerge. Even so, there are still assembly factors whose functions have yet to be identified.

This Special Issue on the Biogenesis/Assembly of Respiratory Enzyme Complexes is not intended to be comprehensive, rather it presents a wide-ranging collection of review and research articles that demonstrate the multiplicity of fascinating biological processes involved in the assembly of these energy generating machines, and the diversity of experimental approaches. The issue purposefully brings together studies of both prokaryotic and eukaryotic systems in order to emphasize how the comparison of the two enhances our understanding. Given that mitochondria arose from bacteria, plus the fact that the α proteobacteria, in particular, contain respiratory complexes with high similarity to those of mitochondria, it is not surprising that many of the assembly proteins present in bacteria have been retained in mitochondria. Hence, information gained from studies in bacteria has provided important insights into assembly processes in mitochondria, including human mitochondria, and such translation of information will continue. Nonetheless, bacteria are not mitochondria. Assembly of the respiratory complexes in mitochondria adds complexities, including the involvement of two genomes, the import of most mitochondrial proteins, the lack of direct access to copper and iron in the external environment, a greater number of subunits in each complex and the absence of alternative respiratory complexes with redundant activities. Hence, it is also not surprising that mitochondria contain many more assembly proteins than bacteria and that the assembly processes are more elaborate.

The articles of this Special Issue focus on the assembly of the three proton pumps of oxidative phosphorylation, Complexes I, III and IV, plus key related topics. Articles from the Ryan and Friedrich groups discuss the assembly of eukaryotic and prokaryotic Complex I, respectively; the former with particular attention to information gleaned from disease-causing variants and the latter via systematic disruption of each of the 13 genes for the structural subunits. The Winge group presents an analysis of the assembly of Complex III, and the roles of recently characterized assembly proteins. Barrientos and colleagues have done the same for the catalytic core of mitochondrial cytochrome *c* oxidase (C*c*O). Daldal and colleagues have reviewed the assembly of the prokaryotic cbb_3-type C*c*O, with informative comparisons to the assembly of the aa_3-type C*c*O. The cbb_3-type C*c*O also requires the assembly of *c*-type cytochromes, for which the Kranz group has contributed a novel research article involving two of the three known cytochrome *c* assembly pathways. In further news of Complex IV biogenesis, Lars Hederstedt outlines molecular analyses of heme A biosynthesis, while the Ludwig group provides a detailed analysis of Surf1 function in heme A assembly. Widely variant perspectives on the copper chaperones involved in C*c*O biogenesis are presented by three groups: the plasticity of copper–sulfur clusters (George), a molecular mechanism for copper release from a chaperone (Hill) and the cellular relevance of different combinations of copper chaperones (Hosler). Finally, Luirink et al. present a thorough analysis of the machinery for membrane protein insertion, folding and assembly in prokaryotes.

I am privileged to have been invited by BBA Bioenergetics to guest edit this Special Issue and I am deeply indebted to all of the authors for creating such extraordinary contributions. Special thanks to Sandra Tokashiki of BBA Bioenergetics for having done everything possible to keep the project on schedule.

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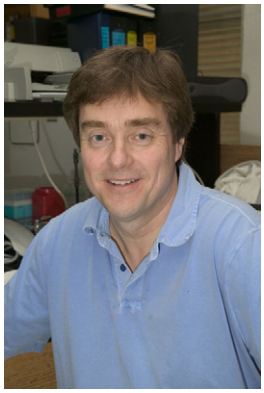

Jonathan Hosler has been a professor of Biochemistry at the University of Mississippi Medical Center since 1995. Hosler received his Ph.D. in 1983 from the University of Michigan, working with Charles Yocum on ferredoxin-mediated energy transduction pathways in chloroplasts. He then moved to Duke University to pursue questions of chloroplast protein synthesis with John Boynton and Nick Gillham, before joining the laboratory of Shelagh Ferguson-Miller at Michigan State University in 1987, where he began studies on the *aa* -type cytochrome *c* oxidase of *Rhodobacter sphaeroides*. His current research interests include the mechanisms of copper center assembly in respiratory oxidases, the process of proton uptake into long-range proton transfer pathways and the effects of antifungal drugs on mitochondrial function.

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