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International workshop on non-mitochondrial cytochromes *c*

A short foreword with some history

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A brief description of the informal workshop on non-mitochondrial cytochromes *c* is given. The organization of the meeting, the personnel participating and the scope of research effort are discussed. A brief historical account is included to place the Symposium reports in context.

Cytochrome *c* as a mediator of coupled electron transport in animal and plant mitochondria has been a focus of attention for biologists concerned with bioenergetics since its discovery by David Keilin during his epochal researches in the mid '20's. Its apparent occurrence in non-mitochondrial systems in bacteria, protozoa and chloroplasts was noted but it was tacitly assumed that such heme proteins did not differ essentially from the unique prototype of cytochromes *c* as a mitochondrial component. Relatively few studies, practically none on isolation and characterization, were reported until a surge of interest developed in the '50's, owing to some discoveries in anaerobic bacterial systems. Thus, in England [1] and Japan [2] sulfate-reducing bacteria were found to contain large quantities of relatively easily soluble *c*-type cytochromes, which were termed 'cytochromes c_3' These findings followed on the discovery of another soluble *c*-type cytochrome, termed 'cytochrome c_2' [3]. Still another anaerobe was added to the list, essentially simultaneously, with the detection and isolation of a *c*-type cytochrome later called 'cytochrome *c*-553' [4].

At the time there were only a few laboratories engaged in research to follow up those discoveries [1] In Japan, a group led by K. Okunuki (the discoverer of cytochrome c_1) included such notable pioneers as T. Horio, K. Yamanaka and I. Sekuzu, among many others.

Also, groups in Nagoya at the laboratories of F. Egami (including R. Sato and S. Taniguchi) and of T. Mori were reporting work on *c*-type cytochromes (including in addition observations of a high-potential non-heme brown protein by T. Hori). However, a systematic effort to probe the nature of variant heme Proteins required a unique combination of skills in microbiology, protein chemistry and structural analytical procedures. Such a situation existed in San Diego, where M. D. Kamen organized researchers to activate an approach which established a basis for comparative biochemistry of *c*-type cytochromes. This laboratory, mainly through the labors of R.G. Bartsch and T.E. Meyer, produced a steady stream of variant *c*-type cytochromes through the following decades which enabled R.P. Ambler and his associates in Edinburgh through determinations of primary structure to propose a working scheme for classification of the many new categories so revealed. The first primary structure of a bacterial cytochrome, that of *Rhodospirillum rubrum* cytochrome c_2, was published in 1968 [5] and its tertiary structure as determined by X-ray diffraction studies [6] is now known.

The widespread notion that heme proteins of the cytochrome *c* type were unique to the mitochondrial respiratory system has been decisively dispelled in the years since the initial discoveries of *c*-type cytochromes in anaerobic systems. Their general function in a wide variety of electron-transport processes with many variations in structure is now firmly established.

In the years which have followed these developments an explosive development of physical biochemistry and molecular biology methodologies has produced a flood of new information as many new workers have flocked to enter the field. The promise of better perceptions of structural bases for the various cytochromes of the *c*-type, and heightened appreciation and insights also

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into mechanisms involving mitochondrial cytochromes *c* now exist. Much of the knowledge gained by study of non-mitochondrial *c*-type cytochromes has been utilized by researchers working on redox mechanisms in mitochondria.

A beginning in compiling and systematizing knowledge in a coherent form was made in 1982 with the appearance of a review by T.E. Meyer and M.D. Kamen [7], although there had been sporadic surveys published previously. The rapid advances in the last few years have been admirably summarized in a two-volume monograph which should be available by the time this issue appears [8]. Many new centers of research on non-mitochondrial systems have sprung up in the last decade and an increasingly accelerated rate of progress in the understanding of electron transport in such systems, as well as in mitochondria, can be anticipated.

It was clear even in 1987 that a meeting to assess studies in the field was urgently needed. This special issue of BBA presents the results, as expressed in minireviews and short papers, and gives some indication of the discussions which took place at the international workshop, organized by M.D. Kamen at the Fogarty Center, National Institutes of Health from July 31 to August 2, 1990. It was possible to assemble a small group of researchers with 'hands-on' experience in isolation and characterization of variant *c*-type cytochromes whose experience covered most of the areas of research now operative. Those who were able to attend were R.G. Bartsch (Arizona), M.A. Cusanovich (Arizona), S.J. Ferguson (Oxford), R.B. Gennis (Illinois), A.B. Hooper (Minnesota), G.O. Hreggvidsson (Edinburgh), H. Iwasaki (Nagoya), R.J. Kassner (Illinois), D.W. Krogmann (Purdue), T.E. Meyer (Arizona), G.R. Moore (East Anglia), J.J.G. Moura (Lisbon), G.W. Pettigrew (Edinburgh), G.M. Smith (UCD), J. Van Beeumen (Ghent), P.C. Weber (Dupont, Delaware), R.J.P. Williams (Oxford), P.M. Wood (Bristol), and T. Yamanaka (Tokyo). R.P. Ambler (Edinburgh), F.R. Salemme (Dupont) and J. LeGall (Georgia) were invited but were unable to attend. Their work was reviewed as needed, thanks to the presence of others familiar with relevant data.

Even this informal workshop required a fair degree of organization. Letters had to be written, programs and a brochure devised, and financial support obtained. The successful prosecution of the meeting was assured by the efforts of Dr. J. Schmidt the Director of the Fogarty Scholars-in-Residence Program who, with his capable staff headed by the Mrs. S. Feldman and R. Singer, saw that all details involved in conducting the meeting were expeditiously handled. A beautiful brochure was produced thanks to the professional skills of Ms. L. Brown and her staff in the Design Section of the support services provided by the NIH. Dr. P. Schambra, Director of the Fogarty Center, provided the help needed financially to make the workshop possible. The support of the Virginia L. Swanson Foundation is also gratefully acknowledged.

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