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Book Review

Mitochondria and Cell Death

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Mitochondria and Cell Death. Edited by GC Brown, DG Nicholls, CE Cooper. Published for the Biochemical Society by Portland Press, London, UK: 1999, Pp. 225, ISBN: 1 85578 1255. £65.00.

Mitochondria, the powerhouses of a cell, have been attracting a lot of attention in the last few years, because evidence has proven that mitochondria play a key role in apoptotic cell death in mammals, by releasing apoptogenic factors during apoptosis, which are otherwise stored safely inside. Apoptosis is also one of the hottest topics in the medical field being filed from a therapeutic application point of view.

The book entitled 'Mitochondria and Cell Death' is published quite timely and covers various aspects of the mitochondrial role in cell death and various neurodegenerative diseases. The book is derived from the annual Symposium organized by the Biochemical Society in 1988 devoted to 'Mitochondria and Cell Death'. The aspects covered by this book are quite extensive: (1) mitochondrial permeability transition; (2) Bcl-2 family, apoptosis regulator; (3) apoptosis and necrosis; (4) neurodegeneration; (5) mitochondrial DNA diseases; (6) free radicals and nitric oxide; and (7) hypoxia/ischemia. One of the purposes of this book is to show clearly the interaction among these multiple phenomena, to understand better the role of mitochondria, apoptosis in neurodegenerative diseases. The several prominent aspects are: Mitochondrial dysfunction may be linked to neurodegenerative diseases including Huntington's disease, Alzheimer's disease, Parkinson's disease and Friedreich's Ataxia. This idea is basically consistent with the notion that the neuronal system utilizes a huge amount of energy. The mitochondrial dysfunction possibly arises through a variety of different pathways, including free-radical generation, impaired calcium buffering, mitochondrial permeability transition and bioenergetic catastrophy, mutations in mitochondrial DNA and mutations in nuclear DNA affecting the mitochondria. For example, inhibition of respiration has been implicated in Parkinson's disease, and respiratory inhibition results in ATP depletion, in turn enhancing glutamate sensitivity that is well known as 'excitotoxicity'. Mitochondria are major cellular sources of reactive oxygen species, and these oxidants can in turn inhibit mitochondrial respiration, induce PT and mutate mitochondrial DNA. Mitochondria are also targets for nitric oxide (NO). NO and its derivative, peroxynitrite ($ONOO^-$), with an ability to inhibit mitochondrial respiration, might contribute to the cytotoxic action of NO. NO-mediated inhibition of respiration of nerve cells results in rapid glutamate release, which may contribute to the neurotoxicicity of NO. A good example of the involvement of radicals in neurodegenerative diseases might be a point mutation in superoxide dismutase gene in amyotrophic lateral sclerosis. It was also shown that the mitochondria undergo permeability transition under various apoptotic conditions such as overloaded Ca^{2+} and oxidants (hypoxia and reperfusion), leading to the release of apoptogenic factors such as cytochrome c (one of caspase-activators) and AIF (nuclear destruction factor). Permeability transition is mediated by the opening of a specific polyprotein channel, called permeability transition pore, the structure and function of which were nicely discussed. Bcl-2 family of proteins, which is the best-characterized critical regulator of apoptosis, targets the permeability transition pore. Apoptosis mechanism is also overviewed, by touching on cytochrome c release, Bcl-2 family, ceramide, and necrosis *versus* apoptosis is also discussed from a bioenergetic point of view, in conjunction with the cell death occurring in tissues. Although it is still to be determined whether apoptosis involves mainly permeability transition, it is an attractive step, to which various pro-cell death stimuli can

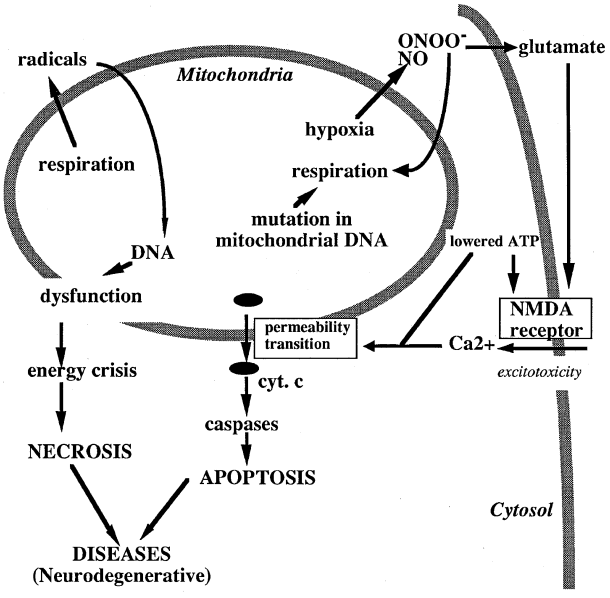

Figure 1

converge, resulting in cell death, one of the causes for various neurodegenerative disorders.

Certainly, various processes described in this book, mitochondrial bioenergetics, permeability transition, Bcl-2 family, apoptosis, necrosis, mitochondrial DNA mutations, free radicals, interact in many ways in the pathology of various neurodegenerative disorders, as shown in Figure 1, and the book will be of a great help to researchers who are interested in the field to get general ideas as well as very updated information, and hopefully stimulate breakthroughs in this field.