

Highlight Issue Guest Editorial

This Highlight Issue focuses on Coenzyme Q. The articles are peer-reviewed minireviews or original papers emanating from the 2nd Conference of the International Coenzyme Q₁₀ Association held in Frankfurt, Germany, on December 1–3, 2000. In a broader sense, that conference represented the eleventh in a series of meetings initiated by Karl Folkers and Yuichi Yamamura in 1976. Sadly, it was also the first of these meetings without Lars Ernster, who contributed so much in his long research career to further the knowledge on different biochemical aspects of Coenzyme Q.

In accordance with the guidelines proposed from the beginning by Karl Folkers, these meetings have endeavored to encourage increased cooperation between basic sciences and medicine in research into Coenzyme Q; the International Coenzyme Q₁₀ Association was founded in 1997 in this spirit. Progress on Coenzyme Q (CoQ) research has been consistent in the past two decades: the classic role of CoQ as a unique carrier for the two-electron transfer within the lipid phase of the mitochondrial membrane, together with its essential function for proton-based energy coupling, has become more deeply understood.

We feel honoured that *Free Radical Research* hosts this series of papers. The role of ubiquinol as inhibitor of the propagation of lipid peroxidation is well established; in addition, ubiquinol can efficiently sustain the antioxidant effect of vitamin E by regenerating the vitamin from the tocopheroxyl radical. Besides its widespread presence in the lipid environment of biological membranes, CoQ is also found in plasma lipoproteins where it exerts its antioxidant protection. Involvement of CoQ in the antioxidant mechanisms protecting low-density lipoproteins from oxidation might be one of the reasons of the anti-atherogenic role of Coenzyme Q₁₀ which has recently been highlighted in ApoE gene knockout mice. Reactivity of ubiquinols but also of ubiquinones towards oxygen and carbon radicals is a field of intensive study. Ubiquinol and ubiquinone analogues have been

shown to regulate the mitochondrial permeability transition pore.

Some basic aspects concerning the mechanisms responsible for extramitochondrial reduction of CoQ are now being clarified. The participation of CoQ in the electron transfer across the plasma membrane is deeply involved with its role in the maintenance of redox signalling of this membrane and in possible prevention of stress-induced apoptosis. CoQ has high synthetic and breakdown rates in all tissues, even in organs where the other mevalonate pathway lipids, cholesterol and dolichol, have a very low turnover. A number of metabolites formed from CoQ may influence apoptosis, down- or up-regulation of CoQ biosynthesis, or other metabolic processes. The ability of CoQ to counteract apoptotic stimuli triggered by different apoptosis transduction signals is also studied. Novel aspects of the antioxidant function of CoQ are currently being investigated at the skin level and in skin surface lipids.

A lowered cellular content of CoQ₁₀ was originally described in some patients affected by heart failure, where the energy-starvation status of the myocardium is supposed to be a dominant feature. This constituted the basis for using CoQ₁₀ as an adjunctive treatment to the conventional therapy in heart disease. In a broader sense, some properties of CoQ₁₀ are investigated as cardiovascular effects, since they may be related to possible interaction of CoQ₁₀ with vascular reactivity and to its antiatherogenic properties.

Defects of the mitochondrial respiratory chain and oxidative phosphorylation have been demonstrated in several neurodegenerative disorders. Some abnormalities of energy metabolism, detectable by NMR techniques, show a pattern which resembles the one seen in some syndromes where free radical-induced damage is involved. Such observation forms the basis for attempting CoQ₁₀ therapy in patients affected by different kinds of mitochondrial dysfunction. In fact, CoQ₁₀ treatment has been shown to significantly improve ATP synthesis in both the skeletal and cardiac muscle of patients affected by

different neurodegenerative disorders. Studies are currently in progress to assess whether this treatment has any disease-modifying effect; from a basal aspect this field offers real possibilities of better understanding the relationship between the classical bioenergetic role and the antioxidant properties of CoQ.

Sincere gratitude is expressed to the following companies which generously contributed to the conference in Frankfurt:

Asahi (Japan), Beiersdorf (Germany), Eisai (Japan), Jarrow Formulas (USA), Kaneka (Japan), Kyowa Hakko (Japan), Mitsubishi (Japan), MS Pharmazeutika (Germany), Nisshin (Japan), Pharma Nord (Denmark).

Gian Paolo Littarru, Ancona
Chairman,
International Coenzyme Q₁₀ Association