HRVATSKA AKADEMIJA ZNANOSTI I UMJETNOSTI
Zavod za kliničku i transplantacijsku imunologiju i molekularnu medicinu u Rijeci

Čast nam je pozvati Vas na predstavljanje prve edicije u izdanju Zavoda

DEBLJINA
JAVNOZDRAVSTVENI PROBLEM I MEDICINSKI IZAZOV

urednik: Daniel Rukavina

četvrtak 27. studenog 2014. u 17,00 sati
Knjižnica Hrvatske akademije znanosti i umjetnosti
Strossmayerov trg 14, Zagreb

P R O G R A M

I. PREDSTAVLJANJE KNJIGE

DEBLJINA
JAVNOZDRAVSTVENI PROBLEM I MEDICINSKI IZAZOV

Urednik: Daniel Rukavina

Zbornik radova sa 2. simpozija HAZU Zavoda za kliničku i transplantacijsku imunologiju i molekularnu medicinu u Rijeci održanog 8. svibnja 2014.

17,00 – 17,50

Uvodna riječ:
Akademik Zvonko Kusić, predsjednik Hrvatske akademije znanosti i umjetnosti

Pozdravna riječ:
Akademik Marko Pećina, tajnik Razreda za medicinske znanosti

O knjizi će govoriti:

Akademik Daniel Rukavina, urednik knjige
Akademik Dragan Dekaris, recenzent
Akademik Željko Reiner, recenzent

17,50 – 18,00 Odmor

II. POZVANO PREDAVANJE / INVITED LECTURE

18,00 – 19,00

Uvod / Introduction: Akademik Daniel Rukavina

Invited lecture:

Giorgio Lenaz, MD., PhD., Professor Emeritus, University of Bologna, Bologna, Italy
„Respiratory supercomplexes: a new challenge for the role of mitochondria in physiology and pathology“

Discussion

GIORGIO LENAZ: Short CV

Born in Padua (Italy) on November 3, 1938.

Medical Degree at the University of Bologna on July 18, 1962, summa cum laude.

"Docent Degree" (libera docenza) in Biochemistry, 1968.

1962 – 1969 Research associate, Institute of Biochemistry, University of Bologna, Italy.

1964 – 1967 On leave for the Institute of Enzyme Research , Univ. of Wisconsin, Madison WI, USA.

1966 – 1967 Assistant Professor, Institute for Enzyme Research, U. Wisconsin, Madison WI, USA.

1969 – 1975 Assistant Professor, Institute of Biochemistry, University of Bologna, Italy.

1975 – 1979 Full Professor of Biochemistry, Medical School, University of Ancona, Italy.

1979 – 1989 Full Professor of Biochemistry, Faculty of Sciences, University of Bologna, Italy.

1989 – 2011 Full Professor of Biochemistry, Medical School, University of Bologna, Italy.

2012 – Professor Emeritus, University of Bologna.

He is author of over 400 publications (>340 of which quoted on Medline since 1963) has been invited as a speaker at over 70 international meetings and is invited author of 25 reviews and 73 chapters of books in the field of Bioenergetics. He has organized some national and international Meetings and has been a member of the executive committee of national and international scientific societies (Italian Biochemical Society, International Coenzyme Q10 Association, President of the Italian Group of Bioenergetics).

His research mainly concerns the structural and functional organization of the respiratory chain in mitochondria, in particular:

- The role of Coenzyme Q in electron transfer
- The presence and function of super-complexes of the respiratory chain, in particular concerning the mechanism of substrate channeling
- Mechanism of electron transfer and production of oxygen radicals by the respiratory chain, in particular by Complex I
- Role of mitochondria in pathological alterations, including cancer, and in aging.

Giorgio Lenaz

RESPIRATORY SUPERCOMPLEXES: A NEW CHALLENGE FOR THE ROLE OF MITOCHONDRIA IN PHYSIOLOGY AND PATHOLOGY

S U M M A R Y

The *electron transfer chain* or *respiratory chain* is a multi-enzyme system that collects reducing equivalents (hydrogen atoms) released from oxidations of intermediary metabolism and conveys them to molecular oxygen reducing it to water. In eukaryotes the respiratory chain is associated to the inner membrane of mitochondria. The energy released by the electron transfer is used to synthesize ATP from ADP and inorganic phosphate (*Oxidative Phosphorylation*). The classic electron transfer chain is the functional sequence of four major multi-subunit complexes designated as NADH-Coenzyme Q reductase (Complex I), succinate-CoQ reductase (Complex II), ubiquinol-cytochrome c reductase (Complex III) and cytochrome c oxidase (Complex IV); the enzyme complexes are connected by two mobile redox-active molecules, i.e. a lipophilic quinone, Coenzyme Q (CoQ), embedded in the membrane lipid bilayer, and a hydrophilic heme protein, cytochrome c (cyt. c), localised on the external surface of the inner membrane.

Contrary to the view of a random organization of the respiratory chain complexes prevailing in the last decades of the past century, evidence has now accumulated that a large proportion of the mitochondrial respiratory chain complexes in a variety of organisms is arranged in supramolecular assemblies called *supercomplexes* or *respirasomes*.

The natural assembly of the respiratory complexes I, III, and IV into supramolecular stoichiometric entities is not just a mere structural feature but has deep functional implications on the properties of the respiratory chain. The most obvious implication is a more efficient way of electron transfer by fixed interactions (*channeling*) rather than by diffusion-mediated collisions of CoQ and cyt. c with the partner enzymes. In addition, supercomplex association enhances the stability of Complex I and limits the generation of reactive oxygen species (ROS) from the respiratory chain.

Supercomplexes have been found to be disrupted during aging and in several disease states accompanied by oxidative stress, such as cardiovascular disease, neurodegenerative diseases, and cancer.

An implication of supercomplex organization as the missing link between oxidative stress and energy loss in disease was first suggested by us: under conditions of oxidative stress a dissociation of supercomplex assemblies occurs, with loss of facilitated electron channeling and resumption of a less efficient random diffusional behavior with electron transfer depending upon the collisional encounters of the free ubiquinone molecules with the partner complexes. Dissociation of supercomplexes has further deleterious consequences, such as disassembly of complex I and III subunits and loss of electron transfer and/or ATP synthesis; the consequent alteration of electron transfer may elicit further induction of ROS generation. These changes may have deep metabolic consequences: an initial enhanced ROS generation due to different possible reasons and originating in different districts of the cell besides mitochondria would induce a catastrophic chain reaction, with supercomplex disorganization leading to decrease of complex I assembly and further ROS generation; both the lack of efficient electron channeling and the loss of complex I would decrease NAD-linked respiration and ATP synthesis and eventually lead to cell death.