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Plasma membrane redox systems

Between March 26 and 29, 2000 approximately 150 participants from more than 30 countries met at the University of Hamburg, Hamburg, Federal Republic of Germany for the 5th International Conference on Plasma Membrane Redox Systems and Their Role in Biological Stress and Disease. This conference continued the series of meetings previously held in Córdoba (Spain) and Antwerp (Belgium) which were dedicated to this topic. A truly multidisciplinary conference, the meeting brought together leading scientists not only from the area of plasma membrane redox but also from ancillary areas of apoptosis, oxidative stress, skin research, and iron metabolism. One of the outstanding features of the meeting was a successful amalgamation and integration of plant, animal, and fungal cell research often alternating in the program. The multidisciplinary character is reflected in the papers of this issue.

The organizers of this conference and the guest editors of this issue would like to thank *Protoplasma*'s editor in chief, D. Menzel, F.-W. Bentrup, and Silvia Schilgerius for their enthusiasm to support this special issue.

The meeting in Hamburg brought out new thrilling aspects of plasma membrane redox function. In many ways it emphasized more precise biochemical definitions of enzymes involved in redox phenomena which had been discussed in previous plasma membrane redox meetings. Functions which had previously been unclear or unrecognized were brought up and expanded. A dramatic entree was provided by Angelo Azzi with his description of a specific ligand-based role of α-tocopherol in control of cell signaling: Its function can easily be related to redox control of gene expression. It remains to be seen if the ligand is associated with the plasma membrane and if α-tocopherol undergoes redox change. The radical introduction was followed by the cytochrome explosion. Both plant and animal plasma membranes have now got cytochromes which are good for something. Except for the low-potential b_{558} cytochromes of neutrophils, the small amount of cytochrome in other plasma membranes originally had little meaning. Thanks in large part to the persistent studies by Han Asard (in this issue), a new aspect of plant membranes was detected: the role of cytochrome b_{561} in ascorbate-based ascorbate radical reduction in plant plasma membranes analogous to the well-known role of cytochrome b_{561} in adrenal chromaffin granules. Furthermore, Beatrix Meier (in this issue) discussed the presence of the low-redox-potential *b* cytochromes in animal plasma membranes other than neutrophils which allow peroxide generation for gene activation. The evidence for an iron site on the outer surface of the membrane and its possible involvement in reduction of oxygen through the quinone-dependent system was reviewed by Hans Löw. Thus we end up with two competing mechanisms for superoxide generation in animal plasma membranes. On the other hand, reduction of hydrogen peroxide by ascorbate peroxidase was shown by Paolo Trost (in this issue). There were several posters on the nature and function of plant cytochrome b_{561} (Paolo Trost, Alajos Berczi, Sabine Lüthje, Wim Verelst, all in this issue). Cytochromes P-450 and b_5 were also discussed and have potential for further development.

The NADPH oxidase of neutrophils was examined in relation to activation by phosphorylation and NADPH binding by Lin Dang. This is a clue to future developments in relation to the homologous superoxide-generating system in fibroblasts (Beatrix Meier) and the iron transport reductase system in plants (Petra Moog).

A new development is control of membrane enzymes by redox in the membrane. A glimpse of this is seen in inhibition of cerimide formation and apoptosis by ubiquinol formation in the plasma membrane (Sergio-Francisco Martin-Gonzalez). Redox control of membrane configuration is ready for more extensive examination.

Enzyme purification and new assay procedures are bringing out the diversity of transplasma membrane

redox systems. Clearly there are pyridine nucleotide dehydrogenases sufficient to accomplish the reduction of quinones, cytochromes, iron, nitrate, and oxygen at the plasma membrane. It appears that the list of transmembrane redox functions has greatly expanded with the introduction of the ascorbate radical-cytochrome b_{561} system and the low-potential cytochrome b_{558} system in addition to quinone-dependent enzymes, the inducible enzymes involved in iron reduction (the old "turbo" system) and nitrate reductase.

A mystery enzyme of great potential importance is the external NADH (or hydroquinone) oxidase, which was discussed by James D. Morré and by Mike Berridge. Its proposed oscillation and oxygen radical generation are possible clues to regulatory functions. Gene expression could be controlled by peroxide production and by the action of this enzyme as a protein disulfide isomerase. The later interaction brings up the possibility of reverse electron transport driving electrons from the redox level of quinone to the level of the cellular sulfhydryl pool. In other words, redox signaling to control protein phosphatases and transcription factors.

The obverse side of peroxide production is: If it gets out of control, it can be a basis for oxidative stress and ageing (Aubrey Grey). Redox-based energy transduction independent of ATP formation is seen in the report by Hans Nohl and Lars Gille (in this issue) on the redox-driven acidification of lysosomes. Is this a clue that part of the proton transport associated with plasma membrane electron transport represents a redox-linked energy transduction? It certainly suggests a redox support for membrane potential. The possibility for redox-driven transport of protons is also apparent in the report by Lydia Henderson (in this issue) on the neutrophil NADPH oxidase combined with the demonstration of the low-potential oxidase in fibroblasts by Beatrix Meier.

The role of the redox systems in regeneration of antioxidants such as ascorbate and α-tocopherol was also brought up. Reduction of coenzyme Q in low-density lipoproteins by thioctic acid was proposed as a basis for maintaining coenzyme Q in the reduced form in blood to protect tocopherol. The antioxidant function in protection of skin was discussed by Karin Schallreuter and the role of thioredoxin was considered. The role of membrane redox systems in regeneration of antioxidants is indicative of an area of major importance.

Several authors discussed mechanisms for cell defense against invading parasites using peroxide production at the plasma membrane (respiratory burst). Przemylsław Wojtaszek (in this issue) gave evidence for two different processes in plants based on external peroxidase or plasma membrane redox.

Control of the plasma membrane redox in plants by blue light was further developed in a poster (Alison Taylor). Posters on control of the inducible iron reductase involved in iron uptake in plants continued the development of this concept. Although one can expect that redox-driven proton translocation will be related to membrane potential and ion transport, there was a notable lack of major developments in control of membrane potential and ion transport – with a number of remarkable exceptions: Tomonori Kawano presented a monoamine oxidase possibly related to Ca^{2+} transport, and Adriana Katz and Uri Pick suggested an Na^{+}-coupled redox system in the halotolerant alga *Dunaliella* sp.

The 13 lectures and 78 posters presented at the meeting provided significant material on diverse aspects of cellular redox functions, much more that can be covered in this short review. As a successor to the previous international plasma membrane redox meetings, this meeting carried on a tradition of interdisciplinary exchange of ideas and recognition of new possibilities. Furthermore, it provided solid material for understanding the mechanisms and significance of plasma membrane redox systems.

The next meeting in the series will be held in 2002 in Bologna and organized by Paolo Trost and Paolo Pupillo.

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