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Conference Report

Redox 2000: The 5th International Conference on Plasma Membrane Redox Systems and Their Role in Biological Stress and Disease

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THE LAST WEEK OF MARCH brought to a cold but only occasionally damp Hamburg almost everyone currently active in plasma membrane (PM) redox biology. As is inevitable for a rather small research community, such gatherings are relatively infrequent (in this case biennial) and are correspondingly unmissable. Our hosts on this occasion were the group of Michael Böttger, a specialist in the role of electron transport in nutrient uptake in maize. I mean "group" in two senses, because Professor Böttger was assisted not only by his official co-organisers, Olaf Döring and Sabine Lüthje, but also by his family, who were constantly on hand at the coffee bar and elsewhere and who contributed greatly to the smooth running of the meeting.

Many more PM redox laboratories worldwide are working with plants than with animals, and this was naturally reflected in the participation in this conference. If we exclude the NADPH oxidase of neutrophils, there has been substantially more success in characterizing plant PM redox systems at the molecular level than their animal counterparts. Plants use PM redox not only for nutrient uptake in roots, but also for several processes above ground; examples which were discussed include the opening and closing of stomata (Alison Taylor), anti-pathogen response (Jörg Durner), and uptake of oxidised ascorbate for intracellular reduction (Nele Horemans). This last function of PM redox systems was also discussed in the context of animal cells, in back-to-back talks by James May and Hans Goldenberg. Among new results reported was a role for nitric oxide in gene regulation of antifungal enzymes, suggesting very ancient origins for signaling by NO in biological systems.

Only one talk centered on the neutrophil NADPH oxidase, but the quantity of such material was well compensated by the quality. Lydia Henderson reported the identification of the proton pathway in the gp91 subunit, which allows electrons to be pumped into the phagosome electroneutrally and without acidification of the phagocyte cytosol. The pathway relies on the action of two critical histidine residues in the *N*-terminal 230 amino acids, which can perform the proton channel function. There was also a fascinating discussion by Przemyslaw Wojtaszek of the oxidative burst in plants. One enzyme involved here is a peroxidase rather than a superoxide generator. We learned in a poster by Fayida Minibayeva that the same enzyme can also exist free in the apoplast space and may generate superoxide there.

Superoxide generation by nonphagocytes was also the topic of the talk by Beatrix Meier. However, this discussion focused not on superoxide's toxicity but on its role in signal transduction. Fibroblasts were demonstrated to generate superoxide when dividing rapidly, especially in arthritic tissue. Moreover, both sub-

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units of the enzyme have been cloned, sequenced, and found to be highly homologous to counterparts in the phagocyte enzyme, despite having different substrate specificity (the fibroblast enzyme being able to oxidise NADH with higher affinity than NADPH).

Extracellular superoxide production is a topic of particular interest to those of us concerned with aging and age-related diseases, since it may mediate many of the underlying molecular degenerative processes. This issue was addressed by Marilyn Merker, whose group have developed a highly elegant *in vivo* model of the control of extracellular oxidative damage by endothelial cells. It has been known for 15 years that endothelial cells can effectively eliminate oxidation of LDL in whole blood (that is, when endogenous levels of antioxidants are present), whereas LDL oxidises rapidly if endothelial cells are not present. Merker used a system of isolation of enzymes from the outer PM surface involving stripping them off by attaching biotin moieties which are then exposed to avidin-coated beads. Proteins isolated in this way were shown to be able to act as NADH-quinone oxidoreductases, using water-soluble quinones with short or zero-length isoprenoid chains. It remains to be shown whether these enzymes can also reduce water-soluble species present *in vivo*, such as dehydroascorbate.

The second day concluded with the conference dinner. The chairman announced at the start of the day's proceedings that the talk by Jim Morré had been scheduled directly prior to the conference dinner, because it was sure to evoke so much discussion, and he was absolutely right. Morré's group have been a mainstay of mammalian PM redox research for many years, and his talk discussed a finding which, if presented by someone of lesser stature, would probably be considered artefactual. As is also reported in the article from Morré's group which appears in this issue of *ARS* (A.D. Peter *et al.*), the two proteins shown by them to be able to oxidize extracellular NADH in favor of oxygen possess a second activity, a protein disulphide isomerase, and alternate between the two activities with a strictly regular periodicity of 24 minutes for the constitutive enzyme and 23 minutes in the case of the tumor-specific one. This has the macroscopic effect of an oscillation in the rate of growth (elongation) of plant cells, but is also readily measured as the rate of consumption of exogenous NADH. Morré made a preliminary report of this finding at the last PM redox conference two years ago, and inevitably encountered widespread skepticism. This time, when he was able to announce a number of advances including the cloning of the tumor-specific enzyme, he was again showered with questions. And just as the chairman had predicted, they continued unabated for the rest of the evening.

A criticism that has been leveled, not always fairly, at the animal PM redox community is that they seem to be taking a very long time to characterize their objects of interest at the molecular level. This period of frustration may be nearing its end, with Morré's success in cloning the tumor-specific surface oxidase being accompanied by the report from Mark Baker, of the Lawen laboratory, that the transmembrane NADH:ferricyanide oxidoreductase of lymphoblastoid cells has been isolated by two-dimensional gel electrophoresis and some internal amino acid sequence obtained, despite its apparent refractoriness to N-terminal sequencing.

As in the past, this conference brought together nearly the entire PM redox community for the first time in two years, and was thus virtually guaranteed to provide numerous novel findings. That it did not only this, but also entertained us in style (including a tour of a museum dedicated to the era of Danish rule of the suburb of Hamburg in which the meeting took place), is a testament to the care which the organizers took in their arrangements. I apologize to those participants whose contributions I have not had the space to summarize here. I will surely be in Bologna in two years for the next in this valuable conference series, and I encourage readers to do the same.

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