Function of Calcium-independent Phospholipase A\textsubscript{2} in Oxidative Stress in Phagocytes

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October 7, 2004

This a transcription of the talk presented on Thursday, October 7, 2004 in Berlin, Germany at the 2nd International Conference on Phospholipase A\textsubscript{2}.

Group VIA calcium-independent phospholipase A\textsubscript{2} (iPLA\textsubscript{2}) has been shown to play a major role in regulating basal phospholipid deacylation reactions in certain cell types. Proposed iPLA\textsubscript{2} roles have rested heavily on the use of bromoenol lactone as a selective iPLA\textsubscript{2} inhibitor, but this compound actually inhibits other enzymes and lipid pathways unrelated to PLA\textsubscript{2}, which makes it difficult to define the contribution of iPLA\textsubscript{2} to specific functions. In previous work we used antisense technology to decrease cellular iPLA\textsubscript{2} activity as an alternative approach to study iPLA\textsubscript{2} functions. In the present study we have prepared U937 cells that exhibit enhanced iPLA\textsubscript{2} activity by stably expressing a plasmid containing iPLA\textsubscript{2} cDNA. Compared with control cells, the iPLA\textsubscript{2}-overexpressing U937 cells show elevated responses to hydrogen peroxide with regard to both arachidonic acid mobilization and incorporation of the fatty acid into phospholipids. Long-term exposure of the cells to hydrogen peroxide results in cell death by apoptosis, and this process is accelerated in the iPLA\textsubscript{2}-overexpressing cells. Increased phospholipid hydrolysis and fatty acid release also occur in these cells. However, abrogation of U937 cell iPLA\textsubscript{2} activity by either MAFP or an antisense oligonucleotide does not delay or decrease the extent of apoptosis induced by hydrogen peroxide. Thus iPLA\textsubscript{2} may actually be dispensable for the apoptotic process to occur.

Work supported by Grants BMC2001-2244 and BFU2004-01886 from the Spanish Ministry of Science and Technology, Grant CSI-4/02 from the Education Department of the Autonomous Government of Castile and León, and Grant 011232 from Fundació La Marató de TV3).
REFERENCES


