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Meeting Report

DATELINE Shanghai

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First International Symposium on Programmed Cell Death
Shanghai, China, September 8–12, 1996.

The meeting, organized by David Scott, Yufang Shi, Yun-Bo Shi, and Yonghua Xu, was the first meeting on this topic to be held in China and was also the first opportunity for many of the international speakers to visit this beautiful, rapidly developing country and discuss apoptosis with Chinese scientists and their students. The organizers should be commended for doing a remarkable job of providing a wonderful mix of excellent science and most gracious hospitality. The meeting had a truly international flavor, with speakers from the U.S., Canada, Great Britain, Japan, China, Taiwan, Singapore and Germany. The quality of the science was quite high, with a series of new developments in apoptosis reported.

The meeting had three general foci: apoptosis in development, apoptosis in the immune system and activation of apoptotic pathways. The developmental studies focused on two systems, amphibian metamorphosis and *Drosophila* development. Yun-Bo Shi presented elegant studies defining the role of matrix metalloprotease activation during thyroid hormone induced apoptosis. Jamsed Tata provided evidence for developmental regulation of thyroid receptors which modulate the sensitivity to thyroid hormone. Shi and colleagues also made the startling observation that the immunosuppressive drug cyclosporin blocks thyroid hormone induced tadpole tail resorption. Similar observations were made by Doug Green and Yufang Shi for cyclosporin and FAS mediated apoptosis in T cells. The molecular basis for this interesting observation, however, remains to be established, Zehei Song reported on the cloning of an ICE-like protease, DCP1 from *Drosophila*. This protease is widely expressed in fly and is of maternal origin. The protease DCP1 induces apoptosis following transfection and appears to be essential for embryonic development.

On the immune front, a series of speakers made important contributions to the meeting. John Ashwell further refined his 'glucocorticoid receptor'/T cell receptor antagonism model, providing new insights on the role of glucocorticoid and positive and negative selection of T cells in the immune system. He also presented data indicating that at least in lymphocytes, jun kinase activation was a response to apoptosis and not a trigger as previously thought. Davis Scott provided convincing data showing that FAS pathways to apoptosis differ in B and T cells. Doug Green and Jeffrey Yen also presented data on myc and apoptosis, but there did not appear a clear consensus among the studies. Scott suggested that loss of myc was associated with apoptosis in B cells. Green suggested that myc regulates FAS, and Yen suggested that myc is essential for cell survival in human erythroleukemic cells. The only thing clear about myc and apoptosis is that it has a remarkable cell specificity. In other studies, Thomas Rothstein presented some elegant work describing B cell resistance to FAS mediated apoptosis. He showed that engagement of B cells by antigen or IL4 treatment generates states of FAS resistance associated with undefined intracellular changes. Alterations in the sensitivity to apoptotic signals are likely to be an area of future intensive investigation.

The meeting had a strong contingent of speakers working on proteases and apoptosis. Barbara Osborne presented evidence for involvement of proteases acting to alter either signal transduction or perhaps to be involved in protease activation. Junying Yuan described her recent work on the Ich-3 knock-out mouse. The animal has properties similar to ICE knock-outs and, interestingly, Ich-3–animals were resistant to LPS induced apoptosis/in septic shock, suggesting Ich-3 likes upstream of ICE. Three speakers, Arnold Greenberg, Chris Bleackley and Pierre Henkart, addressed mechanisms of CTL killing by granzyme B and perforin (death by murder). Greenberg and Bleackley both presented new evidence showing that granzyme B enters targets in the absence of perforin but only translocates to the nucleus in its presence. Bleackley and Henkart also showed that CPP32 inhibitors block DNA damage induced by granzyme B but not membrane effects, as measured by chromium release. These observations suggest that during death by murder, such as in the CTL system, there may be features distinct from classical cell suicide.

Finally in a related topic, Carl Bortner and Francis Hughes provided data on the role of cell shrinkage and ion fluxes during apoptosis. DNA damage was shown to occur only in cells that had shrunken as a consequence of K+ exclusion. Further data were presented showing that K+ concentration inside non-apoptotic cells inhibited nuclease activity in several in vitro systems. These findings suggest that ion movement may be an early necessary event for subsequent apoptotic events.