

## COMMENTARY

This work examines the effect of IFN-gamma treatment and Fas ligation upon the induction of apoptosis in antineoplastic drug-resistant or drug-sensitive cell lines. They show that IFN upregulated Fas antigen expression in KG-1a cells, and that this resulted in an increase in Fas-mediated apoptosis. IFN and anti-Fas were able to induce apoptosis even in drug-resistant cell lines, an effect which was additive when combined with antineoplastic drugs. Interestingly, Bose et al. (1) have shown that daunorubicin-mediated apoptosis involves the production of ceramide; Fas-mediated apoptosis also involves ceramide production (2-4). The observation that drug-resistant cell lines are still susceptible to anti-Fas despite the (presumably) shared ceramide signalling pathway suggests that drug resistance could be bypassed in order to induce apoptosis.

The authors also examine glutathione content (by flow cytometry) and find a dramatic reduction in GSH content in cells treated with anti-Fas antibody, and effect which is synergistically enhanced by the addition of interferon-gamma. One limitation of flow cytometric analysis is that it reflects absolute content of GSH rather than concentration of GSH. Thus, as cells lose volume during the induction of apoptosis, it is possible that the concentration of GSH could remain the same while the absolute content decreases. GSH content is not measured by other methods in this work. However, if the interpretation is correct that GSH is depleted, then the finding is quite interesting, as it suggests that oxidative stress is a feature of Fas-mediated apoptosis. Although the

production of reactive oxygen intermediates is widely recognized to occur in apoptosis mediated by tumor necrosis factor alpha, it has not yet been demonstrated for apoptosis mediated by Fas (5).

## REFERENCES

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