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From the editor

The pursuit of cancer cell death by cancer chemotherapy dates to the earliest observations in the 1940s that mustard gas could shrink lymph nodes and to the synthesis of derivatives such as nitrogen mustard that ultimately found application in the curative therapy of Hodgkin's disease. Other than hormonal or immunologic approaches, the cancer therapies developed in the last four decades of the 20th century were considered cytotoxic therapy, and often, DNA was the chosen target. Simultaneously, study of the molecular biology of the cancer cell advanced, allowing molecularly targeted agents to be the drugs of promise for the 21st century.

This issue of *CCR Focus* explores cell death pathways and strategies aimed at exploiting those pathways as molecular targets. It is dedicated to the late Dr. Stanley Korsmeyer, whose seminal work has led us to understand that aberrations in these pathways are a critical derangement in cancer, is highlighted. With Drs. Edward Benz and David Nathan as guest editors, this issue presents articles by the editors and by Dr. Nika Danial that describe the intrinsic pathway of apoptosis and efforts to restore the cell's ability to initiate programmed cell death. The editors argue that material damage to a cancer cell, even at a critical target, will fail if apoptosis is impaired and that agents activating cell death pathways are needed in combination with conventional therapy. Drs. Greg Verdine and Loren Walensky highlight the difficulties inherent in targeting the anti-apoptotic molecule bcl2, and strategies that have been identified to overcome them. Dr. Ravi K. Amaravadi and Craig Thompson expand this line of discussion to note that cell death occurs along any of three pathways, apoptosis, necrosis, and autophagy, the latter pathway being cytoprotective. To add complexity, any or all three of these pathways may be operating simultaneously in the cancer cell that has been subjected to anticancer therapy. Again, they perceive the need to combine anticancer therapies with agents targeting these pathways. To conclude this issue of *CCR Focus*, Drs. Rixe and Fojo argue that true cytostatic agents do not really exist and that all effective anticancer therapies induce cell death. Taken together, these articles show that cell death pathways are an important target on the way forward.

As with all issues of *CCR Focus*, this feature endeavors to enlighten the interested non-expert, to stimulate the thinking of those working in the field, and to highlight important concepts for future research.

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CCR Focus