

## CONTENTS

# Novel Cytokines for RCC

BY BEVERLY A. CALEY

The human body sometimes produces its own immune response to renal cell carcinoma that results in spontaneous disease remission. (Estimates of the frequency of spontaneous remission vary, but it may occur in as few as 0.08 percent of cases to as many as 7 percent of cases.) Cytokines are proteins produced by the immune system that allow immune system cells to communicate with each other. Researchers are studying numerous cytokines to try to reproduce or enhance this natural response.

For example, in studies in the laboratory and in animals, interleukin-18 (IL-18) showed anti-tumor activity, both as a single agent and in combination with other biologic or chemotherapy agents. A recent phase I study indicates that IL-18 is safe to use in people. The side effects include fevers and chills, which were easily managed and decreased in severity over time, and treatable blood problems and chemical imbalances. Laboratory tests on these patients led researchers to recommend additional studies.

IL-12 is another cytokine that has shown promise in some early human studies, but the response rate in humans has been considerably lower than the rate that was expected, based on the activity of IL-12 in mice and in human cancer cells studied in the laboratory. James Yang, MD, points out that these cytokines are normally part of a complex, multi-component immune network and must function in cooperation with other cytokines and immune cells. A recent phase I study combined IL-12 with low-dose IL-2, and another study combined IL-12 with interferon. Both studies found evidence that IL-12 works better in combination with other cytokines. Yang explains, "We need to explore such strategies to realize their full therapeutic potential. Yet those efforts are severely handicapped by availability, cooperation between companies, and the lack of appropriate flexible oversight regulations."