



Philip M. Farrell, MD, PhD

## Using the power of genetics, genomics and molecular biology to fight cancer

By Philip M. Farrell, MD, PhD

**B**efore his untimely death from a heart attack on February 22, 2002, my friend and colleague Paul Carbone, MD, who served so effectively as long-term director of the University of Wisconsin Comprehensive Cancer Center, convinced me that we are at the beginning of a veritable cancer epidemic among the elderly. Scientists who are aware of this serious problem aren't yet sure how to explain it. It could be that aging immune systems deteriorate, or that, with extended years, multiple carcinogenic factors have the time they need to trigger malignant processes. Paul used to say that since heart disease is no longer killing as many people as before, cancer is now taking over, especially in our growing older population.

At the other end of the age spectrum, we have seen something quite different. We have had the great fortune to witness the reversal of clinical outcomes related to one of the most prevalent, potentially lethal cancers in children—acute leukemia. When I first started out as a young pediatrician in the late 1960s, a diagnosis of leukemia was

like a death sentence for most children. Now we have experienced a night-and-day transformation, with the preponderance of children today surviving the disease (although cancer recurrence remains a risk in these survivors).

Paul Sondel, MD, PhD, head of the Pediatric Hematology/Oncology Division at UW Children's Hospital and the newly named Reed and Carolee Walker Professor in Pediatric Oncology, has been vigorously and productively involved in this reversal. His UW team was one of the initial members of the Children's Oncology Group (COG), which has contributed significantly to more effective cancer treatments and higher cure rates in youngsters. With Dr Sondel serving as immunotherapy leader for the group for many years, COG has enrolled almost half of all childhood cancer patients in the United States in clinical trials, including leukemia drug trials.

We can attribute this remarkable improvement to better treatments stemming from translational research and numerous multi-center clinical trials. But this advance is one of only a handful of success stories in the overall battle against cancer. Cancers of varying kinds continue to challenge researchers around the globe. To achieve even

better results, I believe we must devote more of our attention to the early detection of cancer risk and then take advantage of opportunities to prevent malignancies. In addition, better methods of diagnosing early stages of cancer are sorely needed.

The world-class research program underway in the laboratory of UW Medical School professor William Dove, PhD, the George Streisinger Professor of Experimental Biology at the McArdle Laboratory for Cancer Research and the Laboratory of Genetics, is a prime example, in my mind, of the kind of research that offers the best hope for finding new ways to detect—and prevent and treat—cancer.

The central focus of the Dove team—an interdisciplinary group including basic scientists working with physicians from the UW gastrointestinal clinic—is a mouse model they identified more than a decade ago that contains a genetic mutation rendering the animals susceptible to colon cancer. The gene affected in this "Min mouse" family is very closely related to the major human gene that controls colon cancer, so it clearly points the way to a better understanding of human colon cancer.

The researchers are looking for marker molecules expressed in the

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tumor-bearing animals, hoping to learn whether the molecules can be detected in fecal or serum samples before the tumors proliferate. This has obvious potential for application to early detection of colon cancer in humans.

Dr Dove and his colleagues also have found a gene that offers resistance to intestinal cancer in the Min mouse model, making the colon tumors grow more slowly or less efficiently. The group is expanding its search for additional resistance fac-

tors for colon cancer. We can reasonably imagine that such a modifying gene in humans might be used in gene therapy or as a lead compound for the development of traditional drug therapies.

Dr Dove has spearheaded the Wisconsin Symposia on Human Biology, which are held on campus alternate spring semesters. He and I co-chaired the symposium last spring, titled "From DNA to Molecular Medicine." This gathering of

more than 500 participants had a strong continuing medical education component. So in addition to the many basic and translational scientists who attended the meeting, clinicians from throughout Wisconsin also came to learn about applying the power of genetics, genomics, and biology to their practices. My hope is that we can use the same revolutionary knowledge to find new ways to prevent, detect, and treat human cancers.



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