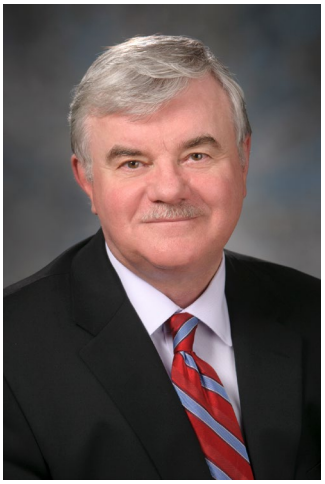
Title: The Origin of Bladder Cancer

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Identifying the mechanisms of cancer initiation is essential for the development of early detection and prevention strategies to intercept carcinogenesis in its occult phases before it progresses to a clinically aggressive and incurable disease. We used bladder cancer as a model for such studies as the simple anatomy of the organ facilitates the mapping of precursor lesions and field effects in microscopically intact adjacent mucosa on the scale of the entire organ. We performed whole-organ mapping of molecular changes in the evolution of human bladder cancer by multi-platform genomic analysis. This approach identified over 100 dysregulated pathways affecting immunity, tissue differentiation, and transformation as early events of bladder carcinogenesis. Extensive dysregulations of interleukin signalling combined with aberrant methylation of HOX genes in a background of multiple activated oncogenic pathways were the dominant features of the field effects. There were three types of mutations based on their geographic distribution and frequencies of variant alleles. The most common were low-frequency mutations restricted to individual mucosal samples. Two additional types of mutations were associated with clonal expansion. The first exhibited low mutational frequencies and the second increased in their frequencies with disease progression. Time modeling showed that bladder cancer evolves over 10-15 years and its development can be divided into dormant and progressive phases. The progressive phase lasted 1-2 years and was driven by a specific subset of mutations involving genes with high proliferative advantage. This is the first comprehensive characterization of bladder cancer evolving from field effects on the whole-organ scale.

Biography

Bogdan Czerniak, MD, PhD, is a Professor of Pathology in the Department of Pathology at The University of Texas MD Anderson Cancer Center, Houston, Texas. He received his MD, PhD from the Pomeranian Medical Academy in Szczecin, Poland in 1973 and 1976 respectively. In 1982-1984 he was an NIH Fellow at Montefiore Medical Center in New York. Since 1993, he has been working at The University of Texas MD Anderson Cancer Center. His laboratory conducts research on mechanisms of bladder cancer development with a focus of early incipient events of urothelial carcinogenesis.

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Category: **Keynote Lecture**