EDITORIAL

The Nobel Prize; An Exclamation Point For Urologic Practice

The Nobel Prize in physiology or medicine is arguably the apogee of medical scientific achievement. Alfred Nobel, a Swedish chemist, engineer and inventor amassed a fortune during his lifetime and provided funds for the prize that bears his name. The original Nobel Prizes in physics, chemistry, physiology or medicine, literature and peace were first awarded in 1901.

In 1968, Sweden's central bank, the Sveriges Risbank provided funds to the Nobel Foundation to support a prize in economics. The first Nobel Prize in Economics was awarded in 1969. Throughout the slightly more than a century of physiology or medicine awards, the scientific subjects have been wide-ranging. However, on four occasions, individuals were recognized for work that would directly impact urologic practice. These were Charles B. Huggins in 1966, Andrew Schally and Roger Guillemin in 1977, Joseph E. Murray in 1990 and Joseph P. Allison and Tasuku Honjo in 2018.

Charles B. Huggins was born in Canada and graduated from Acadia University and Harvard Medical School. As a urologist at the University of Chicago, he demonstrated the relationship between androgens and prostate function. He further demonstrated the beneficial effect of androgen ablation on metastatic prostate cancer.[1] He published his early findings in the first issue of Cancer Research.[2] The work of Huggins introduced an entire era of prostate cancer treatment in urologic practice starting with simple bilateral orchiectomies, followed by oral estrogen therapy and then anti-androgens.

Andrew Schally was born in Poland in 1926 and following World War II, he moved to Canada and received his doctorate from McGill in 1957. He continued his professional career primarily at Tulane University. Roger Guillemin was born in France in 1924 and received his M.D. from the Medical Faculty at Lyon in 1949 and a PHD from the Universite de Montreal in 1953. He then moved to the Baylor College of Medicine and eventually the Salk Institute.

Schally and Guillemin were scientific rivals and separately discovered the structures of TRH (thyrotropin releasing factor) and GnRH (gonadotropin releasing hormone). Schally and Guillemin were jointly awarded the Nobel Prize in 1977 "for their discoveries concerning the peptide hormone production of the brain" along with Rosalyn Yalow "for development of radioimmunoassays of peptide hormones." The discovery of Schally and Guillemin introduced a generation of GnRH agonists and antagonists that have been used to achieve chemical castration in the treatment of prostate cancer.

Joseph E. Murray was born in 1919 in Milford, Massachusetts and graduated from Holy Cross College and Harvard Medical School. On December 23, 1954, he, along with J. Hartwell Harrison and the rest of the renal transplant team, performed the first successful human kidney transplant between identical twins at Peter Bent Brigham Hospital in Boston. Murray was awarded the Nobel Prize in physiology and medicine in 1990. Aside from serving as the practical underpinning for the era of transplant surgery that would occupy the last half of the 20th century, Murray's work continues as the foundation for both renal transplants and donor nephrectomies that represent a major component of urologic training and practice.

In 2018, James P. Allison and Tasuku Honjo were jointly awarded the Nobel Prize in physiology and medicine "for their discovery of cancer therapy by the inhibition of negative immune regulation". Allison was born in Alice, Texas and received his B.S. and PHD from the University of Texas, Austin. Most of his professional career was spent at M.D. Anderson Medical Center. He identified the CTLA-4 protein. Tasuku Honjo was born in Kyoto in 1942 and received his M.D. in 1966 and his PHD from the Faculty of Medicine, Kyoto University. He received part of his postgraduate training at the National Institutes of Health, Bethesda, Maryland. He identified the programmed cell death protein (PD-1).

The clinical implications of the identification of the immune checkpoint inhibitors, CTLA-4, PD-1 and PD-L1 and their potential roles in cancer therapy cannot be overstated. For decades, cancer therapy has been limited to "cut, burn or poison"[3] whereby surgery, radiation or chemotherapy would treat cancer, but would also unavoidably damage healthy tissue as well. Now, for the first time, the foundation of anti-CTLA-4, PD-1 and PD-L1 drugs aim at the manipulation of the body's immune system rather than directly treating the cancer cell. These immune checkpoint inhibitors are in various stages of development. Some have been approved for clinical use, some are in ongoing phase 3 investigations and some are in the pharmaceutical developmental pipeline.

It is hard to imagine the practice of clinical urology today without the underpinning of androgen ablation in the treatment of prostate cancer or the management of donor nephrectomies, renal transplants and their sequelae. It is always treacherous to predict the future of clinical progress, but given the fundamental changes that occurred in urologic practice due to the discoveries acknowledged by the Nobel committees in 1966, 1977 and 1990, it is neither naïve or reckless to speculate that the Nobel Prize in physiology or medicine in 2020 signals a watershed moment in oncological treatment. Only the future will answer what will be the full impact of checkpoint inhibitors on the management of urologic cancer. However, there is every reason to believe that 2020 will signal a new era in urologic cancer care and will serve as an exclamation point for the practice of clinical urology.

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