

## A Noble Nobel

I was seeing patients in clinic on October 7th when I learned that the 2019 Nobel Prize in Physiology or Medicine had been awarded to Dr Gregg Semenza, Sir Peter Ratcliffe, and Dr William Kaelin Jr—three scientists who led seminal studies that described how cells sense and adapt to changing oxygen availability. I was floored, not by the fact that this work warranted such an honor—it unfolded over more than two decades and has tremendous implications in medicine, from oncology to kidney disease. No, I was floored because I knew this work so well, and in particular one of the researchers, Bill Kaelin.

I first met Bill in 1998 when I arrived at the Dana-Farber Cancer Institute as an instructor in medicine and joined the genitourinary oncology group under Dr Philip Kantoff. At the time, I was interested in signal transduction (this was before the days of imatinib) and kidney cancer. The outlook for kidney cancer was so bleak that I remember an older colleague in oncology asking me why I would ever want to specialize in it. I was undeterred, however. I had read about VEGF and was excited to work with Dr Kaelin, who had recently elucidated much of the elegant biochemistry of how the VHL protein regulated intracellular oxygen levels at the protein level. Biallelic loss of VHL function is central to kidney cancer carcinogenesis, progression, and VEGF overexpression in clear cell kidney cancer. This biology eventually translated to the approval of several VEGF signal transduction inhibitors for advanced kidney cancer. As for me, what I learned from Bill Kaelin was one of the most important lessons of my career.

After completing two years of laboratory-based training at Johns Hopkins, I came to Dana-Farber and signed up to work part-time in the Kaelin Laboratory. It quickly became apparent that I was not committed or accomplished enough to work there. Bill took me aside and told me flat-out that the lab was not for me. At that point he could have released me back to clinic to see patients, but he did not. We discussed my interests, skills, and opportunities and decided I should focus on the clinical translation of his work. Bill introduced me to collaborators at Novartis and gave me an opportunity to lead a phase 1 study of a first-in-class VEGF tyrosine kinase inhibitor. Although that certainly would have been more than enough assistance, he didn't stop there. Bill kept in touch with me throughout the study, wanting to learn details regarding everything from patient tolerance to clinical efficacy and correlative studies. His genuine

interest in the translation of his discoveries into treatments is something he modeled for me that I have never forgotten.

This study and Bill's mentorship did not contribute to his later Nobel Prize, but they did contribute mightily to my career and indirectly to the many people I have since influenced. Mentorship will probably never be recognized by the Nobel Committee, but to me it is perhaps one of the most important contributions we can make to our field. In case I haven't said it enough, thank you, Bill, for all you have done.

Although most advances do not qualify for Nobel Prizes, our field continues to progress. This issue of *Clinical Advances in Hematology & Oncology* includes an interview with Dr Hope Rugo of the UCSF Helen Diller Family Comprehensive Cancer Center on the treatment of early-stage hormone receptor-positive breast cancer. We also address the topic of cognitive impairment among men with prostate cancer, in an interview with Dr Charles Ryan of the University of Minnesota. Dr Margaret Kasner of the Kimmel Cancer Center at Thomas Jefferson University discusses outpatient administration of liposomal daunorubicin and cytarabine in patients with secondary acute myeloid leukemia, and Dr David Hong of the University of Texas MD Anderson Cancer Center addresses the targeting of the *KRAS* G12C mutation in patients with advanced solid tumors.

Moving on to our review articles, Drs Max Mendez-Lopez, Tabea Sutter, Christoph Driessen, and Lenka Besse of the Cantonal Hospital St Gallen in Switzerland describe the latest research on the use of HIV protease inhibitors for the treatment of multiple myeloma. Finally, Drs Raetasha Dabney, Mustapha Khalife, Kamran Shahid, and Alexandria Phan from the University of Texas Health Science Center at Tyler review the importance of molecular pathways and targeted therapy in cholangiocarcinoma.

Whether our contributions to medicine include laboratory research, clinical trials, patient care, or all of the above, we all need inspiring colleagues and mentors—even if they can't all be Nobel Prize winners.

Sincerely,



Daniel J. George, MD

