Meeting Report

A Tribute to George F. Vande Woude, a Man of Character:
2006 Scientific Symposium Winning the War against Cancer: From Genomics to Bedside and Back

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In April 2006, the American Academy of Arts and Sciences announced the election of new Fellows and Foreign Honorary Members to its illustrious roster. Included among the honored were former Presidents of the United States George H.W. Bush and Bill Clinton, Supreme Court Chief Justice John Roberts, and Dr. George F. Vande Woude. Although he may not have achieved the same level of public recognition, Dr. Vande Woude is no less deserving of the accolades. Well known to Cancer Research readers as a former director of the ABL-Basic Research Program at the National Cancer Institute (NCI), a member of the National Academy of Sciences, and the founding Director of the Van Andel Research Institute, but also as an outstanding scientist, Dr. Vande Woude has made significant and substantial contributions to our current understanding of the molecular biology of cancer.

Dr. Vande Woude began his career as a retrovirologist. Early on, George used newly emerging recombinant DNA technology to isolate integrated forms of acute transforming retroviruses and compare their oncogenes to cellular proto-oncogenes. His laboratory isolated and determined the sequence of proviral long terminal repeats (LTR) and showed the enhancer function of the LTR promoter, showing its usefulness as an expression vector in eukaryotic cells. In 1981, he further showed that the LTR of the Moloney sarcoma virus provirus covalently linked to c-mos was sufficient to transform mammalian cells. This ability of proviral LTR to activate the transforming potential of c-mos suggested that viral LTR-like elements could activate other normal cell sequences with oncogenic potential.

Later, Dr. Vande Woude’s laboratory showed that the c-mos oncogene normally functions during oocyte maturation and plays an essential role for entry into cell cycle arrest at metaphase II. These novel observations provided a fresh perspective on meiotic cell cycle regulation and some of the first clues to the molecular basis of cancer.

In the early 1980s, Dr. Vande Woude’s laboratory discovered the human MET oncogene, a member of the tyrosine kinase growth factor receptor family that is ubiquitously expressed in mammalian tissues. His laboratory also discovered that the Met ligand is a hepatocyte growth factor (HGF), providing the context for the importance of this ligand-receptor pair in the mitogenic, morphogenic, and morphogenetic behavior of epithelial cells. His laboratory was the first to show that inappropriate Met expression occurs in human tumors and that cells inappropriately expressing HGF/Met autocrine signaling display potent metastatic activity in vivo. Based in large part on work published by his laboratory, we now know that inappropriate Met signaling is involved in most types of human cancers and that Met expression often correlates with poor prognosis.

Through the course of his 40-year scientific career, Dr. Vande Woude has mentored more than 70 postdoctoral fellows, students, and visiting scientists. His laboratory has published over 300 research articles that have been referenced on more than 8,500 occasions. Remarkably, he provides no indication that his pace will ever slacken. On the contrary, and like his favorite oncogenes, Dr. Vande Woude is constitutively active and continues his research on the molecular basis of cancer, focusing on the properties of oncogene activation, tumor growth, invasion, and metastasis.

For these reasons and on the occasion of his 70th birthday, Dr. Vande Woude was celebrated in the 2006 Scientific Symposium Winning the War against Cancer: From Genomics to Bedside and Back, held September 10 to 12, 2006 at the Van Andel Research Institute in Grand Rapids, Michigan. The meeting drew more than 250 participants from the Americas, Europe, and Asia.

The lasting themes of Dr. Vande Woude’s research were reflected in the outstanding scientific presentations from 25 leading cancer scientists.

Protein Kinases and Cell Cycle Progression

Dr. Vande Woude’s laboratory defined the role of the oncogene mos in vertebrate meiosis, helping to establish the key roles of protein kinases in cell cycle progression and development. Tony Hunter (The Salk Institute, La Jolla, CA) presented an engaging retrospective on his discovery of tyrosine phosphorylation and related his more recent findings on the role of Raf1 in cell movement and acini formation in ducal carcinoma in situ. Highlighting the role of receptor tyrosine kinases in tumorigenesis, Morag Park (McGill University, Montreal, Quebec, Canada) discussed how mutations that block CBL-mediated ubiquitylation of Met can alter its half-life and activity. Tony Pawson (Mt. Sinai Research Institute, Toronto, Ontario, Canada) showed how the modular structure of proteins allows the creation of novel signaling molecules using oncogenic chimeric proteins as an example. Talks by Tim Hunt (Clare Hall Laboratories, Herts, United Kingdom), Jim Maller (University of Colorado, Denver, CO), and Martine Roussel (St. Jude Children’s Research Hospital, Memphis, TN) outlined current efforts to identify key substrates of master cell cycle regulatory complexes.

p53, Genome Integrity, and Cell Death

Dr. Vande Woude was among the first to describe the effects of loss of p53 function on centrosome duplication and genomic instability. Loss of p53 tumor suppressor function is now recognized as an important early step in tumor progression.

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Reinforcing this, Arnold Levine (Cancer Institute of New Jersey, Princeton, NJ) described the roles of single nucleotide polymorphisms in MDM2 and p53 in tumorigenesis and how these polymorphisms influence tumor phenotype. Karen Vousden (Beatson Institute for Cancer Research, Bearsden, United Kingdom) provided an intriguing discussion about strategies to reactivate p53 through inhibition of MDM2. Paul Marks (Memorial Sloan-Kettering Cancer Center, New York, NY) showed how inhibition of histone deacetylation causes tumor growth arrest and decreased angiogenesis in vivo. David Livingston (Dana-Farber Cancer Institute, Boston, MA) presented exciting data on the binding protein of BRCA2, PALB2, and its functions through interaction with BRCA2 and its role in Fanconi anemia. Craig Thompson (University of Pennsylvania, Philadelphia, PA) described different aspects of cancer cell metabolism, their functions in cancer, and how one can target cancer cell metabolism to suppress cancer growth. Steve Hughes (NCI, Frederick, MD) elegantly showed how HIV type I reverse transcriptase is able to develop resistance to nucleoside analogues. Suzanne Cory (Walter and Eliza Hall Institute, Parkville, Victoria, Australia) and Joan Brugge (Harvard Medical School, Boston, MA) described the involvement of Bcl-2 family proteins in B-cell malignancies and breast cancer models, respectively. Jerry Adams (Walter and Eliza Hall Institute) described how BH3-only proteins interact with prosurvival proteins and trigger apoptosis. Michael Dean (NCI, Frederick, MD) discussed the importance of ABC transporters in detoxification of stem cells.

Animal Models of Cancer

Reflecting Dr. Vande Woude’s interest in developing robust models of Met-mediated tumorigenesis, much attention was given to discussion about new animal models of cancer. Michael Bishop (University of California, San Francisco, CA) outlined how new mouse models for liver and breast cancer can provide clues to improved prognostics and illuminate issues in therapeutics. Bill Muller (McGill University) showed that endogenous models of breast cancer, in which active ErbB2 is knocked in, provide a better model of ductal carcinoma in situ than do ectopic models, in which HER2 is expressed under the control of the mouse mammary tumor virus promoter. Finally, Anton Berns (Netherlands Cancer Institute, Amsterdam, the Netherlands) presented results from an interesting study, in which he did insertional mutagenesis on mice having p53 and p19ARF null backgrounds to identify genes that promote tumorigenesis.

New Directions

It would not be a stretch to describe Dr. Vande Woude as a visionary scientist and several compelling talks picked up on this theme, shining a light on new paths to discovery. Janet Rowley (University of Chicago, Chicago, IL) described the 98% of DNA to which no known function has been attributed as our “dark matter,” and challenged her audience to take a more global approach to analyzing signaling pathways as they set out on this new frontier of discovery. Phil Sharp’s (Massachusetts Institute of Technology, Cambridge, MA) talk explored the new world of microRNAs, which associate with as many as 50 to 100 mRNAs and regulate their expression. James Allison (Memorial Sloan-Kettering Cancer Institute, New York, NY), the meeting’s self-described sacrificial immunologist, asked why, if an immune system can reject a transplanted kidney or heart, it cannot reject a tumor? This simple question set him on an interesting investigational journey that led to novel approaches to strengthen T-cell response for the treatment of cancer. Finally, Ed Harlow (Harvard Medical School), Lou Staudt (NCI, Bethesda, MD), and Bruce Ponder (Cancer Research UK, Cambridge, United Kingdom) each described imaginative high-throughput screens to identify novel associations between genes and human disease.

The Life of the Party

Dr. Vande Woude is known as much for his science as he is for his youthful exuberance and joy of life, so the Symposium would not have been complete without a party or two. On the first evening, a special reception was held for Tony Hunter and Tony Pawson as they were jointly presented the 2005 Daniel Nathans Memorial Award in recognition of their landmark studies on protein modification and its role in intracellular signaling. This award was established by the Van Andel Institute in 2000 to recognize individuals who emulate the contributions made by the late Daniel Nathans, a founding member of its Scientific Advisory Board, to biomedical and cancer research. Prior recipients include Richard Klausner, Francis Collins, Larry Einhorn, Robert Weinberg, and Brian Druker.

The next evening, a long line of associates took turns, “roasting” their 70-year-young friend at a gala banquet. Those Cancer Research readers who know Dr. Vande Woude can easily envision the sorts of barbed tributes he received. For the minority who has not yet met this “man of character,” we leave you with your imaginations and the following key words: bear hugs, The Picture of Dorian Gray, and shotguns. The rest is up to you.
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