David Kaul, MD: Assessing prostate cancer growth with mRNA of spermine metabolic enzymes

Statistical data from prostate cancer (PCa) clinics indicates that a large patient population discovered by annual prostate specific antigen (PSA) screening may have a latent form of the disease. However, current medical tests cannot differentiate slow from fast growing PCa, resulting in many unnecessary radical treatments and morbidities. It is thus necessary to find new screening tests that enable us to differentiate between fast- and slow-growing tumors. Inspired by the reported functions of spermine in carcinogenesis, we analyzed spermine and mRNA expression levels of rate-limiting enzymes in the spermine metabolic pathway for nine cases of PCa with accurately defined PSA velocity (Vpsa). Using MR spectroscopy, histopathology, laser-capture microdissection and real-time PCR techniques, we analyzed relationships between changes in spermine levels, mRNA expression levels of spermine anabolic and catabolic enzymes and human prostate cancer growth rates represented by serum Vpsa. The expression levels of spermine anabolic enzymes: ornithine decarboxylase (ODC1) and S-adenosylmethionine decarboxylase (AMD1) in benign epithelia surrounding cancer glands was logarithmically reduced with the increase of Vpsa (ODC1, $p < 0.016$; AMD1, $p < 0.048$), and antizyme (OAZ1) expression in cancer cells was increased with the increase of Vpsa ($p < 0.001$). Finally, we observed an inverse correlation between ODC1 and OAZ1 ($p < 0.019$) measured in cancer cells. These correlations may function to evaluate the aggressiveness of human prostate cancer, and assist patients and clinicians to select appropriate treatment strategies based on biological activities of individual tumors.