Androgen receptor and its coactivators in prostate cancer

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A major obstacle in the treatment of prostate cancer is the development of androgen-independent disease. We have recently shown that Lef1, a transcription factor activated by WNT signaling, induced expression of the AR gene in androgen-independent prostate cancer cell line, and consequently enhanced cell proliferation and invasion. This suggests that inhibition of Lef1 by blocking WNT signaling may represent a new therapeutic approach in combating androgen-independent prostate cancer. While the majority of studies on AR focus on its action in epithelial cells, we are also examining the function of AR in prostate stromal cells. We have shown, using an epithelial-stromal cell coculture system, that AR expression in stromal cells inhibits prostate epithelial cell growth and invasion. We also found that androgen ablation prevented AR in the stroma from suppressing epithelial growth and invasion. Therefore, the lack of stromal AR signaling may, in turn, facilitate the survival, growth, and invasion of a sub-population of the epithelial prostate cancer cells, eventually leading to androgen-independence.

In addition to changes in AR expression, alterations in the level or splicing of AR coactivators could also contribute to androgen-independent prostate cancer cell proliferation. Taken together, our findings lend new insights into the development of androgen-independent prostate cancer and could lead to the development of novel therapies against the disease.

Biography

Dr. Lee is Professor in the Department of Pathology and Urology at New York University School of Medicine and Director of Molecular Pathology at New York Harbor Healthcare System and co-Director of Genetic Program, Center of Excellence of NYU Urological Disease. He obtained his MD degree from Beijing Medical University (Peking University, School of Medicine) and PhD from SUNY Downstate Medical Center. Dr. Lee was trained as a postdoctoral fellow with Dr. Robert Roeder at the Rockefeller University. Following his residency in Pathology at NYU Medical Center, he completed a Surgical/Oncologic Pathology fellowship at the University of Texas, M. D. Anderson Cancer Center. He is a specialized in Surgical, Oncologic, Genitourinary and Molecular Pathology. Dr. Lee is on editorial board for several peer reviewed journals.

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