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## Semenogelin I as an androgen receptor coactivator is a novel molecular target for the treatment of prostate cancer

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A seminal plasma protein, semenogelin I (SgI), contributes to sperm clotting, upon binding to Zn<sup>2+</sup>, and can be proteolyzed by prostate-specific antigen (PSA), resulting in release of the trapped spermatozoa after ejaculation. In contrast, the role of SgI in the development and progression of any types of malignancies remains largely unknown. Immunohistochemistry in radical prostatectomy specimens revealed overexpression of SgI in prostatic carcinoma, which was significantly correlated with biochemical recurrence after the surgery. In prostate cancer LNCaP cells, zinc treatment was found to enhance SgI expression. Using prostate cancer cell lines stably expressing SgI, we further investigated its biological functions, in conjunction with zinc (that could generally inhibit cell growth) and androgen/androgen receptor (AR) (that could generally promote cell growth). SgI overexpression resulted in significant increases in AR-positive cell proliferation and PSA expression. Luciferase reporter gene assay showed even slight inhibitory effects of SgI in the absence of zinc versus its significant stimulatory effects in the presence of high levels of zinc on dihydrotestosterone-enhanced AR transactivation. Co-immunoprecipitation then demonstrated dihydrotestosterone-induced physical interactions between AR and SgI. These results suggest that SgI, together with zinc, functions as an AR coactivator and thereby promotes androgen-mediated prostate cancer progression. Additionally, as seen in some of other steroid hormone receptor co-regulators, the LxxLL motif (L=leucine; x=any amino acids) present in SgI appeared to be essential and sufficient for mediating the interaction with AR. Our findings may thus provide a new therapeutic target for androgen-sensitive prostate canceras well as castration-resistant tumor.

### **Biography**

Hiroshi Miyamoto, MD, PhD, is an American board-certified pathologist and is currently an Associate Professor of Pathology and Urology at Johns Hopkins University School of Medicine. He completed his medical school and urology residency training, followed by clinical urology practice, all in Japan. In 1996, he moved to the United States to conduct postdoctoral research. He then completed pathology residency training at University of Rochester Medical Center and clinical fellowship in genitourinary pathology at the Johns Hopkins Hospital. Since 2009, he, as an independent investigator, has been conducting research projects involving molecular biology of steroid hormone receptors in genitourinary tumors.

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