Interactions Between Vitamin D and Androgen Receptor Signaling in Prostate Cancer Cells

Nancy L. Weigel, Ph.D.
Professor, Molecular and Cellular Biology
Baylor College of Medicine

Prostate cancer is an androgen dependent disease and androgen blockade is the primary treatment for metastatic prostate cancer. However, the tumors become resistant and additional therapies are needed. There is good evidence that vitamin D reduces risk for prostate cancer. The active metabolite of vitamin D, 1,25-dihydroxyvitamin D_3 (1,25D), inhibits the growth of many prostate cancer cell lines although the extent to which growth is inhibited varies from line to line. A report by Zhao et al. (Zhao et al. [1997] *Endocrinology* 138:3290–3298) showed that the growth inhibitory effects of 1,25D in the androgen dependent prostate cancer cell line, LNCaP, were reduced by treatment with the androgen receptor antagonist, Casodex, although Casodex has some growth inhibitory actions of its own.

We sought to determine whether this response was a general phenomenon in prostate cancer cell lines as well as to determine the basis for this differential action. We found that other cells derived from the LNCaP lineage showed the same response, but two other independently derived AR containing cell lines (LAPC-4 and 22RV1) did not. In an analysis of 1,25D action in LNCaP cells, we found that an androgen-induced gene that inhibits cell growth (AS3/APRIN) was also induced by 1,25D. Moreover, Casodex reduced induction by 1,25D. In contrast, AS3 is not induced by either androgens or 1,25D in 22RV1 cells and there is no Casodex reversal of 1,25D mediated growth inhibition. The LNCaP lineage is more responsive to 1,25D than are most other prostate cancer cell lines. Thus, there appear to be both androgen dependent and androgen independent actions of 1,25D that contribute to growth inhibition in prostate cancer cells.