

OVERVIEW

Chemoprevention Strategies

The medical management of prostate cancer was fundamentally changed by the observations of Huggins and Hodges in 1941 [1] demonstrating that androgen deprivation caused tumor regression. Despite the importance of this finding, complete cure of the disease is not common due to the frequent emergence of hormone refractory cells. Recognizing the limitations of medical therapy and the natural history of the disease, attention has now turned to strategies for prevention. Chemoprevention, or the use of chemical agents to prevent the development or growth of prostate cancer, represents one such strategy.

In the papers to follow, several approaches to chemoprevention are outlined. The first paper, by Dr. Isaacs, outlines the importance of androgens in the process of carcinogenesis and the unique role of dihydrotestosterone (DHT) as the major intraprostatic androgen. The potential use of 5α -reductase inhibitors for chemoprevention is introduced. The paper by Dr. Geller expands on the potential use of 5α -reductase inhibitors by comparing the intraprostatic levels of testosterone and DHT in human prostate tissue from patients with untreated benign prostatic hyperplasia and patients with prostate cancer treated with either

surgical castration or a 5α -reductase inhibitor. The paper by Dr. Gormley completes the rationale for the use of 5α -reductase inhibitors by providing clinical data from recent studies on the safety and efficacy of one such inhibitor. This is followed by Dr. Fair's paper suggesting a role for neoadjuvant hormonal therapy prior to prostatectomy as a means of decreasing post-operative recurrence.

In his paper, Dr. Kadman presents evidence that difluoromethylornithine (DFMO) can prevent the development of prostate cancer in a unique animal model. Finally, Dr. Logothetis describes the inhibition of prostatic neural peptides as a chemoprevention strategy.

REFERENCES

1. Huggins C, Hodges C: Studies on prostate cancer. *Cancer Res* 1:293-297, 1941.

Glenn J. Gormley, M.D., Ph.D.
Merck, Sharp & Dohme
Research Laboratories
Iselin, NJ 08830