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## Frank French

### *Cancer Cell Biology*

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Cancer of the prostate (CaP) is initially dependent on androgen for growth. Androgen stimulation of growth is mediated by an androgen receptor (AR) stimulated gene network. CaP regresses following androgen deprivation therapy, but eventually its growth recurs in the absence of testicular androgen. We are working with a human CaP xenograft, CWR-22, that retains these properties including dependence on androgen for growth and recurrence of growth several months following removal of testicular

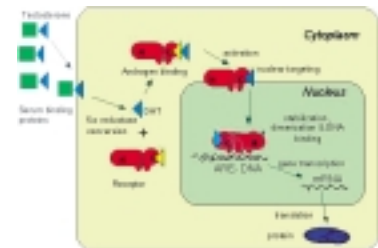
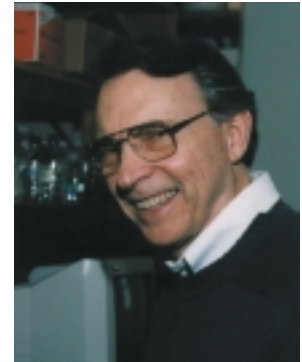
androgen by castration of tumor bearing male mice. AR expression in the recurrent tumor is equal to that in the androgen dependent tumor. We found that expression of androgen regulated genes in CWR-22 decreases following androgen deprivation but increases in association with tumor recurrence in the absence of testicular androgen. This novel observation in the recurrent tumor suggested that either the AR is reactivated in an androgen independent manner or expression of the network of androgen regulated genes is upregulated by a mechanism unrelated to AR. Current work in our laboratory is to further define the network of androgen regulated growth promoting genes and to identify the mechanism that stimulates expression of this gene network in recurrent CaP. Experiments are designed to prevent AR expression in the recurrent tumor using an anti-AR specific ribozyme. Further evidence in support of androgen-independent activation of AR will lead us to focus on the mechanism of this activation.

#### REFERENCES

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Mechanism of androgen action  
(schematic diagram by Catherine S. Choong M.D.)