



MAYO CLINIC

Hormone Refractory Prostate Cancer

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11. P. Red
in 51. Acetamin

820 C
Fis
20

last prot.
Thurs 3/10

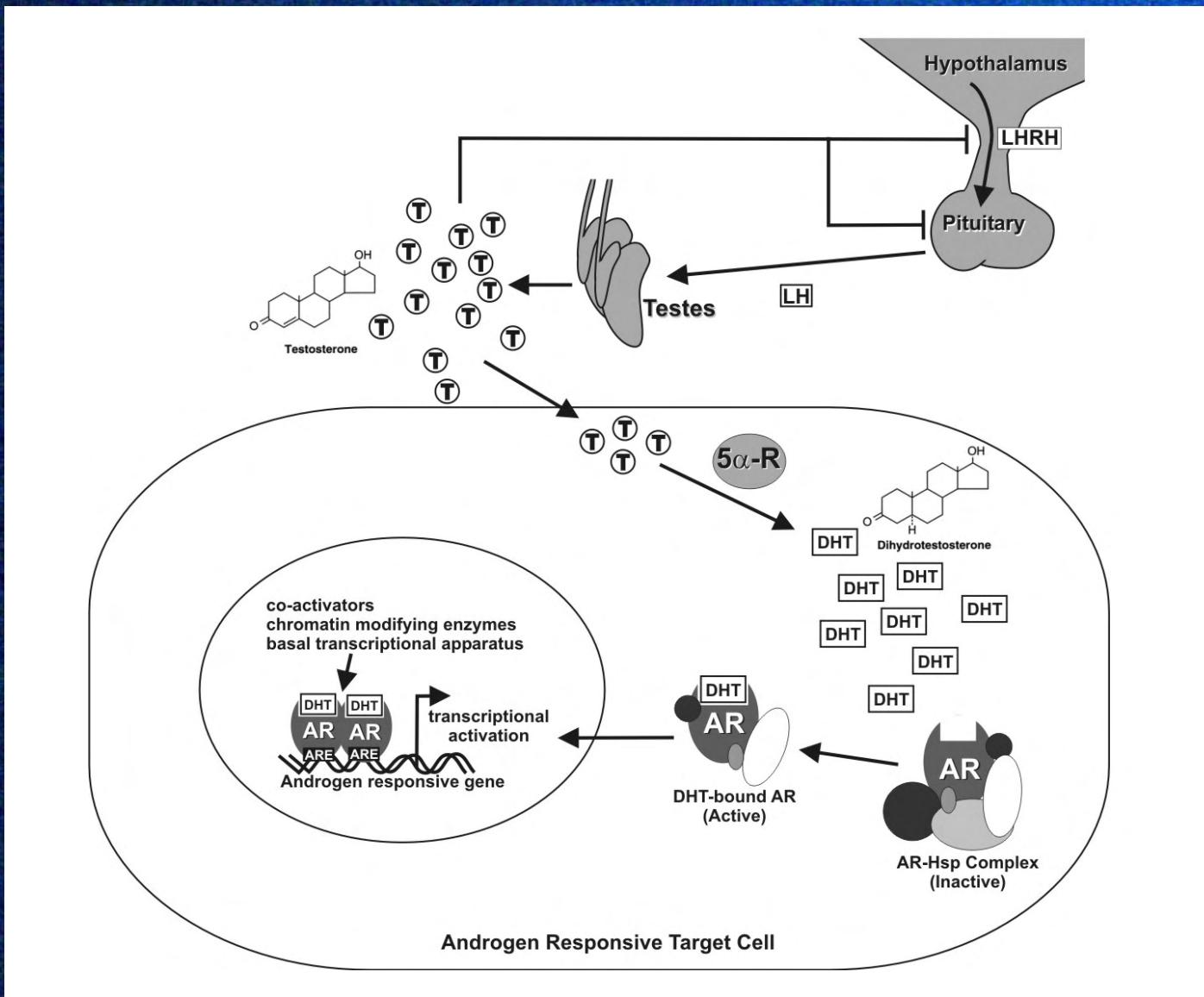
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2A

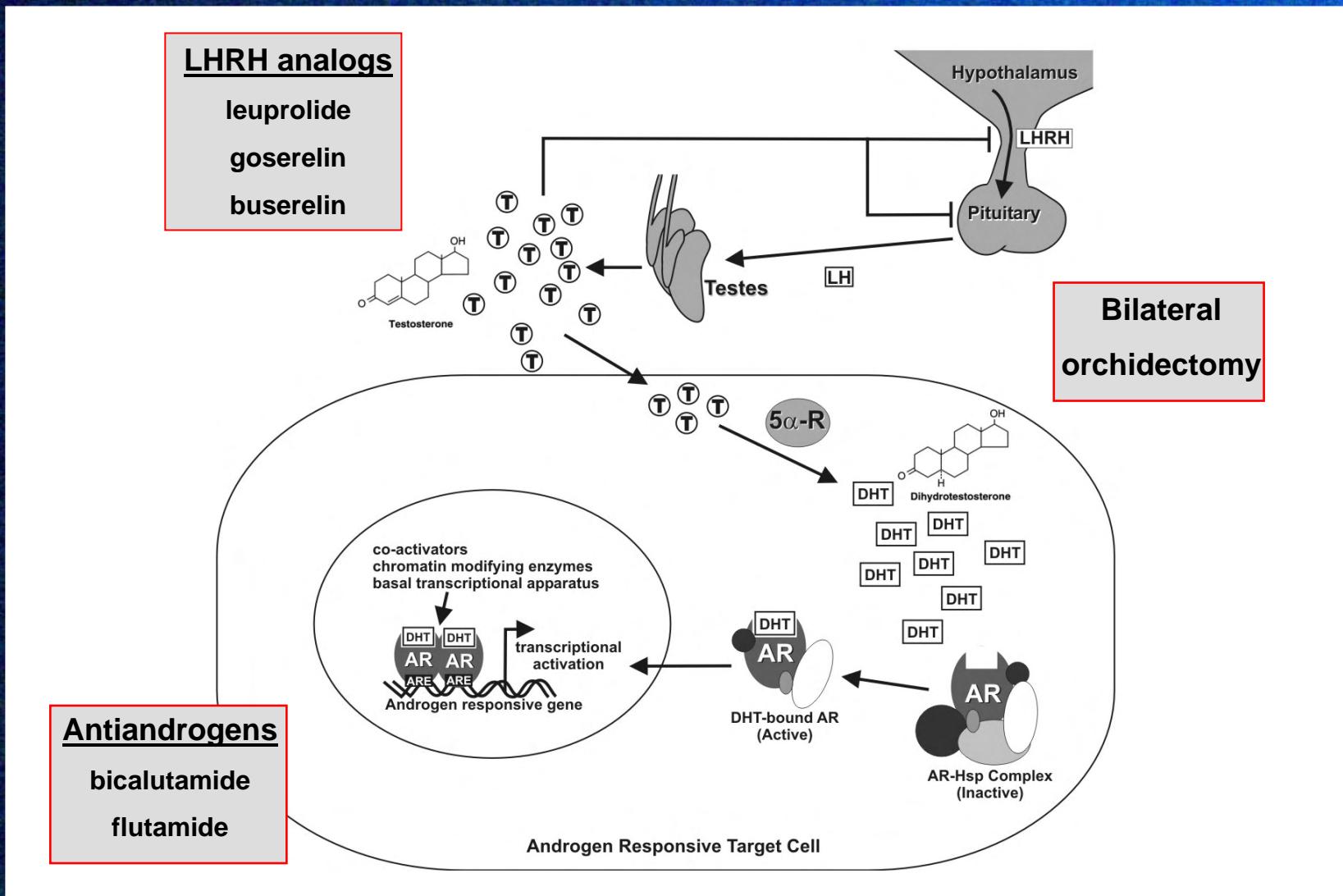
700



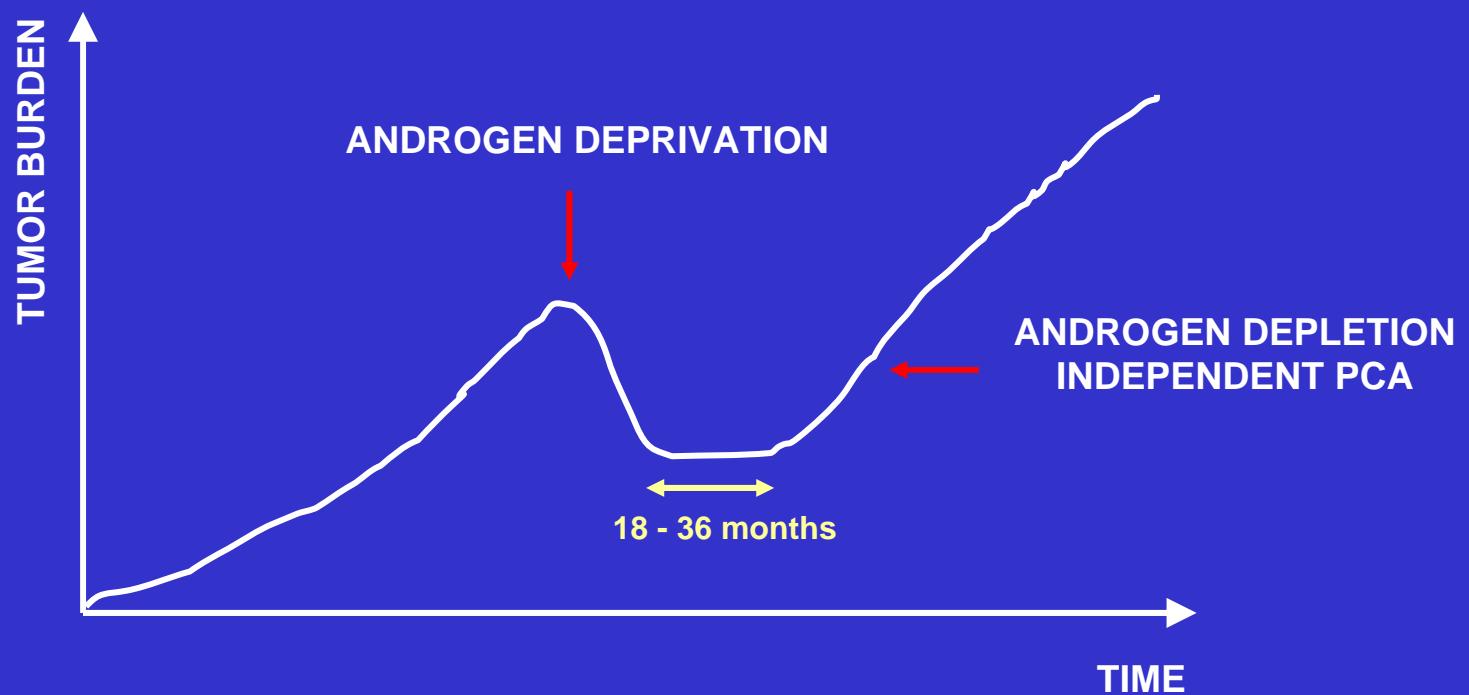
Regulation of AR Activity



AR and Systemic Prostate Cancer Therapy

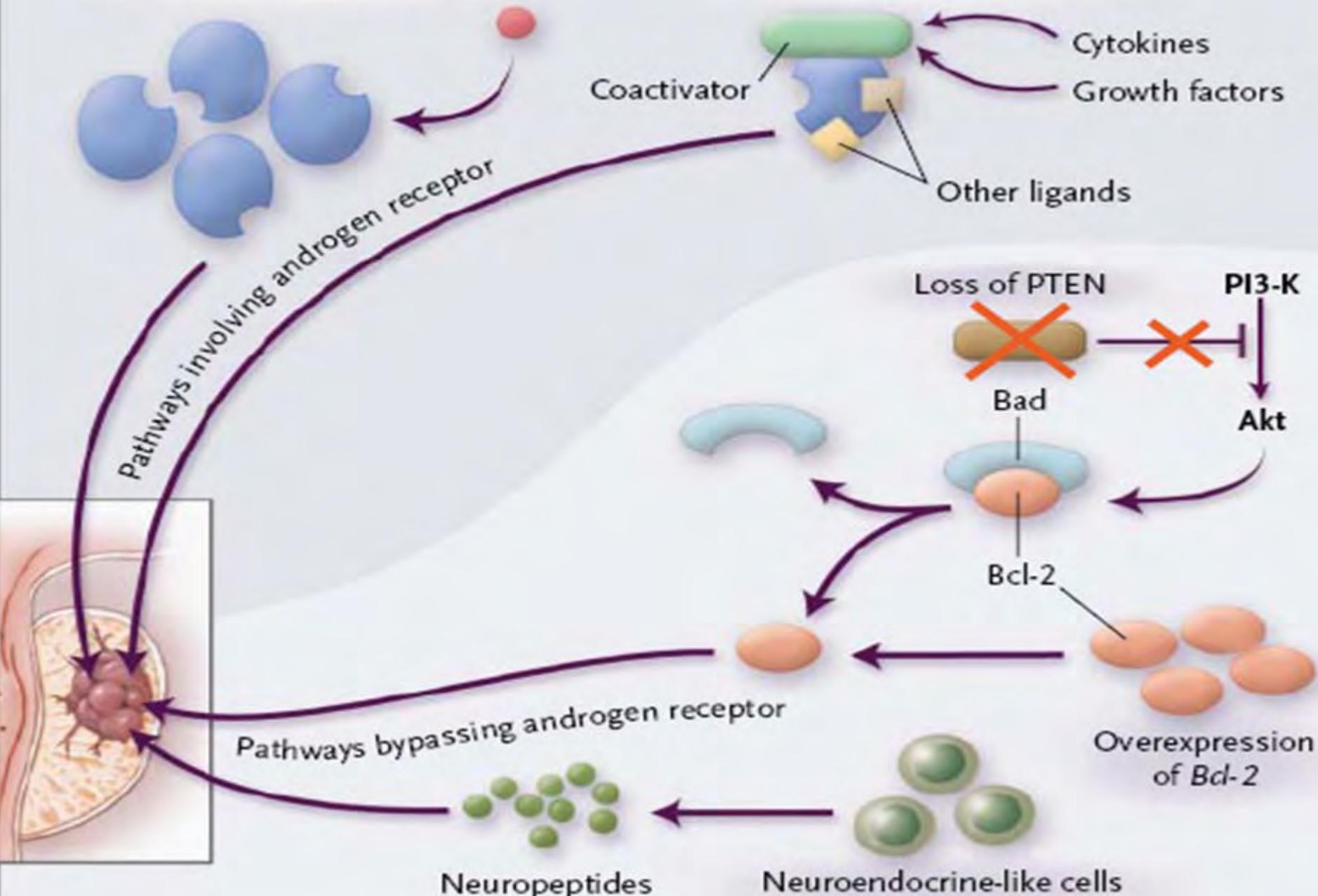


PROSTATE CANCER AND ANDROGEN RECEPTOR

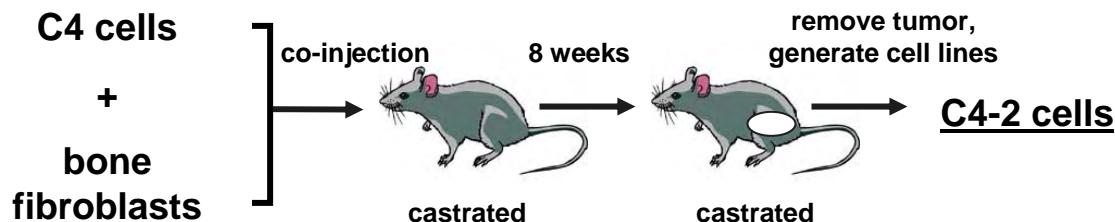
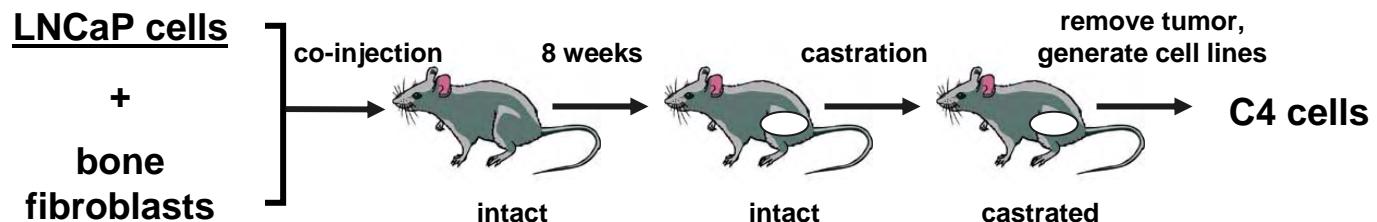


Amplified androgen receptors

Mutated androgen receptor



Model of Prostate Cancer Progression



- ADL growth *in vivo* and *in vitro*
- AR positive
- AR dependent
- express PSA

PSA mRNA Expression

LNCaP C4-2

PSA mRNA

GAPDH mRNA

28S rRNA

18S rRNA

α -AR

α -ERK-2

1nM Mib: - + - +

EtOH: + - + -

AR siRNA
Ctrl. siRNA

α -AR

α -ERK-2

1 2

PSA mRNA

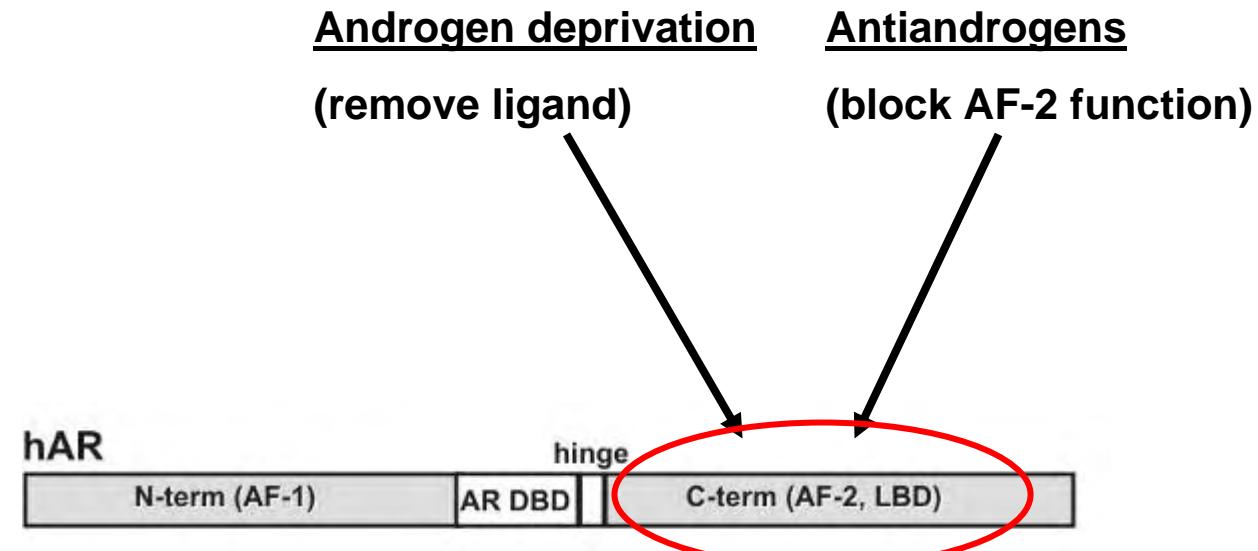
GAPDH mRNA

28S rRNA

18S rRNA

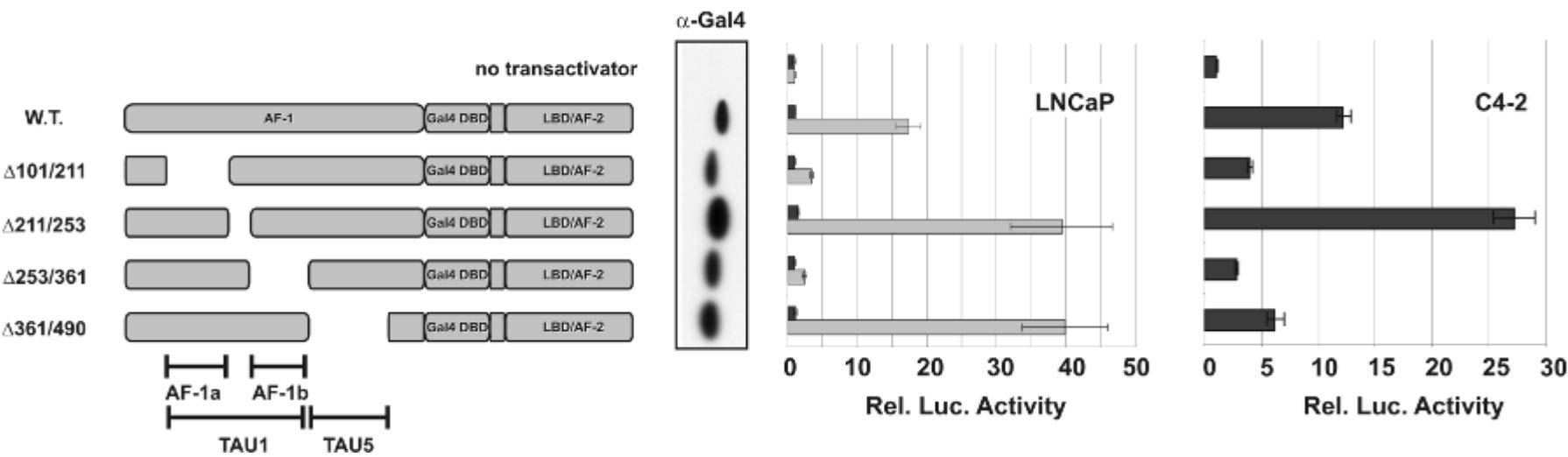
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Key Findings

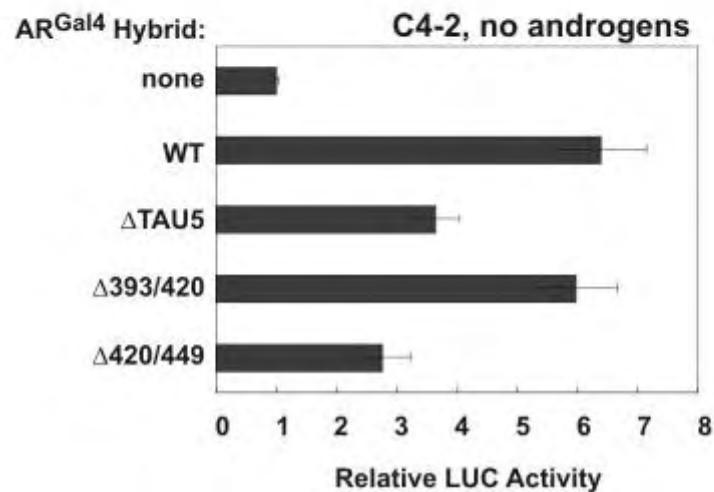
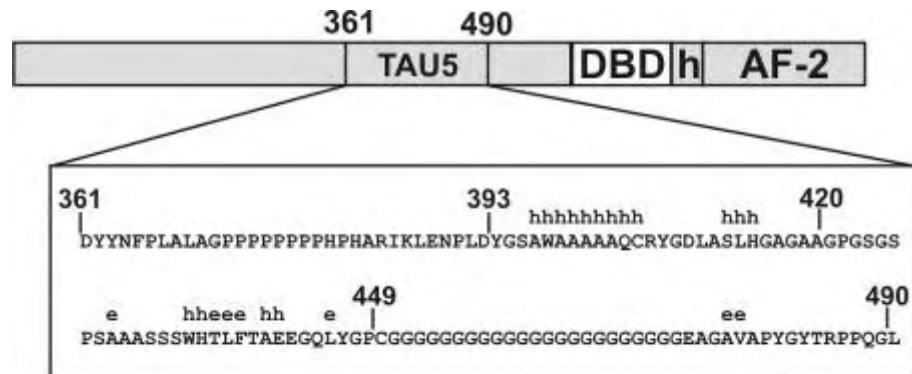


Dehm and Tindall, *JBC*, 2006

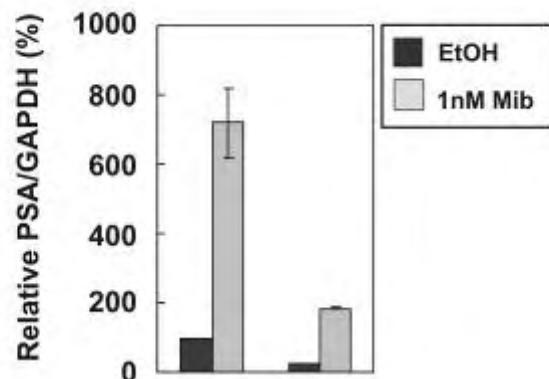
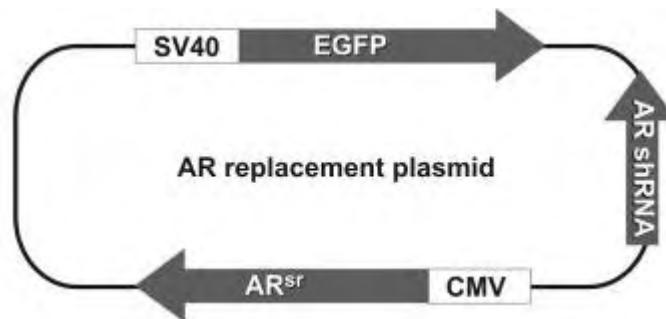
Role of the AR NTD



TAU5 Characterization



Role of AR WHTLF and TAU5 on Chromatin



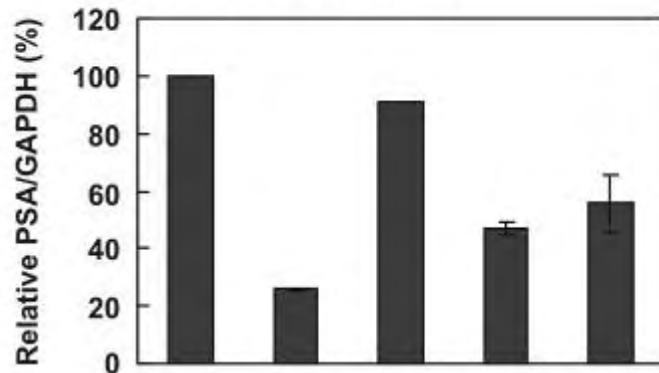
AR replacement
plasmid feature

AR shRNA: - +
EGFP: + +

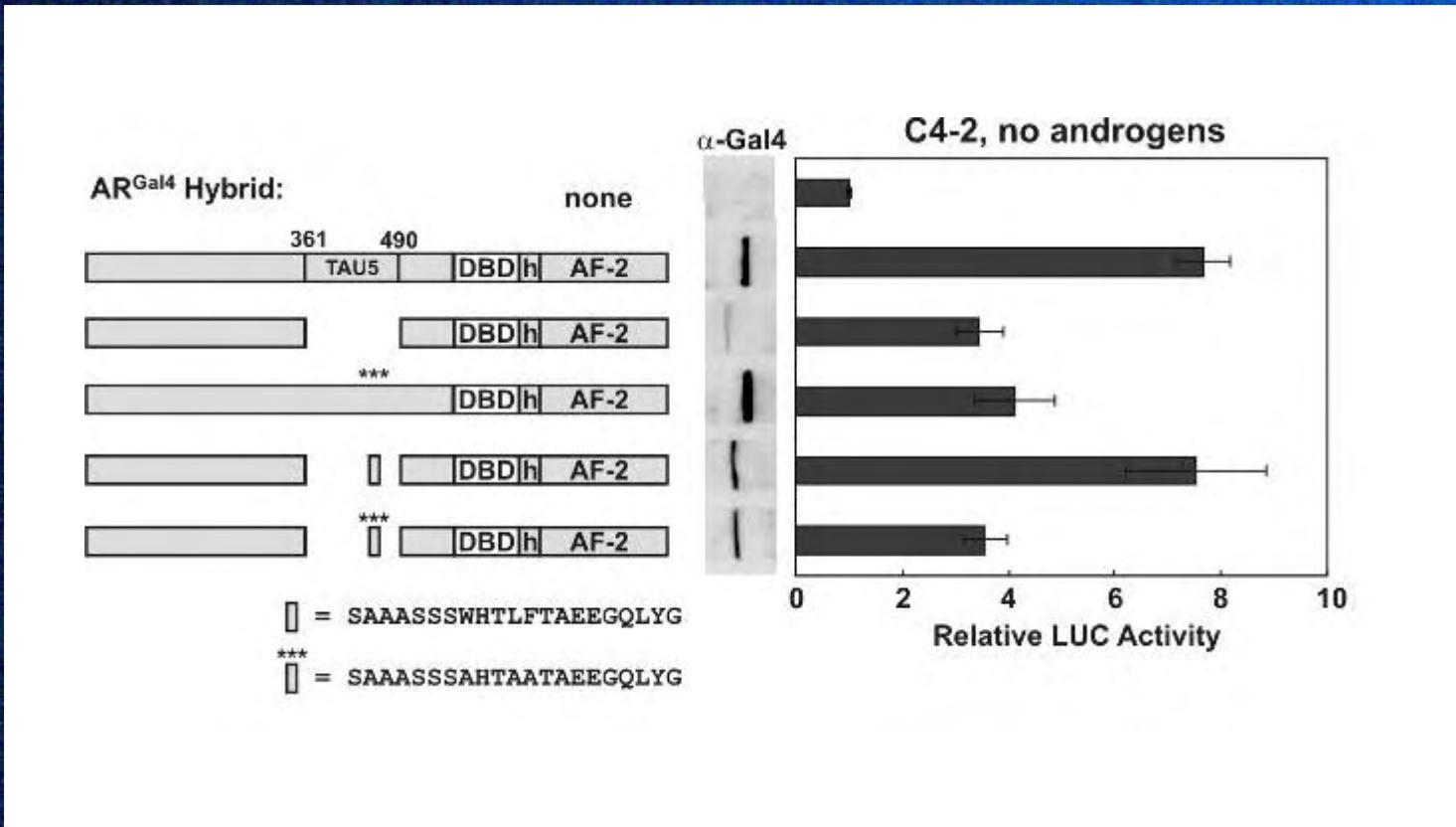
AR replacement
plasmid feature

AR shRNA:	-	+	+	+	+	+
AR ^{sr} :	-	-	w.t.	Δ TAU5	AHTAA	
EGFP:	+	+	+	+	+	+

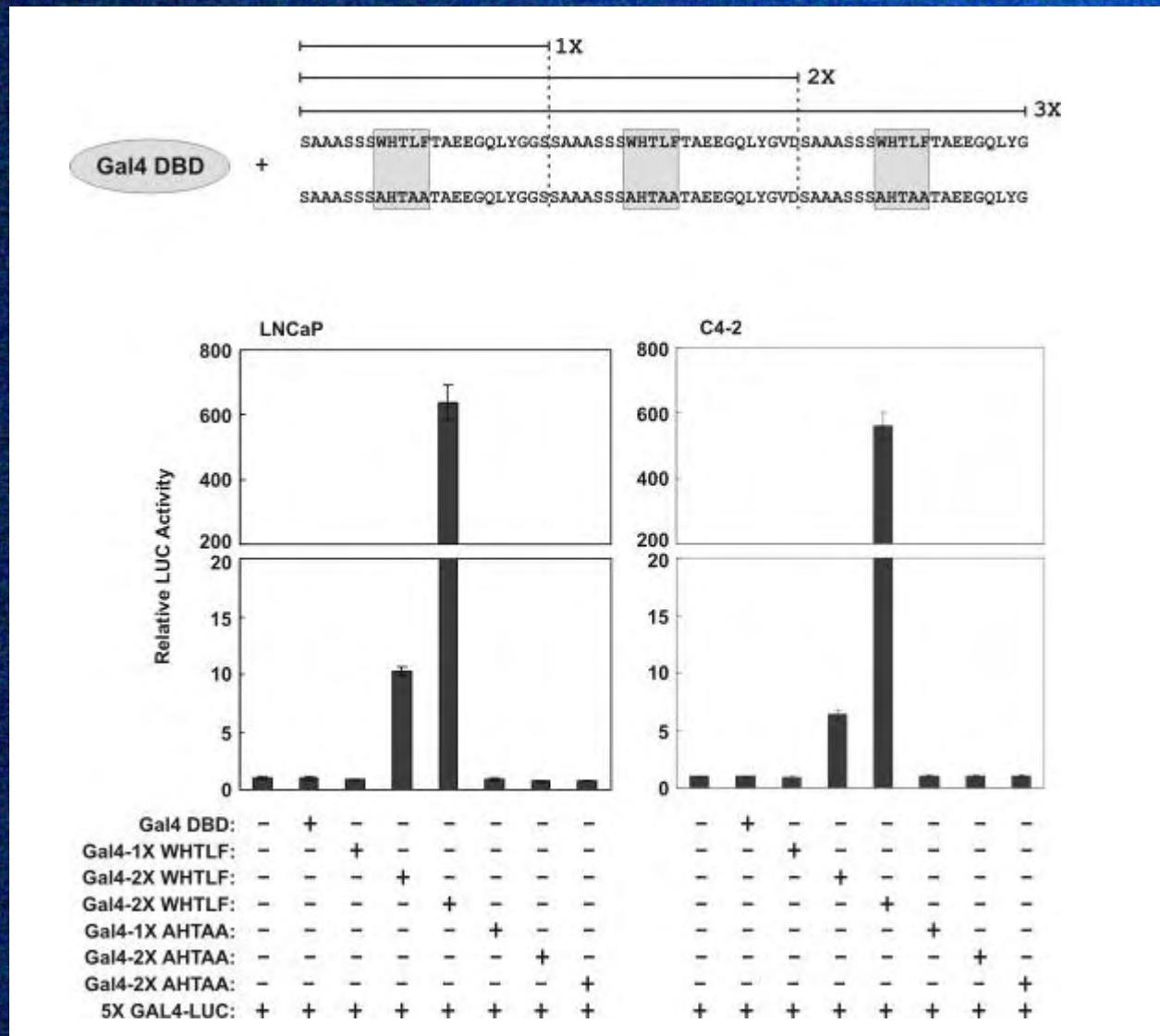
C4-2, no androgens



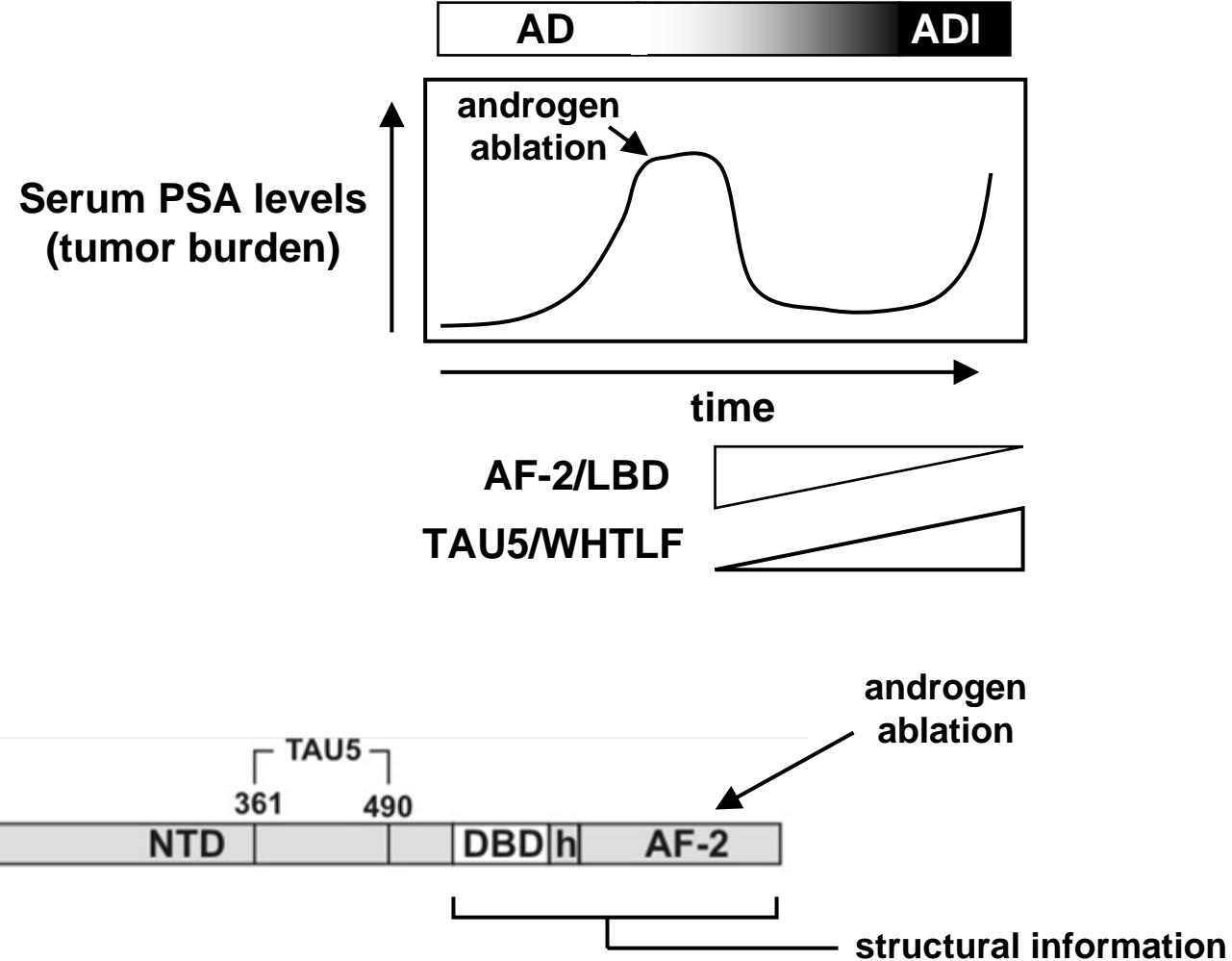
WHTLF Mediates TAU5 Activity



WHTLF is an Autonomous Transactivation Domain



Summary and Conclusions



Acknowledgements

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