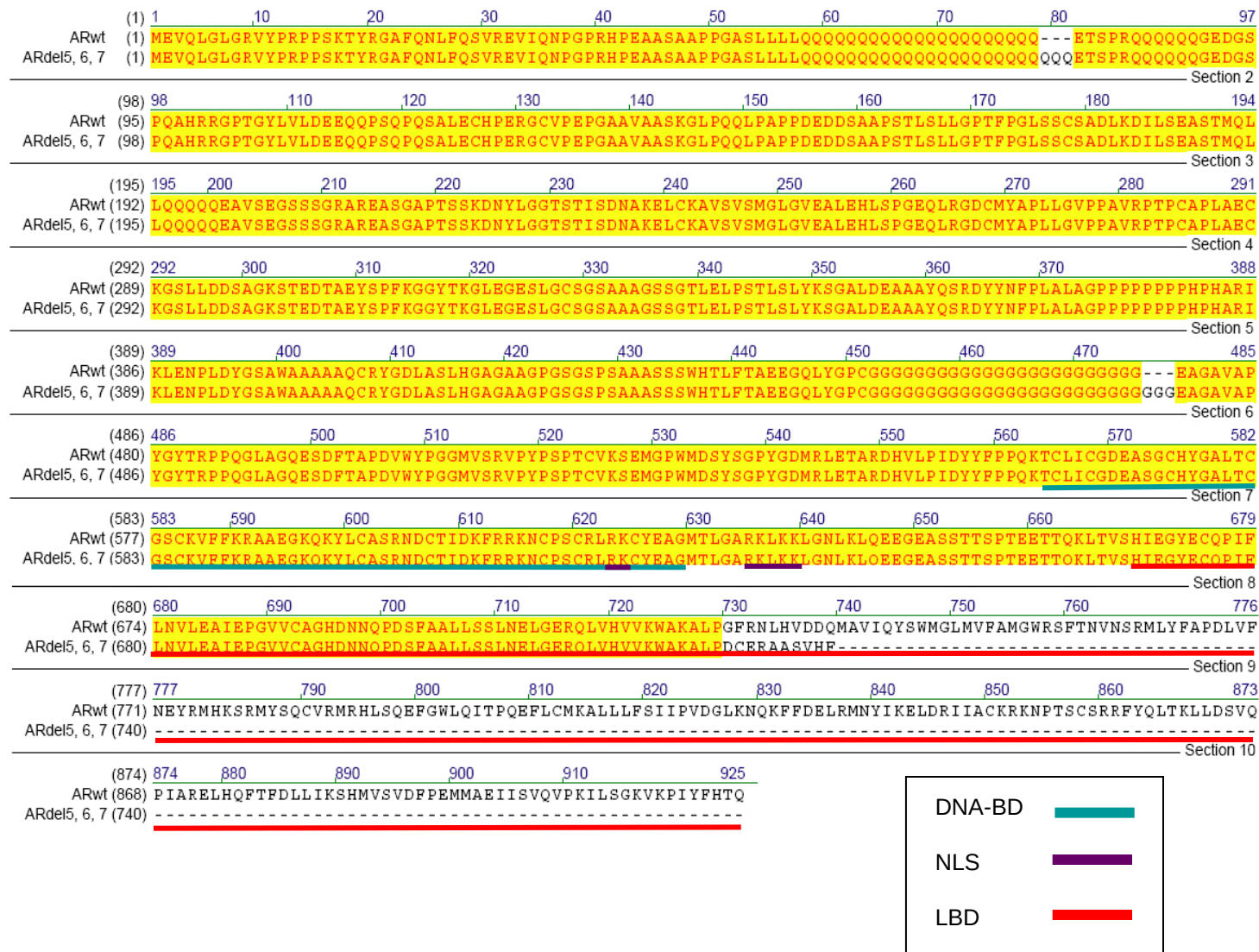
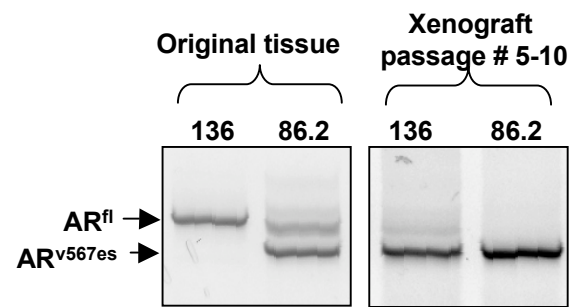




Supplemental Figure 1: Diagram of full-length and predicted variant AR amino acid sequences. The predicted amino acid sequence of AR^{v567es} is compared to the known amino acid sequence for full-length AR. The DNA binding domain (DNA-BD), nuclear localization sequence (NLS), and ligand binding domain (LBD) are marked. Note that AR^{v567es} contains the entire DNA-BD and both NLS clusters, but it is missing the majority of the LBD and contains at its C-terminal end a unique amino acid sequence due to a frame-shift in the nucleotide sequence caused by the splicing of exon 4 to exon 8.



Supplemental Figure 2: Expression of full-length AR and AR^{v567es} in LuCaP 86.2 and LuCaP 136 primary and xenograft tissue. AR mRNA expression in the original tumor tissue and in xenograft passages 5 and 10 in castrate SCID mice. Note the marked increase in AR^{v567es} expression in the castrate xenografts compared to original tissues. Image shown is inverted from the original agarose gel image.

LuCaP #	Source	Tissue Type	Histology	Xenograft Androgen Status	PSA Producer
23.1	RAP	Lymph node	adenocarcinoma	dependent	Yes
23.1AI	NA	Androgen independent	adenocarcinoma	independent	Yes
23.12	RAP	Liver met	adenocarcinoma	dependent	Yes
35	OR	Inguinal LN	adenocarcinoma	dependent	Yes
35V	NA	Androgen independent	adenocarcinoma	independent	Yes
49	OR	Omental fat met	Small Cell CA	independent	No
58	OR	Lymph node	adenocarcinoma	dependent	Yes
69	OR	Bowel met	adenocarcinoma	dependent	Yes
70	RAP	Liver met	adenocarcinoma	dependent	Yes
73	OR	Prostate	adenocarcinoma	dependent	Yes
77	RAP	Femur met	adenocarcinoma	dependent	Yes
78	RAP	Peritoneal met	adenocarcinoma	pending	Yes
81	RAP	Right Pelvic lymph node	adenocarcinoma	pending	Yes
86.2	OR	Bladder met	adenocarcinoma	independent	Yes
92.1	RAP	Peritoneal met	adenocarcinoma	pending	Yes
93	OR	TURP	Small Cell CA	independent	No
96	OR	TURP	adenocarcinoma	dependent	Yes
96AI	NA	Androgen independent	adenocarcinoma	independent	Yes
105	RAP	Rib mets R5, L5	adenocarcinoma	dependent	Yes
115	OR	Lymph node	adenocarcinoma	pending	Yes
136	OR	Ascites Fluid (cells)	adenocarcinoma	dependent	Yes
141	OR	Prostate (TURP)	adenocarcinoma	pending	Yes
145.1	RAP	Liver met	adenocarcinoma	pending	Yes
145.2	RAP	Lymph node	adenocarcinoma	pending	Yes
147	RAP	Liver met	adenocarcinoma	pending	Yes

Supplemental Table 1: Characteristics of the LuCaP xenograft series. Samples were obtained at surgery (OR) or during a rapid autopsy (RAP) as indicated. Xenografts marked NA refer to xenografts that were derived from the regrowth of xenografts in castrated SCID mice (e.g. 96 to 96AI). “V” and “AI” both denote xenografts that are castration-resistant. Column labeled “Xenograft Androgen Status” refers to the response of the xenograft to castration when grown s.c. in SCID mice. “PSA Producer” indicates whether PSA was detected in the blood of mice bearing the xenograft.

GENE CATEGORY	VENN I		VENN II		VENN III		VENN IV		VENN V		VENN VI	
	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR
GO_CC_plasma membrane	0.0006	<0.01							0.0068	<0.01		
GO_CC_integral to plasma membrane	0.0007	<0.01										
GO_CC_integral to membrane	0.0012	<0.01										
GO_BP_response to chemical substance	0.0044	<0.01										
GO_BP_ion transport	0.0047	<0.01										
GO_BP_cell communication	0.0048	<0.01					0.0003	<0.01			7E-05	<0.01
GO_CC_endoplasmic reticulum	0.0055	<0.01										
GO_BP_steroid biosynthesis			4.691E-11	<0.01								
GO_BP_sterol metabolism			7.363E-11	<0.01								
GO_BP_steroid metabolism			5.091E-10	<0.01								
GO_BP_sterol biosynthesis			1.017E-09	<0.01								
GO_BP_cholesterol metabolism			2.968E-08	<0.01								
KEGG_Sterol biosynthesis			3.03E-08	<0.01								
GO_BP_lipid biosynthesis			1.934E-07	<0.01								
GenMAPP_Hs_Cholesterol Biosynthesis			2.791E-07	<0.01								
GO_BP_lipid metabolism			5.286E-07	<0.01								
GO_BP_cholesterol biosynthesis			5.599E-07	<0.01								
KEGG_Lipid Metabolism			2.65E-06	<0.01								
GO_BP_alcohol metabolism			4.327E-06	<0.01								
GO_BP_isoprenoid biosynthesis			3.323E-05	<0.01								
GO_BP_isoprenoid metabolism			3.323E-05	<0.01								
KEGG_Terpenoidbiosynthesis			5.371E-05	<0.01								
GO_BP_biosynthesis			0.0019614	<0.01								
KEGG_Biosynthesis of Secondary Metabolites			0.0026882	<0.01								
GO_MF_oxidoreductase activity			0.0068188	<0.01								
GO_BP_macromolecule biosynthesis			0.0110713	<0.01								
GO_MF_catalytic activity			0.0161017	<0.01								
GO_MF_protein tyrosine/serine/threonine phosphatase activity					0.0041	<0.01						
GO_MF_transcription factor activity					0.0042	<0.01	0.0028	<0.01				
GO_MF_transcription regulator activity					0.0054	<0.01						
GO_MF_amino acid permease activity					0.0054	<0.01						
GO_MF_neutral amino acid transporter activity					0.0054	<0.01						
GO_MF_cell adhesion molecule activity							0.0001	<0.01				
GO_BP_cell adhesion							0.0002	<0.01				
GO_BP_digestion									2E-05	<0.01		
KEGG_Pentose and glucuronateinterconversions									0.0003	<0.01		

Supplemental Table 2. GO analysis for genes differentially regulated by ARv567es compared to full-length AR.

GENE CATEGORY	VENN I		VENN II		VENN III		VENN IV		VENN V		VENN VI	
	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR	EASE score	Global FDR
GO_BP_development									0.0003	<0.01	0.0012	<0.01
GO_MF_glucuronosyltransferase activity									0.0003	<0.01		
GO_CC_membrane									0.0009	<0.01		
KEGG_Androgen and estrogen metabolism									0.0009	<0.01		
GO_BP_morphogenesis									0.0011	<0.01	0.001	<0.01
GO_BP_cell surface receptor linked signal transduction									0.0015	<0.01		
GO_BP_xenobiotic metabolism									0.0022	<0.01		
KEGG_Porphyrin andchlorophyll metabolism									0.0023	<0.01		
GO_BP_response to xenobiotic stimulus									0.0031	<0.01		
KEGG_Starch and sucrosemetabolism									0.0036	<0.01		
GO_CC_extracellular									0.0036	<0.01		
GO_BP_Wnt receptor signaling pathway									0.0043	<0.01		
GO_MF_signal transducer activity									0.0052	<0.01		
KEGG_Metabolism of Cofactors and Vitamins									0.0082	<0.01		
GO_MF_chymotrypsin activity									0.0088	<0.01		
GO_MF_transmembrane receptor protein phosphatase activity									0.0091	<0.01		
GO_MF_transmembrane receptor protein tyrosine phosphatase activity									0.0091	<0.01		
GO_CC_nucleosome											1E-17	<0.01
GO_BP_nucleosome assembly											1E-17	<0.01
GO_BP_chromatin assembly/disassembly											4E-14	<0.01
GO_CC_chromatin											5E-11	<0.01
GO_BP_establishment and/or maintenance of chromatin architecture											4E-09	<0.01
GO_BP_chromosome organization and biogenesis (sensu Eukarya)											7E-09	<0.01
GO_BP_nuclear organization and biogenesis											8E-09	<0.01
GO_BP_DNA packaging											1E-08	<0.01
GO_CC_chromosome											3E-07	<0.01
GO_BP_cellular process											2E-06	<0.01
GO_CC_obsolete cellular component											1E-05	<0.01
GO_BP_DNA metabolism											0.0001	<0.01
GO_MF_oxidoreductase activity\, acting on single donors with incorporation of molecular oxygen											0.0001	<0.01
GO_BP_cell organization and biogenesis											0.0004	<0.01
GO_BP_signal transduction											0.0009	<0.01
GO_BP_anti-apoptosis											0.001	<0.01
GO_BP_negative regulation of apoptosis											0.001	<0.01
GO_BP_organogenesis											0.0011	<0.01
GO_MF_oxidoreductase activity\, acting on paired donors\, with incorporation or reduction of molecular oxygen											0.0048	<0.01
GO_BP_neurogenesis											0.0064	<0.01
GO_BP_cyclic nucleotide metabolism											0.0103	0.0286

Supplemental Table 3. GO analysis (continued) for genes differentially regulated by ARv567es compared to full-length AR.