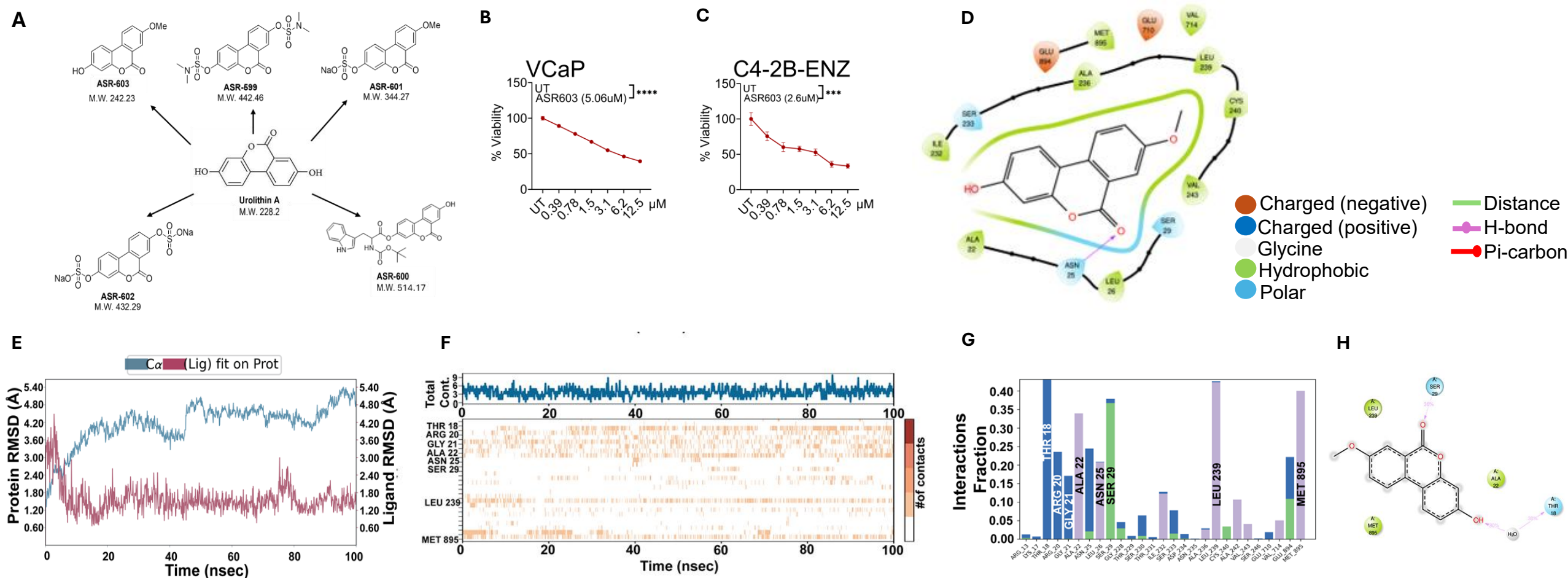
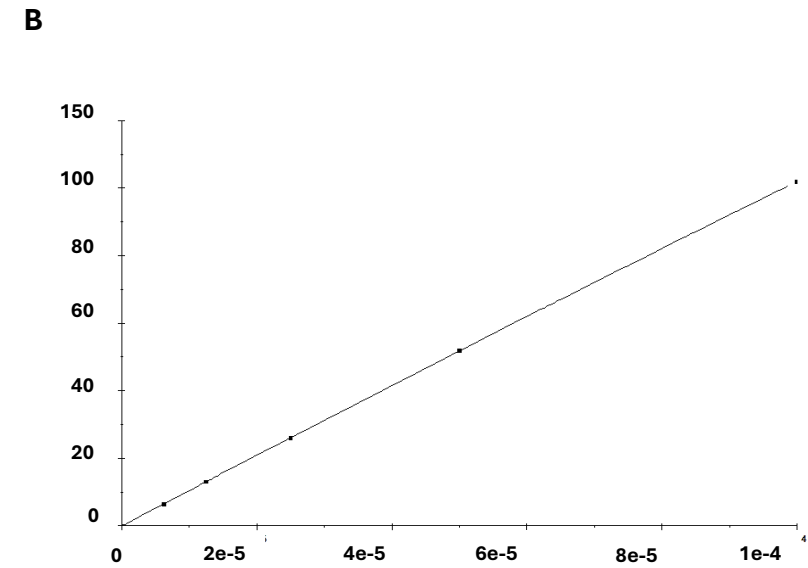
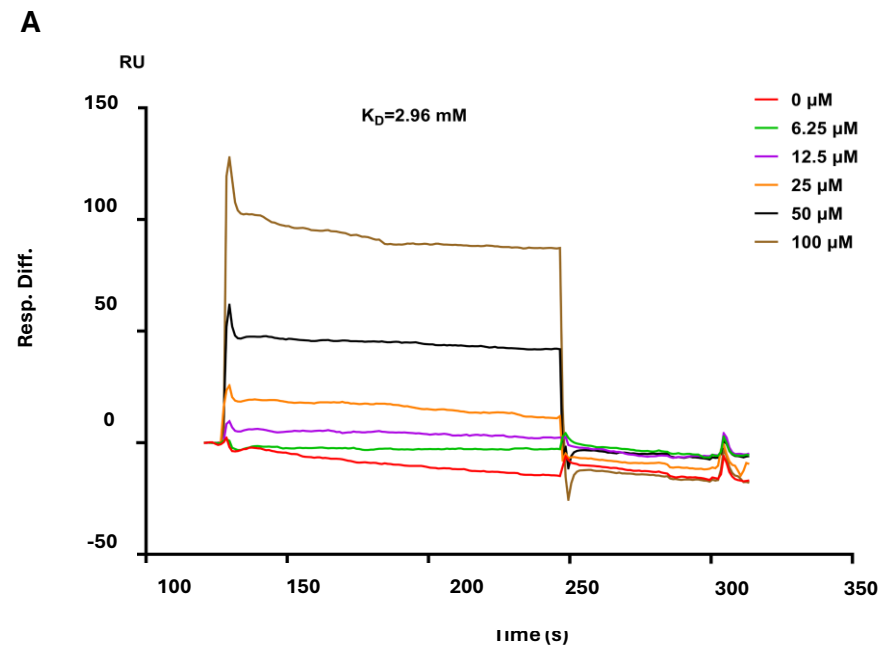
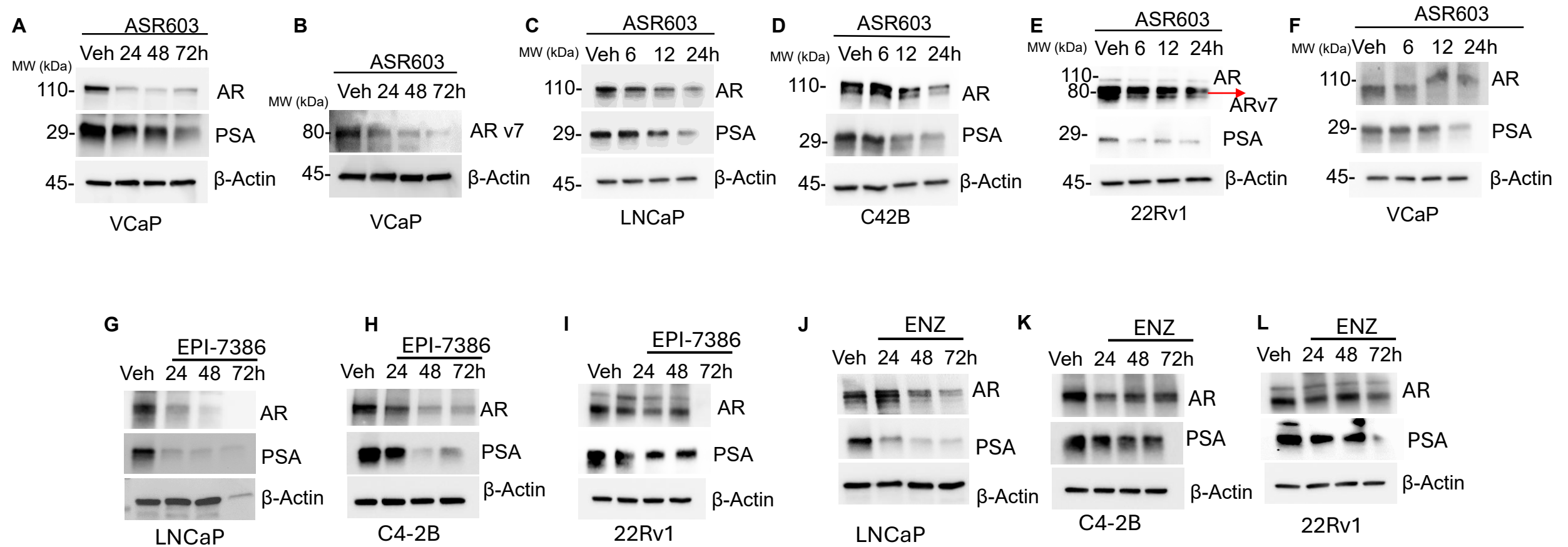




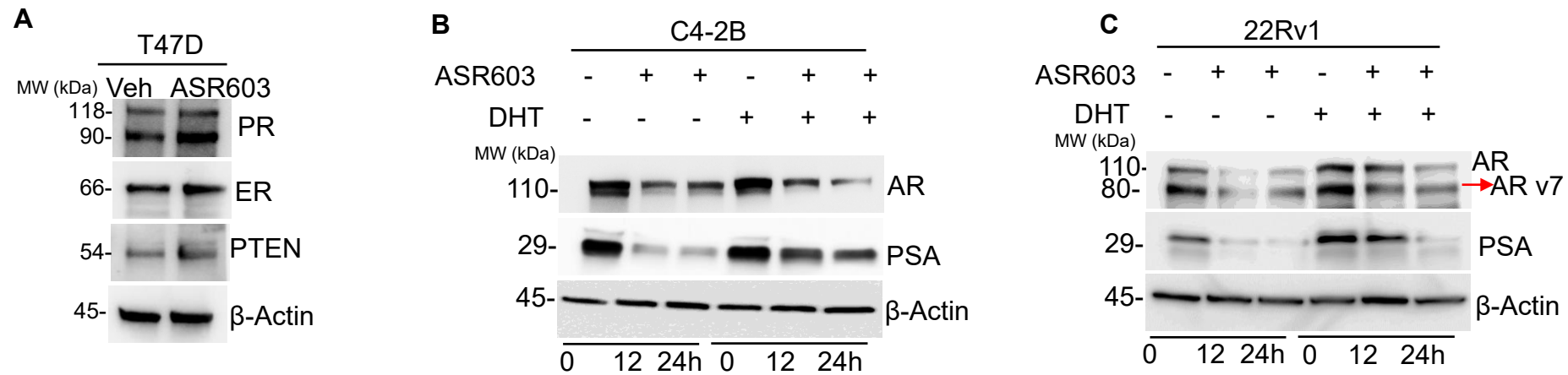
Supplementary Fig. 1: Synthesis and binding of ASR603 to AR-NTD: **A)** O-methylated, amino acid (tryptophan) and sulfonamide-/sulfoxide- conjugated analogs of UroA were synthesized. MTT viability assay was performed for **B-C)** VCaP cells that express ARv7 and C4-2B-ENZ cells that express AR and are resistant to enzalutamide. **D)** 3D and 2D interactions of the ligand with the protein. **E)** The RMSD of the C α atoms in the AR-NTD exhibited initial fluctuations between 3.7 Å and 4.8 Å up to approximately 42 ns. Following this period, the RMSD values stabilized between 4.8 Å and 5.4 Å, remaining within an acceptable range for structural stability throughout the remainder of the 100-ns trajectory. These results suggest that the presence of ASR603 does not significantly perturb the protein's structural integrity. Ligand RMSD analysis further demonstrated that ASR603 remained stably bound within the identified pocket. The RMSD values for the ligand remained consistently below 3.0 Å for the entire duration of the simulation, indicating that ASR603 maintained a stable binding pose without diffusing from the pocket **F)** Interaction timeline analysis confirmed persistent contacts with MET-895, LEU-239, and SER-29 (2–3 contacts throughout): THR-18 emerged as the most interactive residue, displaying a total interaction fraction (IF) of 0.45, primarily via water-bridge-mediated interactions. LEU-239 and MET-895 followed closely, with IF values greater than 0.40, both contributing through persistent hydrophobic contacts. Other key residues included ALA-22 and ASN-25, exhibiting IF values of 0.33 and 0.25, respectively, involving both water bridges and hydrophobic interactions. Interaction timeline analysis further highlighted the consistency of ligand contacts with MET-895, LEU-239, and SER-29, with each maintaining 2 to 3 contacts throughout the simulation period. **G)** Number of protein-ligand contact of active site residues of NTD-AR with ligand molecules during 100 ns MD simulation. The stacked bar charts are normalized over the course of the trajectory: for example, a value of 0.40 suggests that 40% of the simulation time the specific interaction is maintained. H-Bond (Green), Ionic (magenta), Water Bridges (blue) and Hydrophobic (light violet). Among these, hydrogen bonding is especially significant due to its impact on drug specificity, absorption, and metabolism. **H)** 2D interaction diagrams of the ligands with protein residues. All error bars represent means $\pm$ SD. Statistical significance: *P < 0.05; **P < 0.01; ns, not significant.



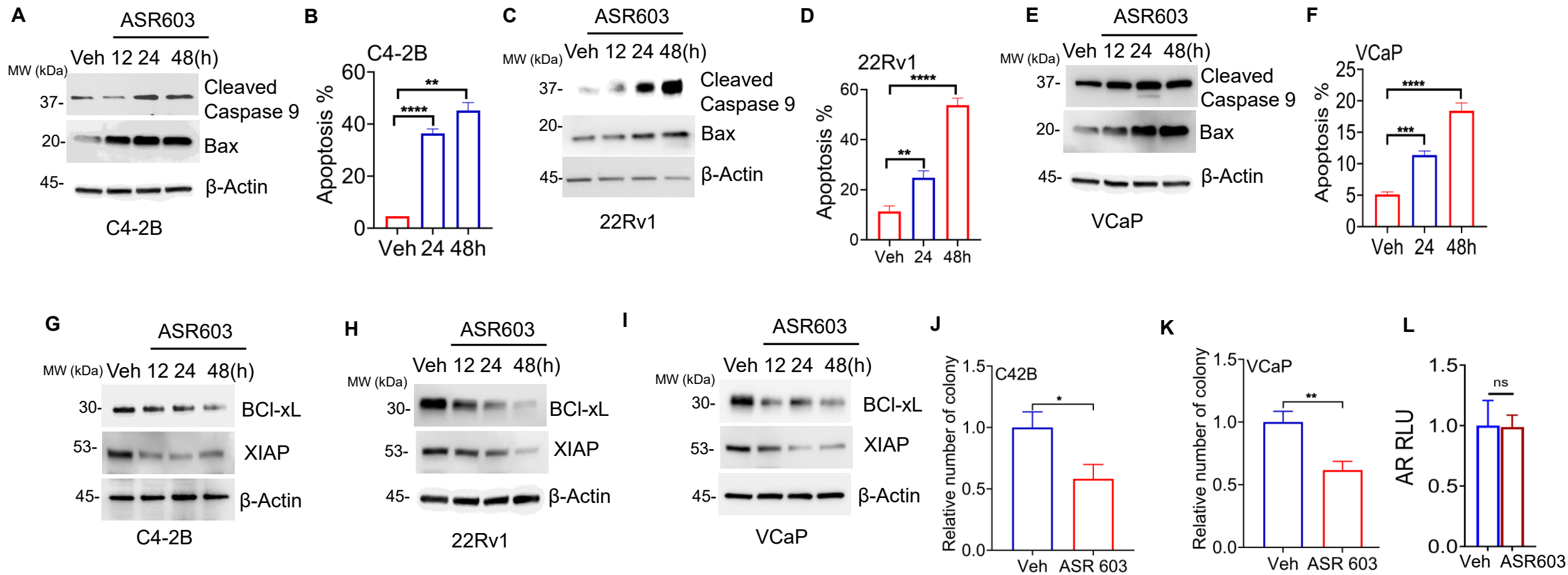
Supplementary Fig. 2: SPR analysis of binding of ASR603 with AR: A) Sensogram curve for binding of ASR603 with AR. **B)** a steady-state analysis fitting curve.



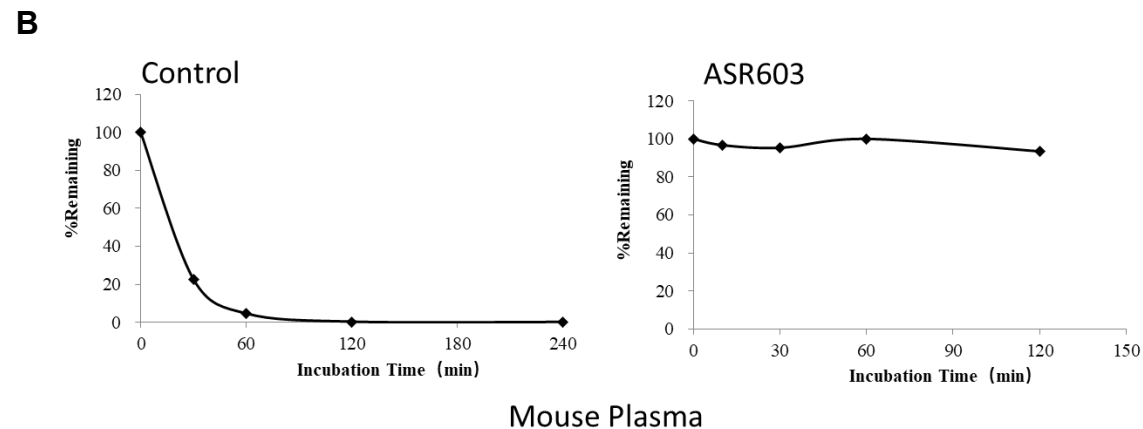
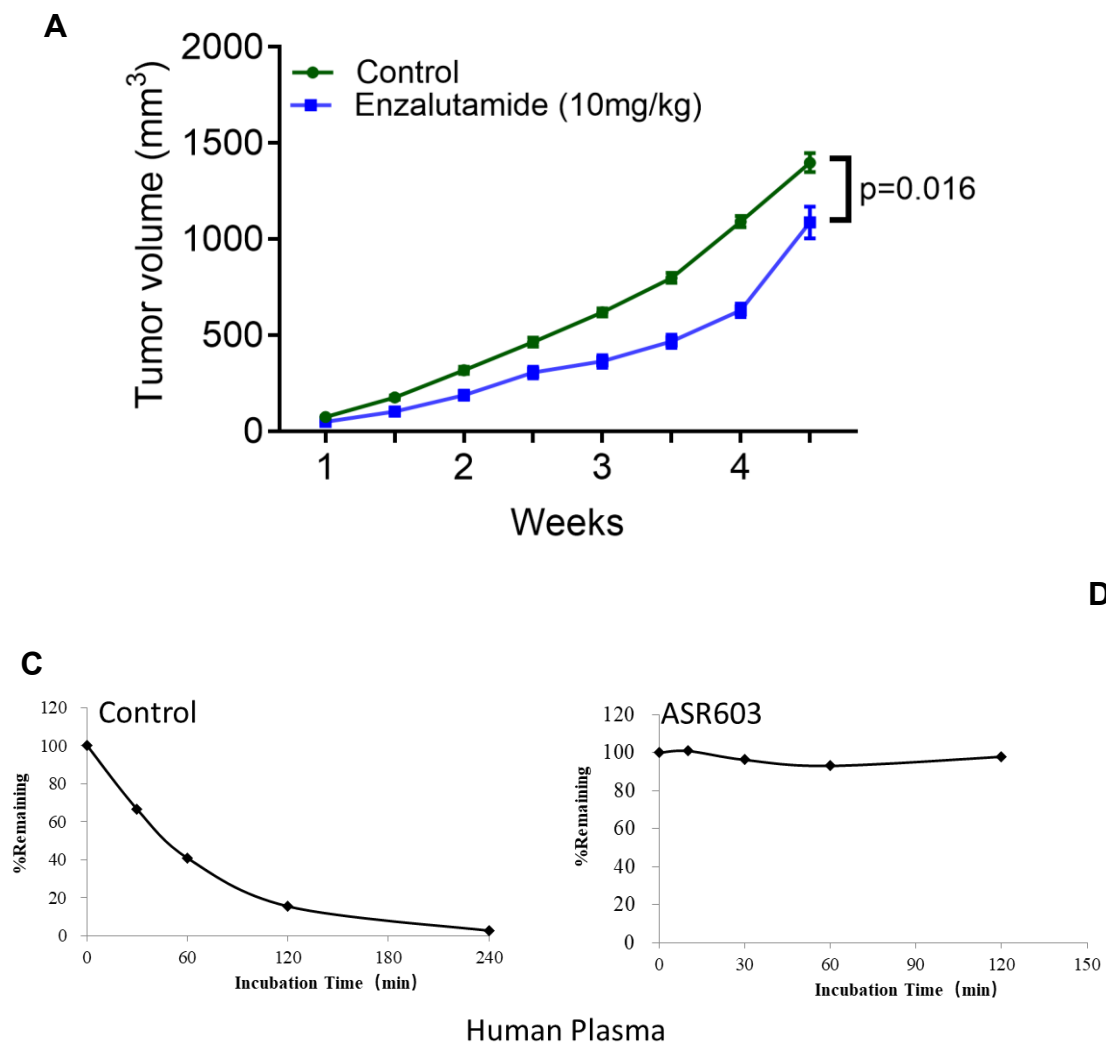
Supplementary Fig. 3: ASR603 inhibits AR signaling: Western Blot analysis of VCaP cells treated with Vehicle (Veh) or ASR603 for 24, 48, and 72 hours and expression of **A)** AR, PSA and **B)** ARv7 was analyzed. Western Blot analysis for expression of AR and PSA in **C)** LNCaP, **D)** C4-2B, **E)** 22Rv1, **F)** VCaP cells treated with Vehicle (Veh) or ASR603 for 6, 12, and 24 hours. **G-I)** Western Blot analysis for expression of AR and PSA with vehicle or EPI-7386 for the indicated time in LNCaP, C4-2B and 22Rv1 cells. **J-L)** Western Blot analysis for expression of AR and PSA with vehicle or Enzalutamide (ENZ) for the indicated time in LNCaP, C4-2B and 22Rv1 cells.



Supplementary Fig. 4: ASR603 specifically inhibits AR signaling: **A)** Western Blot analysis for expression of Estrogen Receptor (ER), Progesterone Receptor (PR) and PTEN in T47D breast cancer cells treated with either vehicle or ASR603 for the indicated time. **B & C)** C4-2B and 22Rv1 cells were treated with Veh (Vehicle) or DHT and ASR603 as well as DHT+ASR603, for 24 and 48 hours and Western Blot analysis for AR, AR-V7 and PSA expression. DHT, a potent androgen and ligand of AR, stabilizes AR protein and activates downstream signaling. DHT increased AR-FL/AR-V7 and PSA expression in both the C4-2B and 22Rv1 cell lines but ASR603 treatment attenuated these effects, indicating its ability to inhibit both ligand-bound AR-FL and constitutively active AR-V7 under androgen-stimulated conditions.



Supplementary Fig. 5: ASR603 inhibits AR function: **A)** Western Blot analysis for expression of Cleaved Caspase9 and Bax in C4-2B cells at indicated time points **B)** FACS analysis of C4-2B cells treated with either vehicle or ASR603 and stained with Annexin-FITC **C)** Western Blot analysis for expression of Cleaved Caspase9 and Bax in 22Rv1 cells at 12, 24 and 48h **D)** FACS analysis of 22Rv1 cells treated with either vehicle or ASR603 and stained with Annexin-FITC **E)** Western Blot analysis for expression of Cleaved Caspase9 and Bax in VCaP cells at 12, 24 and 48h **F)** FACS analysis of VCaP cells treated with either vehicle or ASR603 and stained with Annexin-FITC. Consistent with AR depletion, ASR603 treatment inhibited the expression of key prosurvival markers including BCLxI and Xiap in CRPC cells. Western Blot analysis for expression of BCLxI and Xiap in **G)** C4-2B **H)** 22Rv1 and **I)** VCaP cells treated with Vehicle (Veh) or ASR603 for 12, 24, and 48 hours. **J)** C4-2B and **K)** VCaP cells were seeded for anchorage-independent assay and treated with Vehicle (Veh) or IC₅₀ dose of ASR603 and kept for 3 weeks. The number of colonies was counted at the end of the incubation period. **L)** 22Rv1 cells treated with vehicle or ASR603 and luciferase activity measured. All error bars represent means $\pm$ SD. Statistical significance: *P < 0.05; **P < 0.01; ***P<0.001; ****P<0.0001 ns, not significant.



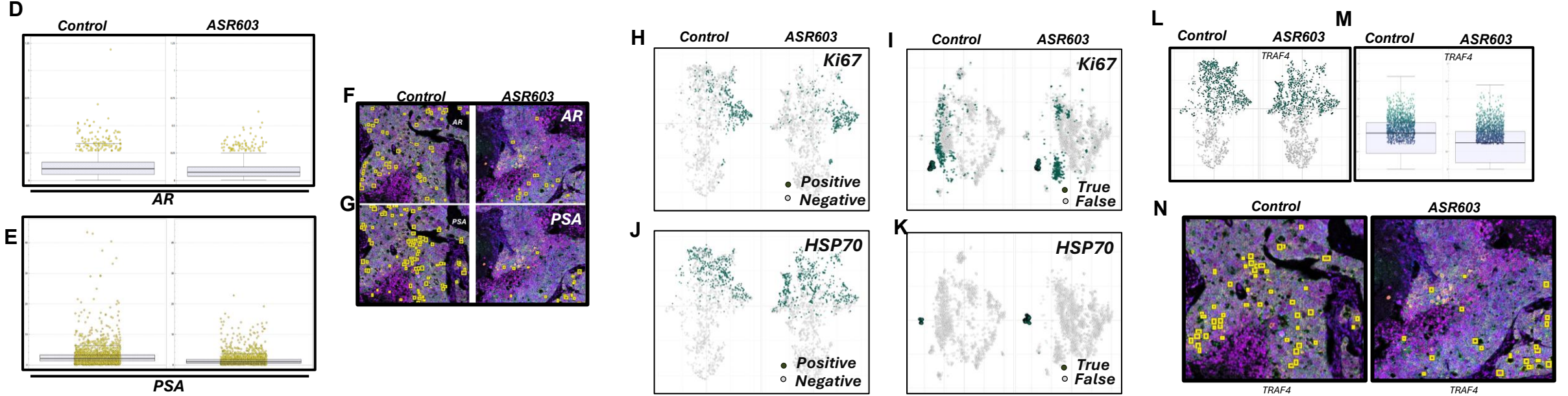
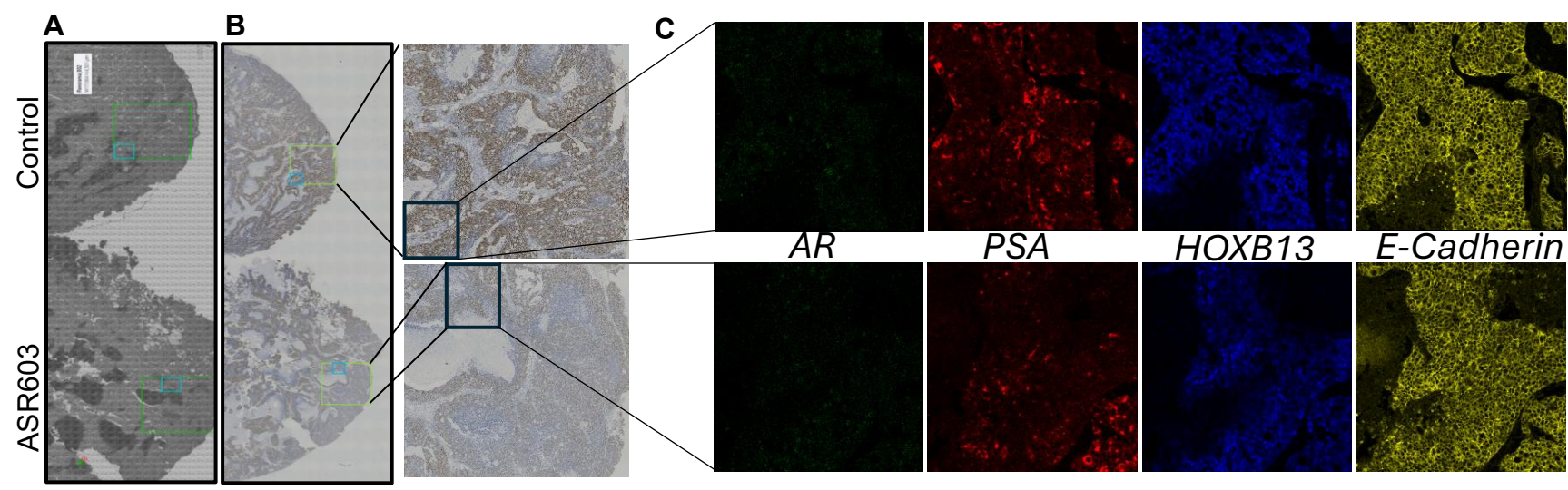
D

Summary

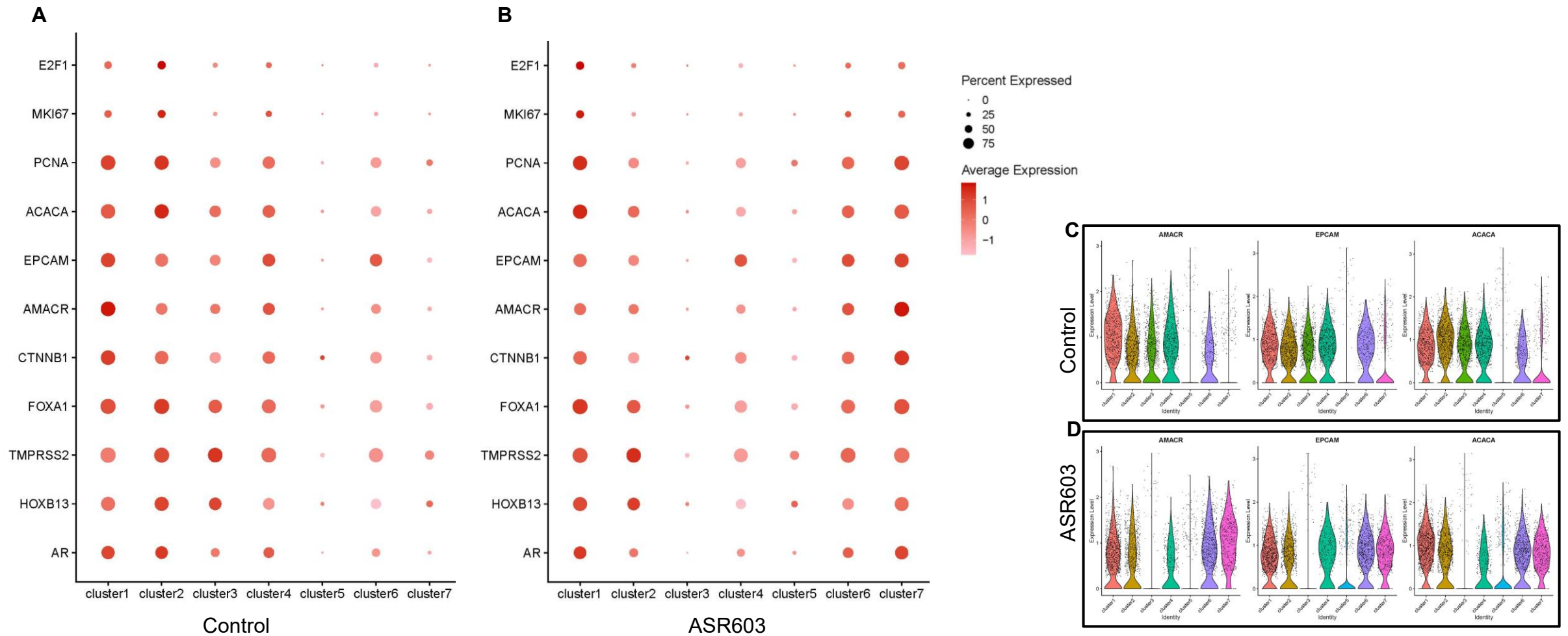
Compound Name	Species	Mouse	
		%Remaining *	T1/2 (min)
Propantheline		0.01	18.50
ASR603		93.40	>240 min

Compound Name	Species	Human	
		Final Remaining (%)	T1/2 (min)
Propantheline		2.79	44.30
ASR603		97.9	>240 min

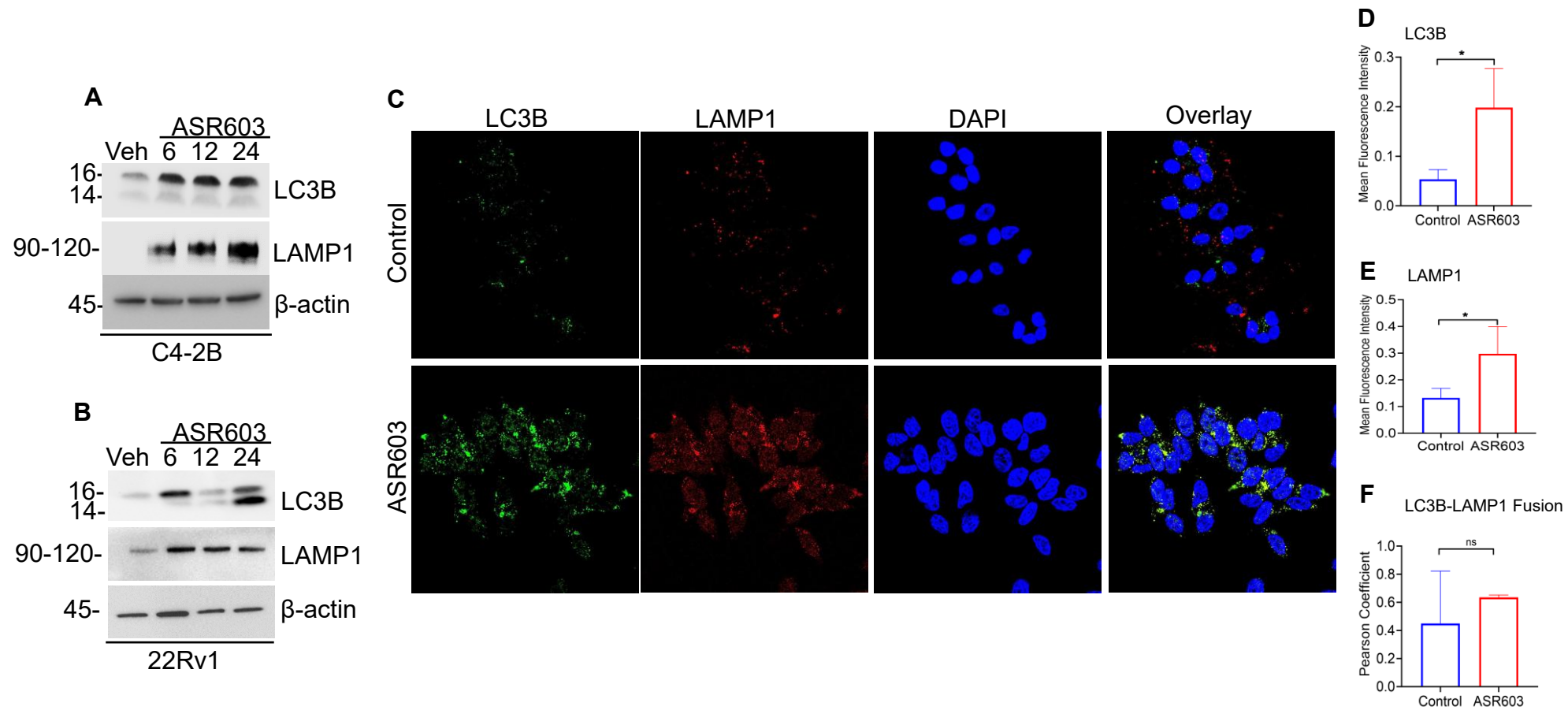
Supplementary Fig. 6 In vivo efficacy of Enzalutamide and Plasma Stability of ASR603: **A)** Tumor growth in vehicle and Enzalutamide treated nude mice. Control (Propantheline) and ASR603 working solution was added into the **B)** mouse plasma and **C)** human plasma to a final concentration of 2 μ M, incubated for the indicated time, and quantified by LC-MS/MS. **D)** The % remaining and T1/2 of the control and ASR603 was calculated in mouse and human plasma.



Supplementary Fig. 7: CyTOF analysis of ASR603-treated PDX tumor: **A)** Control and ASR603 tumors ROIs for CyTOF analysis. **B)** Whole-tissue IHC staining for AR, with magnified insets highlighting AR⁺ and AR⁻ regions in control and treated tumors, respectively, that were selected for downstream spatial profiling **C)** immunofluorescence imaging using metal tagged antibodies for AR (green), PSA (red), HOXB13 (Blue), and E-cadherin (Yellow) in control (upper panel) and ASR603-treated (lower panel) tissues. **D&E)** Scatter-plot and box-and-whisker analyses showing the distribution of androgen receptor–positive (AR⁺) and PSA⁺ single-cell events in control and ASR603-treated CRPC-PDX tumors, quantified by CyTOF and segmented. **F&G)** Spatial maps of AR and PSA protein expression in control and ASR603-treated CRPC-PDX tumors, generated from CyTOF and analyzed. Yellow boxes mark the automated detection of AR⁺ and PSA⁺ cells within segmented tumor regions. UMAP and tSNE projections of **H-I)** Ki67 and **J-K)** HSP70 protein expression from CyTOF analysis, comparing control and ASR603-treated tumors. **L)** UMAP projection and **M)** tSNE projections of box-and-whisker analyses showing the distribution of TRAF4 receptor–positive (AR⁺) and PSA⁺ single-cell events in control and ASR603-treated CRPC-PDX tumors, quantified by CyTOF and segmented. **N)** Spatial maps of TRAF4 protein expression in control and ASR603-treated CRPC-PDX tumors, generated from CyTOF and analyzed.

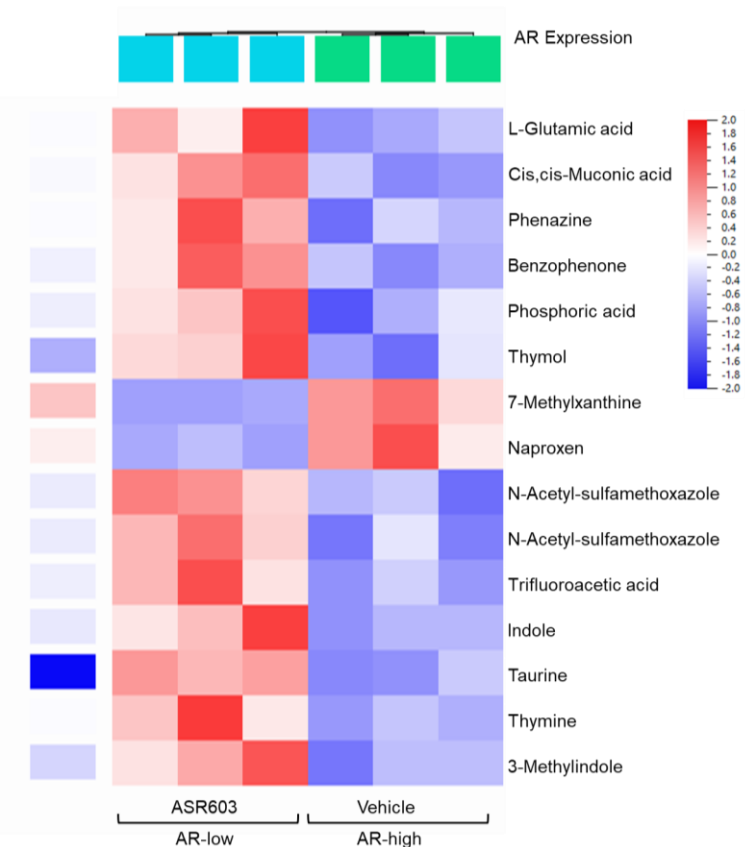


Supplementary Fig. 8: Spatial Transcriptomic analysis of Control vs ASR603-treated PDX tumor: Dot plot visualization of canonical AR pathway components proliferation and prostate adenocarcinoma markers in **A)** control and **B)** ASR603-treated tumors. Dot size indicates the percentage of cells expressing each gene per cluster, and color intensity reflects the average expression level. Violin plots comparing expression of markers of prostate adenocarcinoma across clusters in control **C)** and ASR603-treated **D)** tumors

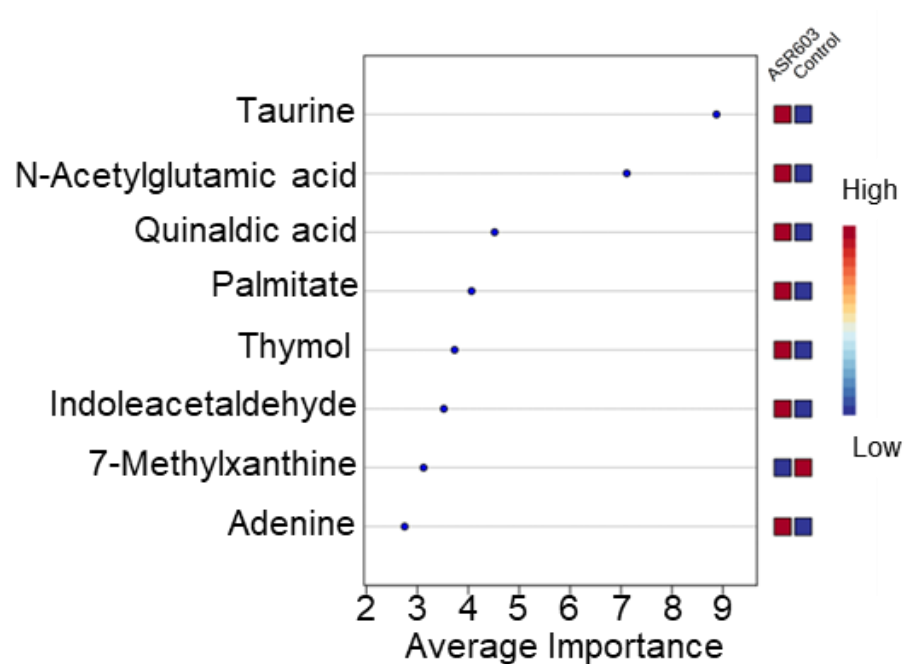


Supplementary Fig. 9: Western blot analysis showing a time-dependent LC3B and LAMP1 protein expression in **A**) C4-2B and **B**) 22Rv1 cells treated with ASR603 or vehicle (DMSO). β -Actin was used as loading control. **C**) Representative images of Single Photon Counting Confocal Microscopy imaging of 22Rv1 cells treated with ASR603 shows LC3B (green) and LAMP1 (Red) expression and LC3B-LAMP1 fusion (Yellow) in response to ASR603 treatment. DAPI is used as nuclear stain (Blue). **D & E**) Mean fluorescence intensity of LC3B and LAMP1 was calculated and represented here in the form of bar graphs. **F**) Colocalization analysis of LC3B (green) and LAMP1(Red) fusion (Yellow) with a non-significant change in Pearson coefficient in ASR603-treated C4-2B cells. All error bars represent means $\pm$ SD. Statistical significance: * $P < 0.05$; ** $P < 0.01$; ns, not significant.

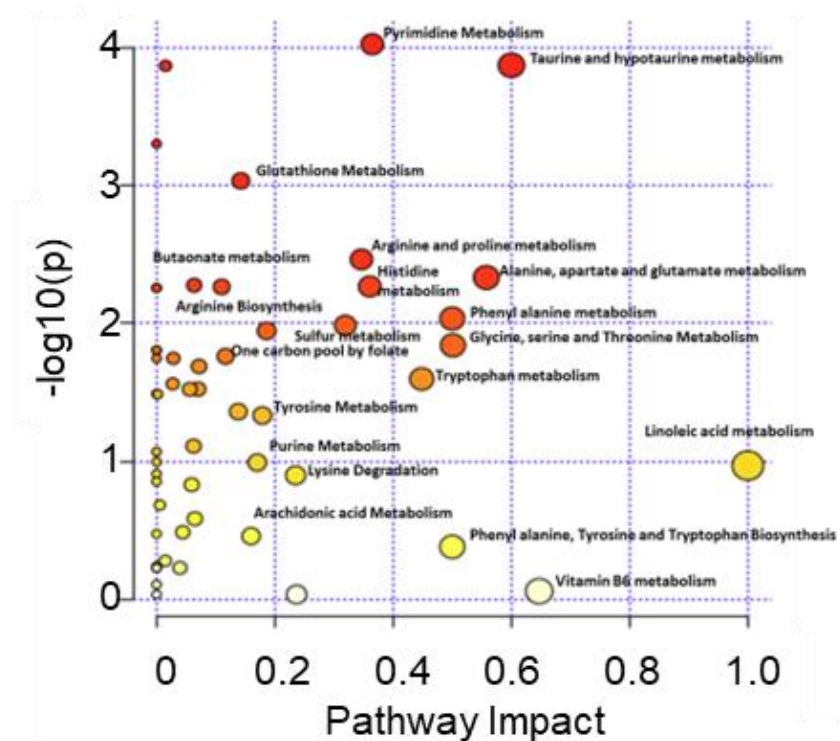
A



B

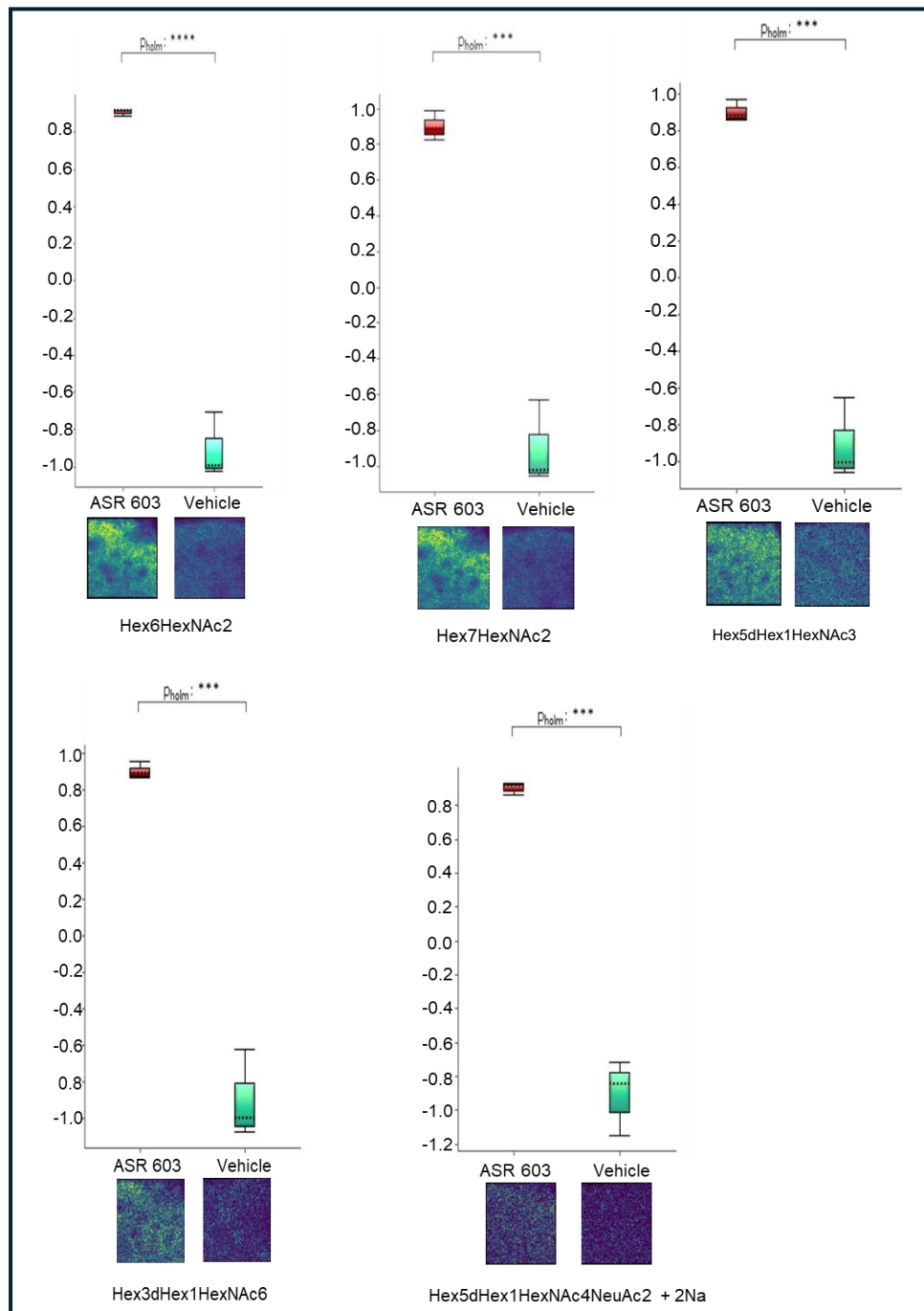


C

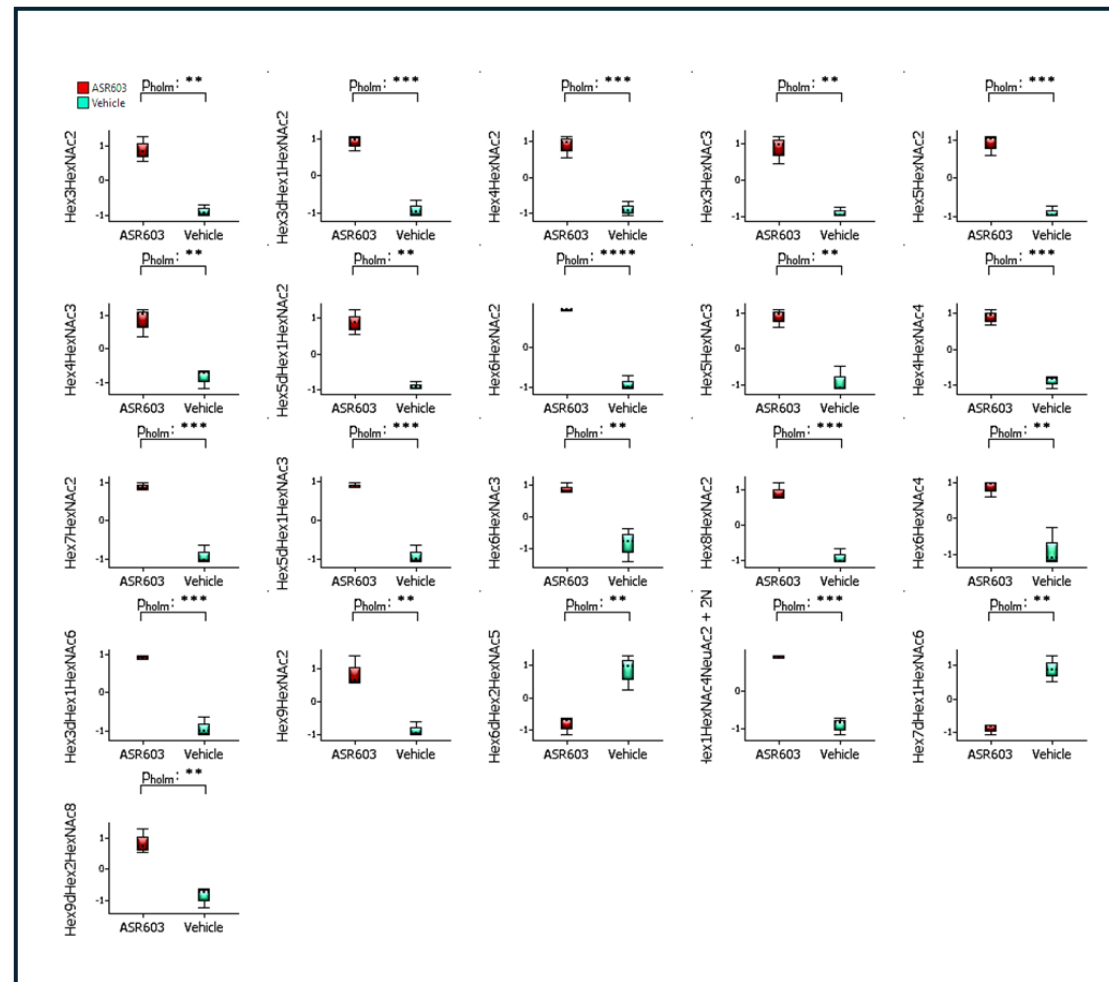


Supplementary Fig. 11: ASR603 treatment altered metabolic landscape in CRPC tumor: A) Hierarchical clustering of metabolites based on abundance in the tumor region with low AR expression. **B)** Variable importance plot highlighting top metabolites contributing to group separation based on multivariate exploratory ROC analysis using the partial least squares-discriminant (PLS-DA) method. The plot illustrates the top metabolites contributing to group differentiation, with color scaling for relative abundance: red reflects high and blue reflects low levels. **C)** Metabolic pathway enrichment and impact analysis identifying significantly altered pathways in ASR603-treated tumors

A



B



Supplementary Fig. 12: Spatial glycome analysis of Control vs ASR603-treated PDX tumor: A&B) Box plots show significantly increased abundance and decline in abundance of indicated glycans in ASR603-treated tumors compared to control.

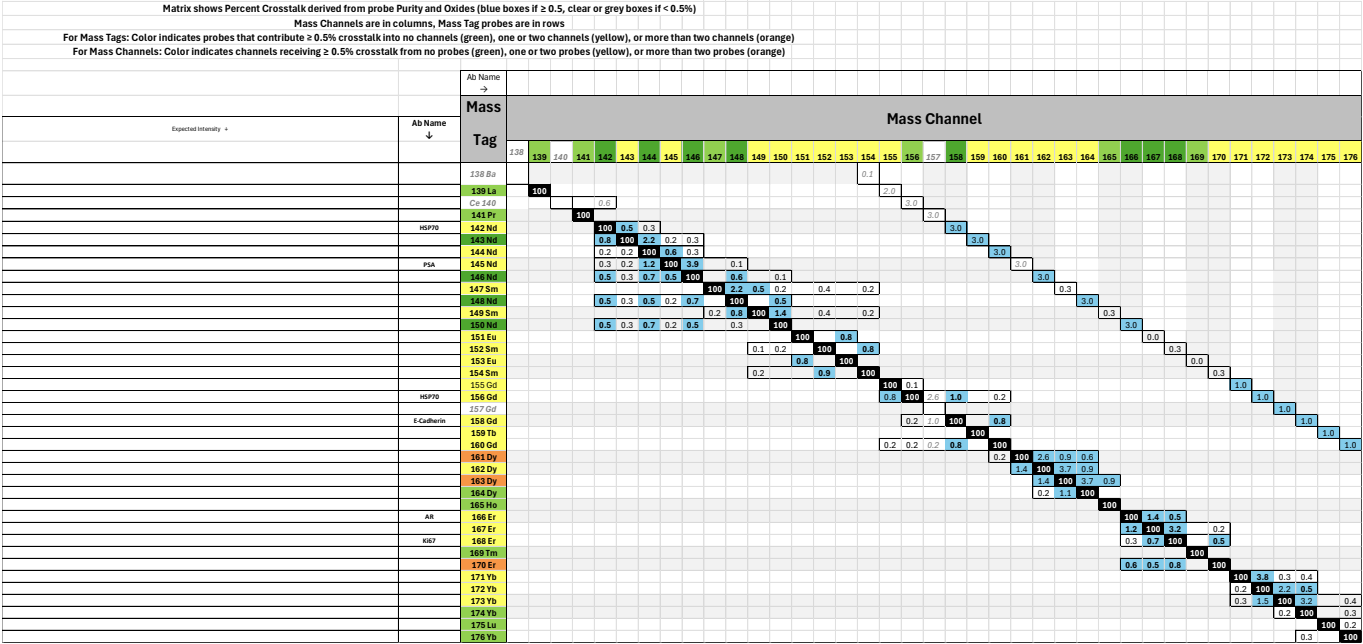
Supplementary Table 1: Binding energy of ASR603 with human N-terminal domain of androgen receptor protein along with interacting residues. Induced-fit docking revealed a top pose with a binding free energy of –54.44 kcal/mol

S. No	Ligand	MM/GBSA ΔG (kcal mol ⁻¹)	Physically Interacting Residue	Spatial Interacting Residue
1	ASR603	-54.44	ASN-25	ALA-22, LEU-26, SER-29, VAL-243, CYS-240, LEU- 239, ALA-236, and ILE- 232

Supplementary Table 2: Antibodies conjugated with lanthanides and used for Imaging Mass cytometry with a planned matrix

Isotope	Mass Channel	Marker	Clone#	staining	stock concentration
142Nd	142	HSP70	3A3	10ug/ml	1mg/ml
156Gd	156	HOXB13	polyclonal	10ug/ml	0.5mg/ml
145Nd	145	PSA	clone A67-B/E3	10ug/ml	1mg/ml
158Gd	158	E-Cadherin	24E10	10ug/ml	0.5mg/ml
166Er	166	AR	polyclonal	10ug/ml	1mg/ml
168Er	168	Ki67	B56	10ug/ml	0.5mg/ml
		Ir DNA-Intercalator			125uM
		Ir DNA-Intercalator			125uM

Ab	mg/ml (100ul)	1mg/ml final conc (ul)	dead vol (column)	Final concentration
HOXB13	0.721	72.1	10	62.1
HSP70	0.439	43.9	10	33.9
TRAF4	0.833	83.3	10	73.3
PSA	0.229	22.9	10	12.9
AR	0.669	66.9	10	56.9



Supplementary Table 3: AR target gene extracted from CHIP-Seq database (GEO database: SRX11222414) for gene-gene correlation analysis

Target_genes	SRX11222414 22Rv1
TRIM49D2	1178
TRIM49D1	1178
FAM107B	1507
CYP3A43	2253
GREB1	1060
C1orf116	810
ZNF341	1316
EPN1	642
UGT2B15	1459
SMARCD2	593
EVA1C	1432
SPIDR	1570
NFKBIA	1801
UGT2B10	719
CROT	1237
DNPEP	709
NFIB	1110
DHX36	1812
MAP3K6	700
FKBP5	2213
SLC13A1	435
C4orf51	802
ZNF547	294
TRAPPC2B	294
PRAME	300
SPINT3	875
CCN5	372
PGC	552
ASPH	610
DAAM1	308
COBLL1	576
DNAJB3	539
CHRNA2	505
SCNN1A	962
NAT1	604
SMAD4	326
AMTN	407
EHF	1205
CDKN1A	432
HK1	283
GLYATL1	630
SPIC	1677

LRRC36	308
HOXC6	269
HOXC4	269
UGT2B11	579
GOLPH3	253
FGD4	528
KAT8	510
RFESD	344
METTL7A	711
SLC45A4	404
C15orf61	579
SLF1	275
KIAA0825	275
TRIQK	302
LTBR	962
HOPX	559
TLE3	488
EPHA7	298
PKP1	555
MTARC1	317
FZD1	280
RABGAP1L	250
MTUS1	716
ANP32E	348
ATF6	1018
HEPACAM2	292
CYP27A1	260
F2	411
ADD3	383
SLC44A4	421
AASS	370
FAM13A	520
HOXA10	358
PRICKLE2	1072
NRTN	279
CYP51A1	254
HSPG2	1242
SQSTM1	268
GBA	299
AHCY	368
SLC31A2	537
MT2A	250
SELENBP1	311
FEZF1	829
SLC44A2	255

SERPINB6	326
RCOR3	266
PRKAA1	337
GPRC5C	364
MXRA8	282
HES1	479
SOCS2	910
SEMA3E	362
TARP	301
SELENOP	250
ZFPM1	303
RAB4A	476
WDR24	405
TSPAN8	712
N4BP2	352
ANKRD53	256

Supplementary Table 4: Metabolic profile from spatially resolved mass spectrometry imaging (MSI) of ROIs from both control and ASR603-treated tumor that matched the ROIs previously analyzed via CyTOF

			Sample ID	Control 1	Treatment 1	Control 2	Treatment 2	Control 3	Treatment 3
			Treatment	Vehicle	ASR603	Vehicle	ASR603	Vehicle	ASR603
			AR expression	High	Low	High	Low	High	Low
Metabolite	Symbol	Name							
Metabolite	C3H4O2	Pyruvaldehyde		0.16159	0.193324	0.142925	0.116658	0.157093	0.239151
Metabolite	C3H6O2	Propionic acid		0.097951	0.162106	0.021009	0.19292	0.112278	0.043682
Metabolite	C2H5NO2	Glycine		0.1281	0.170593	0.039262	0.116951	0.135584	0.175567
Metabolite	C6H6	Benzene		0.879974	0.688729	0.718981	0.45572	0.855071	0.60813
Metabolite	HO3S	Hydrogen sulfite		24.76196	41.32062	23.81787	33.14532	26.65474	35.72116
Metabolite	HO3S	Hydrogen sulfite		6.821421	10.65644	6.59318	8.126444	5.989994	8.482756
Metabolite	C5H8O	Methyl propenyl ketone		0.790464	1.149711	0.81853	0.822663	0.707954	0.757658
Metabolite	C4H7NO	2-Pyrrolidinone		0.398594	0.348975	0.278342	0.275754	0.419888	0.335306
Metabolite	C4H6O2	Diacetyl		1.564826	1.802323	1.406851	1.144223	1.801676	1.30663
Metabolite	C5H10O	Iso-Valeraldehyde		0.202679	0.18979	0.207049	0.239242	0.242067	0.279208
Metabolite	C4H8O2	Acetoin		0.415174	0.637483	0.344497	0.930793	0.306604	0.557395
Metabolite	C3H7NO2	L-Alanine		0.295083	0.405798	0.28177	0.59559	0.323335	0.457966
Metabolite	C3H6O3	L-Lactic acid		17.9497	20.21662	16.90158	24.36798	17.42198	24.581
Metabolite	C3H8O3	Glycerol		0.070062	0.078215	0.044827	0.058473	0.039013	0.023149
Metabolite	C6H7N	Aniline		0.839447	1.098963	0.78721	0.943275	0.662884	1.121557
Metabolite	C6H6O	Phenol		4.810853	5.54665	4.690662	5.014789	3.737299	3.925041
Metabolite	C5H5NO	2-Hydroxypyridine		0.634833	0.654983	0.611003	0.447181	0.526345	0.83925
Metabolite	H3O4P	Phosphoric acid		18.09106	23.9365	16.64749	21.90598	15.11369	21.15839
Metabolite	C6H10O	Cyclohexanone		0.455974	0.73233	0.330202	0.351524	0.274819	0.362356
Metabolite	C5H8O2	Tiglic acid		0.384184	0.674584	0.303908	0.447615	0.445841	0.605488

Metabolite	C6H12O	3-Hexanone		0.158417	0.232061	0.111609	0.202454	0.217689	0.16679
Metabolite	C4H7NO2	1-Aminocyclopropanecarboxylate		1.301032	1.134535	1.314328	1.126782	1.438905	0.866381
Metabolite	C4H6O3	Succinic acid semialdehyde		0.862161	1.064291	1.145013	0.678733	0.807024	0.849253
Metabolite	C5H10O2	Valeric acid		0.409089	0.697621	0.162883	0.540256	0.157373	0.68413
Metabolite	C4H9NO2	Gamma-aminobutyric acid		0.278061	0.485767	0.117281	0.380103	0.127313	0.479729
Metabolite	C4H8O3	Alpha-hydroxyisobutyric acid		0.163916	0.179071	0.256424	0.400377	0.177374	0.198053
Metabolite	C3H7NO3	L-Serine		0.104977	0.126673	0.092278	0.233918	0.032408	0.120826
Metabolite	C7H6O	Benzaldehyde		0.256293	0.231414	0.246187	0.125027	0.175973	0.330649
Metabolite	C7H6O	Benzaldehyde		0.136037	0.171048	0.055312	0.164758	0.096427	0.212723
Metabolite	C6H4O2	Quinone		0.084812	0.109735	0.1482	0.050247	0.062884	0.047408
Metabolite	C7H8O	p-Cresol		0.418674	0.546788	0.473581	0.433121	0.382697	0.427949
Metabolite	C6H4O2	Quinone		1.920684	2.252823	2.034823	2.558851	1.60527	2.281013
Metabolite	C6H7NO	4-Aminophenol		1.264403	1.413179	1.51474	1.14019	1.640236	1.030894
Metabolite	C7H8O	p-Cresol		0.155291	0.199269	0.134283	0.313457	0.243691	0.293989
Metabolite	C6H6O2	Pyrocatechol		0.743474	0.954989	0.795093	0.870498	0.775974	0.57526
Metabolite	C5H5NO2	Pyrrrole-2-carboxylic acid		1.174122	1.256086	0.885817	1.277849	1.081974	1.187916
Metabolite	C4H5N3O	Cytosine		1.929008	2.259512	2.142737	2.809554	2.464906	2.754108
Metabolite	C5H4O3	Pyromucic acid		0.391914	0.524543	0.433325	0.429872	0.394985	0.452184
Metabolite	C4H4N2O2	Uracil		2.451569	2.642928	2.57167	2.635094	2.656224	3.004034
Metabolite	C5H9N3	Histamine		0.365522	0.646768	0.153268	0.398358	0.313533	0.614508
Metabolite	C4H7N3O	Creatinine		0.247924	0.275858	0.141756	0.117596	0.136148	0.22367
Metabolite	C2HF3O2	Trifluoroacetic Acid		5.039485	9.889263	6.151494	12.70516	4.912167	10.94387
Metabolite	C4H6N2O2	Dihydrouracil		1.999577	2.416389	2.312456	2.752054	1.956992	2.836011
Metabolite	C4H7N3O	Creatinine		0.232313	0.3367	0.226003	0.122464	0.038545	0.296002
Metabolite	C7H14O	4-Heptanone		0.137171	0.162462	0.11595	0.08917	0.15732	0.189266
Metabolite	C5H9NO2	L-Proline		0.425744	0.464482	0.350712	0.491996	0.314327	0.826326
Metabolite	C4H4O4	Fumaric Acid		0.270263	0.335287	0.263262	0.323002	0.133712	0.283126
Metabolite	C5H8O3	Levulinic acid		1.283285	1.729515	1.37856	1.364331	1.321096	1.516351
Metabolite	C6H12O2	Isocaproic acid		0.335574	0.419707	0.147903	0.362043	0.113024	0.316923
Metabolite	C4H7NO3	Acetylglycine		0.486597	0.571492	0.264491	0.62726	0.374704	0.615663
Metabolite	C8H7N	Indole		24.95416	34.1076	24.90987	31.3966	24.17119	30.10591
Metabolite	C4H6O4	Succinic acid		0.331494	0.585242	0.535715	0.508103	0.283125	0.725635
Metabolite	C3H7N3O2	Guanidoacetic acid		1.469847	1.76916	1.47096	1.721114	1.551021	2.217965
Metabolite	C4H9NO3	L-Homoserine		0.74689	1.004329	0.762641	0.923791	0.712138	0.991553
Metabolite	C4H8O4	Erythrose		0.509923	0.681884	0.257668	0.497077	0.664984	0.583828
Metabolite	C8H8O	Phenylacetaldehyde		0.797238	1.056491	0.549135	0.935321	0.605277	1.247179
Metabolite	C4H7NO	2-Pyrrolidinone		0.050848	0.101643	0.003653	0.022877	0.036985	0
Metabolite	C7H7NO	Benzamide		1.306499	1.872418	1.278425	1.95387	1.245771	2.052522
Metabolite	C8H8O	Phenylacetaldehyde		0.114725	0.120209	0.094488	0.200253	0.137554	0.341197
Metabolite	C8H11N	N,N-Dimethylaniline		0.030856	0.045083	0.053523	0.023096	0	0.004762
Metabolite	C7H6O2	Benzoic acid		8.368784	7.2783	7.806218	5.497557	6.393098	5.506094
Metabolite	C5H10O	Iso-Valeraldehyde		0.244986	0.308852	0.090447	0.351935	0.303382	0.251195
Metabolite	C8H10O	4-Ethylphenol		0.266025	0.406607	0.275739	0.292141	0.288611	0.28159

Metabolite	C6H5NO2	Nicotinic acid		0.438012	0.517564	0.267824	0.477687	0.792642	0.421403
Metabolite	C6H5NO2	Nicotinic acid		0.334306	0.325937	0.402267	0.27	0.299054	0.356918
Metabolite	C7H8O2	4-Methylcatechol		0.614439	0.743003	0.40776	0.64123	0.468619	0.610755
Metabolite	C2H7NO3S	Taurine		101.2667	133.0891	94.67129	130.4628	94.26434	133.7395
Metabolite	C5H7N3O	5-Methylcytosine		0.394328	0.424362	0.788086	0.343979	0.483872	0.456982
Metabolite	C2H8NO3P	(2-Aminoethyl)phosphonate		0.838938	1.108505	0.459324	1.125298	1.122954	1.303119
Metabolite	C5H6N2O2	Thymine		3.305359	4.112799	3.379969	4.768885	3.230421	4.304528
Metabolite	C5H8N2O2	Dihydrothymine		3.699757	3.975111	3.235018	4.413077	3.452142	4.67864
Metabolite	C8H16O	Octanal		0.201683	0.25072	0.145356	0.373519	0.234155	0.228023
Metabolite	C5H7NO3	Pyroglutamic acid		4.460157	5.23106	4.186209	5.799407	4.340263	5.032649
Metabolite	C6H11NO2	Pipecolic acid		0.466549	0.350596	0.5821	0.458301	0.666389	0.409172
Metabolite	C5H6O4	Itaconic acid		0.286132	0.377073	0.246353	0.466986	0.093901	0.343859
Metabolite	C7H14O2	Heptanoic acid		0.374023	0.646211	0.434679	0.338736	0.32992	0.573605
Metabolite	C6H14N2O	N-Acetylputrescine		0.486513	0.712878	0.425306	0.748489	0.336765	0.834657
Metabolite	C9H9N	3-Methylindole		33.34938	46.12073	33.28786	43.56536	31.0456	41.13126
Metabolite	C6H13NO2	L-Leucine		0.472507	0.669173	0.429297	0.568281	0.399259	0.749708
Metabolite	C5H8O4	Methylsuccinic acid		1.259711	1.75768	0.97803	1.308205	1.241001	1.637104
Metabolite	C4H9N3O2	Creatine		2.105205	2.384212	1.594327	2.489398	2.001883	1.956906
Metabolite	C5H12N2O2	Ornithine		0.395022	0.563986	0.333382	0.603719	0.217639	0.204706
Metabolite	C5H5N5	Adenine		40.39831	52.59111	50.62321	60.77856	46.33786	54.04231
Metabolite	C5H4N4O	Hypoxanthine		0.793732	1.025495	0.751708	1.158119	1.114241	1.157485
Metabolite	C8H8O2	Phenylacetic acid		1.45397	1.881798	1.568064	1.678613	1.556903	1.451716
Metabolite	C4H7NO2	1-Aminocyclopropanecarboxylate		2.476316	3.302035	2.671735	3.623669	2.641487	3.222818
Metabolite	C7H7NO2	p-Aminobenzoic acid		1.575141	1.97544	1.897146	1.580503	1.513797	1.985817
Metabolite	C4H6O3	Succinic acid semialdehyde		2.519084	2.657913	1.881612	2.754032	2.792967	2.635392
Metabolite	C7H6O3	Salicylic acid		8.046651	7.481367	7.0239	5.835555	7.743215	6.46006
Metabolite	C6H6N2O2	Urocanic acid		0.551489	0.781553	0.492681	0.783022	0.428303	0.658919
Metabolite	C8H10O2	Tyrosol		0.334388	0.534247	0.247218	0.476112	0.43232	0.305735
Metabolite	C8H10O2	Tyrosol		0.244881	0.279823	0.277945	0.190951	0.065968	0.302669
Metabolite	C2H5O5P	Phosphonoacetate		0.699635	0.704712	0.595868	0.982815	0.645549	0.491152
Metabolite	C6H8N2O2	1,3-Dimethyluracil		1.183754	1.261093	0.909633	1.35631	0.862993	1.427992
Metabolite	C5H14NO	Choline		0.374337	0.616076	0.198006	0.305895	0.198301	0.660668
Metabolite	C2H8NO4P	O-Phosphoethanolamine		5.447458	5.871227	5.086945	6.88287	5.438948	5.330401
Metabolite	C8H14O2	2-Octenoic acid		0.564262	0.839695	0.430565	0.467748	0.484367	0.513639
Metabolite	C7H12O3	4-Hydroxycyclohexylcarboxylic acid		3.255048	3.650281	3.879119	3.374553	3.591284	3.291791
Metabolite	C8H16O2	Valproic acid		1.429543	1.972364	1.375048	2.457695	1.429101	2.407262
Metabolite	C5H11N3O2	4-Guanidinobutanoic acid		0.972587	1.093348	0.868519	1.011443	1.168996	0.926452
Metabolite	C6H10O4	Methylglutaric acid		1.553828	1.896192	1.539888	1.597842	1.515844	2.048005
Metabolite	C9H10N2	5,6-Dimethylbenzimidazole		4.084116	4.995937	4.526222	5.017305	3.750533	5.412909
Metabolite	C6H14N2O2	L-Lysine		1.277125	1.754521	1.614949	1.639083	1.557967	1.484759
Metabolite	C5H9NO4	L-Glutamic acid		4.062603	6.106211	3.914031	5.079298	3.78018	5.596251
Metabolite	C9H9NO	Indole-3-carbinol		4.309234	5.696332	4.465497	5.0825	3.634235	5.018169
Metabolite	C5H4O3	Pyromucic acid		0.348597	0.519726	0.451185	0.167627	0.281451	0.406431

Metabolite	C9H8O2	Trans-Cinnamic acid		0.615176	0.853622	0.432281	0.888374	0.472031	0.602971
Metabolite	C6H7N5	6-Methyladenine		0.767749	0.772424	1.124587	0.79881	0.818132	1.081459
Metabolite	C9H10O2	Hydrocinnamic acid		0.812148	1.0688	0.524184	0.982954	0.759675	1.057868
Metabolite	C10H14O	Thymol		1.030799	0.989847	0.83958	0.793575	0.890537	0.50654
Metabolite	C5H5N5O	Guanine		32.54195	39.19051	41.77238	48.35362	41.79477	45.16832
Metabolite	C8H9NO2	2-Phenylglycine		0.748548	0.909942	0.524136	1.052984	0.666508	0.790797
Metabolite	C4H4O4	Fumaric Acid		0.596268	0.677979	0.533502	0.578617	0.654908	0.865224
Metabolite	C8H8O3	4-Hydroxy-3-methylbenzoic acid		3.116567	3.859739	3.108727	3.775192	3.490436	3.87496
Metabolite	C10H16O	Perillyl alcohol		0.190322	0.25629	0.277107	0.207143	0.085165	0.091575
Metabolite	C3H7NO4S	3-Sulfinoalanine		2.146647	3.150042	2.646544	3.625022	2.780383	3.125056
Metabolite	C4H7NO3	Acetyl glycine		0.563746	0.706863	0.6355	0.516135	0.636493	0.807855
Metabolite	C7H7NO3	3-Hydroxyanthranilic acid		0.45503	0.534852	0.299172	0.573396	0.380277	0.59026
Metabolite	C8H8O3	4-Hydroxy-3-methylbenzoic acid		0.487705	0.559572	0.379874	0.517473	0.565872	0.886819
Metabolite	C8H11NO2	Dopamine		0.515764	0.578601	0.866334	0.635506	0.657885	0.80296
Metabolite	C4H6O4	Succinic acid		37.74592	38.64493	28.49639	40.094	32.64549	45.31629
Metabolite	C7H6O4	2,3-Dihydroxibenzoic acid		0.897013	1.034779	1.273948	0.947644	0.748014	0.877961
Metabolite	C5H10O3	2-Hydroxy-3-methylbutyric acid		0.804252	0.875358	0.787517	1.081541	0.82987	0.872856
Metabolite	C4H10N2O2	2,4-Diaminobutyric acid		1.916907	2.368664	1.473886	2.569487	1.555445	2.132708
Metabolite	C5H7N5O	FAPy-adenine		1.44613	1.495301	1.206624	1.755356	1.426414	1.271659
Metabolite	C10H18O	Eucalyptol		0.151224	0.222905	0.293892	0.284536	0.060262	0.129856
Metabolite	C10H9NO	Indoleacetaldehyde		63.50208	83.31386	59.82421	75.57278	62.97002	69.87406
Metabolite	C9H7NO2	Indole-3-carboxylic acid		10.58797	13.39042	10.4115	11.24766	12.74832	12.20231
Metabolite	C10H8O2	1,5-Dihydroxynaphthalene		1.858762	2.165302	1.688891	1.827085	1.539643	2.452191
Metabolite	C6H5N5O	Pterin		1.779497	2.275215	1.781698	1.904863	2.172258	2.213227
Metabolite	C9H8O3	m-Coumaric acid		0.46618	0.625736	0.409666	0.821203	0.456	0.464695
Metabolite	C6H5N5O	Pterin		0.974568	1.263667	1.330946	1.08743	0.736755	1.214091
Metabolite	C10H12O2	2-Phenylbutyric acid		0.535439	0.767568	0.616965	0.579168	0.493135	0.644826
Metabolite	C6H4N4O2	Lumazine		0.803554	1.102826	0.434553	0.887641	0.931804	1.024039
Metabolite	C6H7N5O	7-Methylguanine		1.669871	1.602654	2.217439	2.530531	2.743515	1.816961
Metabolite	C9H11NO2	L-Phenylalanine		0.516556	0.654479	0.500561	0.66377	0.358318	0.360605
Metabolite	C10H12O2	2-Phenylbutyric acid		0.239525	0.291715	0.286052	0.122826	0.313025	0.351722
Metabolite	C5H6O4	Itaconic acid		0.431362	0.617254	0.38943	0.470753	0.451267	0.665112
Metabolite	C8H6O4	Terephthalic acid		2.295808	1.766185	1.960543	1.227067	1.745463	1.217489
Metabolite	C6H10O3	2-Methyl-3-ketovaleric acid		0.396022	0.458559	0.330624	0.470576	0.671588	0.415089
Metabolite	C9H10O3	4-Methoxyphenylacetic acid		0.552203	0.681421	0.54581	0.536709	0.707198	0.582524
Metabolite	C6H7N5O	7-Methylguanine		0.783547	0.660709	0.846391	0.685431	1.051372	0.533411
Metabolite	C10H14O2	Perillic acid		0.374579	0.56973	0.341974	0.329242	0.409443	0.359514
Metabolite	C8H18O	Octanol		0.240584	0.277023	0.268452	0.303555	0.185044	0.261486
Metabolite	C8H6O4	Terephthalic acid		0.620662	0.686562	0.582851	0.762252	0.726585	0.739616
Metabolite	C8H9NO3	Pyridoxal		0.868169	0.871029	0.504718	0.616924	1.17106	0.695596
Metabolite	C9H10O3	4-Methoxyphenylacetic acid		1.130019	1.264703	0.839867	1.408816	0.963313	1.500996
Metabolite	C9H13NO2	Phenylephrine		0.471079	0.55864	0.315179	0.485981	0.364778	0.511757
Metabolite	C10H14O2	Perillic acid		0.21665	0.264976	0.112122	0.321679	0.118402	0.134913
Metabolite	C6H12O3	Leucinic acid		1.176432	1.236741	1.004995	0.894936	0.746586	1.434786

Metabolite	C8H12N2O2	Pyridoxamine		0.88591	0.975951	1.345155	1.126329	0.767218	0.709564
Metabolite	C4H7NO4	L-Aspartic acid		0.748165	0.816118	0.711078	0.928519	0.599481	0.747297
Metabolite	C8H8O4	Isovanillic acid		0.792125	0.946815	0.619746	0.887953	0.756912	0.765165
Metabolite	C8H11NO3	Pyridoxine		1.857055	2.048265	1.285954	1.804167	1.979022	1.630974
Metabolite	C9H12O3	1,3,5-Trimethoxybenzene		0.63276	0.703707	0.449924	0.703606	0.476768	0.779342
Metabolite	C8H10O4	3,4-Dihydroxyphenylglycol		1.860139	2.086488	1.69306	2.007746	1.353485	2.267432
Metabolite	C5H4N4O	Hypoxanthine		5.864785	6.589675	4.215846	6.501589	5.01905	6.592995
Metabolite	C10H20O2	Capric acid		5.821392	6.854224	7.418412	6.44527	5.731633	8.468101
Metabolite	C7H9N2O	1-Methylnicotinamide		34.65901	45.56156	32.13389	37.35949	29.16969	38.97632
Metabolite	C10H7NO2	Quinaldic acid		78.83607	101.6922	71.66364	91.06291	74.82874	87.67805
Metabolite	C5H9N3O4	Guanidinosuccinic acid		11.48411	14.26204	12.63942	13.48926	10.2588	11.50843
Metabolite	C10H12N2O	Serotonin		3.000175	3.597571	3.143172	3.383112	2.908385	3.394228
Metabolite	C10H11NO2	5-Hydroxytryptophol		1.041907	1.265871	0.783821	1.319614	0.751581	1.295284
Metabolite	H4O7P2	Pyrophosphoric Acid		1.816551	2.265116	1.334076	2.046242	1.35976	2.21262
Metabolite	C6H6O4	Cis,cis-Muconic acid		5.677898	8.589798	5.556695	8.406251	6.073471	7.690907
Metabolite	C8H14O2	2-Octenoic acid		1.193643	1.589156	1.267975	1.322477	0.930569	1.649769
Metabolite	C11H14O2	5-Phenylvaleric acid		3.114648	2.683022	2.820236	2.688284	2.955038	2.619233
Metabolite	C5H9NO4S	(S)-Carboxymethyl-L-cysteine		0.301912	0.371417	0.242437	0.406154	0.392838	0.348368
Metabolite	C6H5N5O2	Isoxanthopterin		0.449408	0.519278	0.528716	0.434107	0.335083	0.426659
Metabolite	C9H9NO3	Hippuric acid		0.570831	0.604307	0.503555	0.44748	0.423464	0.410203
Metabolite	C6H13NO5	Glucosamine		0.439909	0.417814	0.523809	0.548664	0.430816	0.43629
Metabolite	C6H8O4	3-Hexenedioic acid		1.219716	1.243073	1.415556	1.068884	1.445231	1.246016
Metabolite	C8H8N2O3	Nicotinuric acid		0.602807	0.706408	0.444609	0.704384	0.752639	0.465837
Metabolite	C8H16O2	Valproic acid		0.702099	0.576357	0.867942	0.539528	0.385365	0.683612
Metabolite	C9H8O4	Aspirin		1.168291	1.437588	0.912033	1.465707	0.942937	1.487888
Metabolite	C12H8N2	Phenazine		3.722326	4.801662	3.850209	5.103762	3.479386	4.515272
Metabolite	C13H10O	Benzophenone		2.447318	2.76602	2.837027	2.863554	1.945243	3.113654
Metabolite	C13H10O	Benzophenone		14.89325	20.25245	14.39754	20.89016	15.24527	18.50978
Metabolite	C5H15NO4P	Phosphorylcholine		2.917158	3.204496	2.71742	3.6846	2.714114	2.978704
Metabolite	C9H10O2	Hydrocinnamic acid		3.6227	4.620591	3.025341	3.38796	3.827659	3.966003
Metabolite	C10H14O	Thymol		57.66231	73.656	51.22007	67.41999	53.32848	66.82623
Metabolite	C11H9NO2	Indoleacrylic acid		2.202266	2.369155	1.916219	1.71619	1.696957	2.203079
Metabolite	C9H13NO	Phenylpropanolamine		34.89092	45.73122	35.91779	39.29585	33.4464	45.50719
Metabolite	C9H16O4	Azelaic acid		3.250794	5.296259	1.361425	2.791536	1.941325	2.867304
Metabolite	C10H7NO3	Kynurenic acid		23.7066	33.23404	21.35045	24.8787	22.48485	27.54372
Metabolite	C7H11NO5	N-Acetylglutamic acid		109.2171	146.422	107.4583	127.0007	101.0312	130.503
Metabolite	C10H7NO3	Kynurenic acid		7.06800	9.023099	6.929269	8.414183	6.910922	7.472848
Metabolite	C10H9NO3	5-Hydroxyindoleacetic acid		6.64964	8.361771	6.37675	7.222647	7.63438	7.146955
Metabolite	C11H12O3	Myristicin		1.06449	1.45301	0.90462	1.457726	0.710997	1.031141
Metabolite	C7H13NO3	Isovalerylglycine		0.40179	0.526863	0.491368	0.550012	0.107832	0.465091
Metabolite	C8H17NO2	DL-2-aminooctanoic acid		0.729483	0.800446	0.525393	0.6923	0.46512	0.676639
Metabolite	C6H8O5	Oxoadipate		2.60542	3.408711	2.438601	2.847664	1.929925	3.242677
Metabolite	C8H16O3	Hydroxyoctanoic acid		1.225455	1.36083	1.363544	1.487207	1.284073	1.497317
Metabolite	C6H11NO4	Aminoadipic acid		11.72845	10.79335	10.32863	14.16326	10.2809	12.92706

Metabolite	C12H22O2	5-Dodecenoic acid		0.729627	0.885923	0.63124	1.060673	0.843896	1.537841
Metabolite	C7H9N5	6-Dimethylaminopurine		1.000813	1.300333	0.798937	1.001291	1.223744	1.457381
Metabolite	C5H15N2O4P	Glufosinate-ammonium		1.617492	1.836994	2.075721	1.759026	1.80045	2.210438
Metabolite	C10H14O4	Guaifenesin		1.876898	2.033293	2.129032	2.079767	1.506272	2.070891
Metabolite	C12H24O2	Dodecanoic acid		8.143675	10.34521	9.859406	10.03221	8.441543	9.624538
Metabolite	C10H15NO	Pseudoephedrine		1.311638	1.538539	1.375044	1.487823	1.086256	1.960033
Metabolite	C6H6N4O2	7-Methylxanthine		12.02992	1.797452	16.21133	1.672188	14.66729	1.637056
Metabolite	C10H14O2	Perillic acid		5.328823	7.261998	4.486895	6.809774	5.343595	6.29625
Metabolite	C12H9ClO	2-Hydroxy-5-chlorobiphenyl		1.575843	1.672179	2.396256	2.282494	1.758075	1.505842
Metabolite	C9H12O3	1,3,5-Trimethoxybenzene		27.47665	36.77582	24.28834	34.83897	29.7345	31.79753
Metabolite	C10H7NO4	Xanthurenic acid		2.004663	2.311092	2.119729	2.345141	2.109131	2.036937
Metabolite	C8H15NOS2	Lipoamide		7.044075	9.39562	6.682405	8.083843	6.020585	8.355997
Metabolite	C10H12N2O3	L-Kynurenine		1.249917	1.636853	1.714361	1.684891	1.332085	1.288876
Metabolite	C10H12N2O3	L-Kynurenine		8.281167	11.23762	8.422826	9.362286	8.426014	11.58757
Metabolite	C6H8O6	D-Glucurono-6,3-lactone		4.361266	5.079388	3.245667	4.781973	4.256118	4.504245
Metabolite	C11H14O2	5-Phenylvaleric acid		5.178964	6.485598	6.202876	5.645051	4.585824	5.897495
Metabolite	C6H13NO5	Glucosamine		9.788341	12.7552	8.729466	11.21682	8.298094	10.90933
Metabolite	C7H8N4O2	Theobromine		1.006579	1.501858	1.231893	0.970618	1.220447	1.13377
Metabolite	C11H20O4	Undecanedioic acid		0.501522	0.980176	0.469232	0.615167	0.417058	0.470022
Metabolite	C12H14N2O2	N-Acetylserotonin		0.520284	0.660719	0.357741	0.626447	0.458227	0.584983
Metabolite	C9H13NO3	Epinephrine		0.55619	0.683909	0.531998	0.606146	0.471868	0.616041
Metabolite	C5H15NO4P	Phosphorylcholine		0.912097	1.1561	0.778102	1.065684	0.67289	1.34541
Metabolite	C11H12N2O3	5-Hydroxy-L-tryptophan		0.379483	0.506543	0.344862	0.317363	0.4858	0.307804
Metabolite	C12H14O4	Diethyl Phthalate		11.23987	7.587709	9.705743	6.667312	9.361609	7.45575
Metabolite	C9H20N2O2	N,N,N-Trimethyllysine		1.220225	1.115709	1.099021	0.866869	1.236695	1.205417
Metabolite	C7H11NO5	N-Acetylglutamic acid		0.924532	1.052554	0.759284	0.97187	0.837806	0.931354
Metabolite	C7H15N3O3	Homocitrulline		1.356732	1.655195	1.749991	1.620121	1.166799	1.82237
Metabolite	C7H14N2O4	Diaminopimelic acid		1.593133	1.882793	1.65737	1.889327	1.136953	1.708188
Metabolite	C14H28O2	Myristic acid		27.5971	21.58644	24.59196	16.97812	25.54222	17.21674
Metabolite	C9H12N2O5	Deoxyuridine		1.685778	1.387617	1.405477	1.496273	1.528648	1.287927
Metabolite	C14H14O3	Naproxen		9.711349	5.429649	12.85837	5.951703	11.67183	5.552752
Metabolite	C9H10Cl2N2O	Diuron		0.253965	0.353212	0.084751	0.281073	0.217254	0.15615
Metabolite	C6H12O7	Gluconic acid		0.484412	0.497545	0.819365	0.491546	0.550934	0.520833
Metabolite	C9H17NO4	L-Acetylcarnitine		0.788819	0.780626	0.791239	0.63835	0.921137	0.63891
Metabolite	C10H16N4O3	Anserine		1.052553	1.109226	1.172623	0.751518	0.839695	1.109278
Metabolite	C13H21NO3	Salbutamol		0.611212	0.596826	0.509931	0.728539	0.827228	0.699961
Metabolite	C15H30O2	Pentadecanoic acid		17.56594	19.00585	15.52525	13.38952	15.75705	13.41892
Metabolite	C9H13N3O5	Cytidine		0.740018	0.817518	0.803522	1.120284	0.933406	0.597637
Metabolite	C13H14N2O3	N-Acetyl-DL-tryptophan		1.193407	1.405205	0.894034	1.623925	1.617381	1.232634
Metabolite	C4H13NO7P2	Alendronic acid		0.32962	0.51424	0.38422	0.426139	0.249424	0.145757
Metabolite	C10H18N2O3	D-Desthiobin		1.095725	1.209494	1.004542	1.350242	0.858336	0.798054
Metabolite	C16H30O2	Palmitoleic Acid (16:1)		23.71785	21.90711	19.0892	14.13497	19.14446	14.75782
Metabolite	C15H10O4	Daidzein		0.683336	1.014313	0.712131	0.953804	0.647015	0.799157
Metabolite	C17H21NO	Diphenhydramine		0.596491	0.733043	0.540187	0.826941	0.416927	0.872228

Metabolite	C16H32O2	Palmitate		64.2262	99.04037	50.65106	45.90985	51.21745	51.58711
Metabolite	C10H15N3O5	5-Methylcytidine		1.215133	1.290756	1.006743	1.438583	1.02784	1.599007
Metabolite	C15H20O4	Abscisic Acid		0.354729	0.427075	0.299478	0.325601	0.193685	0.413994
Metabolite	C14H14O3	Naproxen		10.08996	11.15392	10.25582	12.84882	10.14604	13.55111
Metabolite	C20H12O	12-Hydroxybenzo(a)pyrene		2.238836	2.90636	2.194681	3.461231	2.830864	3.329205
Metabolite	C17H34O2	Heptadecanoic acid		4.884684	5.123834	4.493651	2.822623	3.682676	2.668031
Metabolite	C16H19ClN2	Chlorpheniramine		2.442768	2.994813	2.442914	2.890131	2.397037	2.823864
Metabolite	C19H24N2	Imipramine		1.057833	1.334935	0.668273	0.951275	1.051678	1.15929
Metabolite	C18H32O2	Linoleic acid		7.311625	5.875404	6.154376	3.804881	5.71374	4.747208
Metabolite	C18H34O2	Oleic acid		25.76889	22.85026	19.57698	13.5687	21.17846	13.52334
Metabolite	C18H36O2	Stearic acid		21.10962	24.11787	14.5473	13.21236	13.87211	13.85939
Metabolite	C12H20N4O2	Hexazinone		9.971004	12.63836	9.263517	11.07564	10.3588	13.1134
Metabolite	C16H30O2	Palmitoleic Acid (16:1)		0.299082	0.358687	0.397118	0.213823	0.202369	0.404929
Metabolite	C10H14N2O6	Ribothymidine		2.135138	3.169255	2.608549	2.968589	2.816704	3.817702
Metabolite	C12H13N3O4S	N-Acetyl-sulfamethoxazole		14.56062	21.23756	16.39557	22.71128	15.99534	23.10163
Metabolite	C12H13N3O4S	N-Acetyl-sulfamethoxazole		15.87006	22.48938	18.41388	24.37622	15.8383	23.09176
Metabolite	C10H13N2O7P	Thymidine 3',5'-cyclic monophosphate		2.933815	4.013967	2.146016	3.401793	2.412697	3.810895
Metabolite	C20H32O2	Arachidonic Acid (20:4)		5.317878	4.362554	4.278061	5.652152	4.33042	5.40039
Metabolite	C9H12N3O7P	Cytidine-2',3'-Cyclic Phosphate		1.067733	1.169823	1.182278	1.013504	0.780844	1.081599
Metabolite	C15H10O5	Genistein		1.328801	1.501006	1.659959	1.432693	1.125294	1.186219
Metabolite	C20H34O2	8,11,14-Eicosatrienoic acid		1.034288	0.922354	1.087151	1.00023	0.968193	1.066143
Metabolite	C9H14N3O7P	DCMP		0.61438	0.799689	0.512766	0.561952	0.467648	0.761396
Metabolite	C19H16O4	3-(Alpha-acetonylbenzyl)-4-hydroxycoumarin		2.870791	3.408189	3.502152	3.49304	2.872759	3.456047
Metabolite	C20H36O2	Eicosadienoic Acid (20:2)		0.428533	0.386642	0.468292	0.119188	0.281605	0.188766
Metabolite	C20H38O2	Paulinic acid (20:1)		1.170717	1.407461	0.996071	1.639339	0.696184	0.859611
Metabolite	C13H19N3O4	Pendimethalin		5.829165	7.331209	5.756907	6.359449	5.893992	7.016082
Metabolite	C20H32O3	11(12)-EET		0.65866	0.858128	0.639564	0.45712	0.577895	0.831679
Metabolite	C10H15N2O8P	5-Thymidylic acid		1.090636	1.517854	1.448343	1.591099	0.957657	1.200643
Metabolite	C9H14N3O8P	Cytidine monophosphate		1.055744	1.174897	0.972593	0.931497	1.297365	1.189539
Metabolite	C9H13N2O9P	Uridine 5'-monophosphate		1.399841	1.583011	1.073452	1.718999	1.201547	1.206722
Metabolite	C19H28O2	Testosterone		1.685579	1.757886	0.990112	1.326964	1.809048	1.634233
Metabolite	C19H32O2	5a-Androstane-3b,17b-diol		3.978598	4.205161	3.967365	5.337265	4.186068	5.368966
Metabolite	C20H32O4	Leukotriene B4		0.326277	1.162767	0.266276	0.360153	0.21988	0.37497
Metabolite	C22H42O2	Erucic acid		0.647871	0.496305	0.469852	0.271998	0.735394	0.603391
Metabolite	C10H14N5O7P	Adenosine monophosphate		3.48342	4.16961	3.399913	3.740807	3.386494	3.58495
Metabolite	C16H19N3O4S	Ampicillin		1.058911	1.363067	1.163282	1.524806	0.580311	1.370492
Metabolite	C21H30O5	Cortisol		4.055783	3.887468	3.912702	2.952382	3.849413	3.486207
Metabolite	C21H30O5	Cortisol		3.998787	3.948793	3.807113	3.198872	3.854007	3.275217
Metabolite	C20H32O6	Prostaglandin G2		0.984827	1.983528	0.400685	0.687689	0.341123	0.537977
Metabolite	C24H48O2	Tetracosanoic acid		0.225337	0.221161	0.23655	0.138183	0.179512	0.080763
Metabolite	C12H22O11	Cellobiose		0.872524	1.425933	0.85105	0.725605	0.852648	0.64781
Metabolite	C22H23ClN2O2	Loratadine		0.55159	0.662866	0.778123	0.462636	0.503559	0.696209
Metabolite	C12H12O12	Dehydro-L-(+)-ascorbic Acid Dimer		1.429853	1.892916	0.837427	1.435858	1.077348	1.70635
Metabolite	C14H20N6O5S	S-Adenosylhomocysteine		0.88243	1.223076	0.544624	0.865594	0.713484	0.686544

Metabolite	C10H15N5O10P2	ADP		1.24604 5	1.642917	1.13654 4	1.549415	0.85174 1	1.350471
Metabolite	C27H44O2	7-Ketocholesterol		0.36835 6	0.326086	0.25455 4	0.24563	0.20027 1	0.137362
Metabolite	C18H34N2O6S	Lincomycin		1.11478 4	1.275596	1.18489 2	0.898877	0.89120 6	1.124077
Metabolite	C10H15N5O11P2	Guanosine 5'-diphosphate		0.46089 7	0.502375	0.45234 4	0.459433	0.46826 4	0.610674
Metabolite	C23H46NO7P	LPE(18:1)		0.28263 6	0.46332	0.21014 8	0.421245	0.26837 8	0.427927
Metabolite	C18H32N6O7	Poly-DL-(alanine)6		1.14488 7	1.236834	1.02020 4	0.99598	1.12026 9	0.958363
Metabolite	C10H16N5O13P3	Adenosine triphosphate		0.04712 7	0.058673	0.03669 5	0.034357	0.06097 9	0.043224
Metabolite	C29H33ClN2O2	Loperamide		0.66500 9	0.74264	0.91546	0.718125	0.41234 2	0.740177
Metabolite	C27H44NO7P	LPE(22:6)		0.33808 2	0.291576	0.16501 4	0.471579	0.40274 8	0.268169

Supplementary Table 5. List of antibodies used in western blotting

Antibody Name	Company	Dilution
AR-FL	Cell signaling (CST#5153)	1:1000
AR-V7	Cell signaling (CST#196725)	1:1000
PSA	Cell signaling (CST#5365S)	1:1000
BAX	Cell Signaling (CST#2772S)	1:1000
BCL-XL	Cell Signaling (CST#2764S)	1:1000
β -Catenin	Cell Signaling (CST #8480S)	1:1000
C-Caspase 9	Cell Signaling (CST #9505S)	1:1000
C-PARP	Cell signaling (CST#5625S)	1:1000
E CADHERIN	Cell signaling (CST#3195S)	1:1000
LAMP1	Cell signaling (CST#9091S)	1:1000
LC3B	Cell signaling (CST#12513S)	1:1000
Survivin	Cell signaling (CST#2808S)	1:1000
Ubiquitin	Cell signaling (CST#43124)	1:1000
XIAP	Cell signaling ((CST#2045S)	1:1000
β -Actin	Cell signaling (CST#5125)	1:2000
Blocking condition: PVDF membranes are blocked with EveryBlot Blocking Buffer (Biorad#12010020).		
Primary antibodies are incubated overnight at 4°C.		
Secondary antibodies are incubated for one hour at room temperature.		

Supplementary Table 6: Primer Sequences for genes used in qPCR experiments.

Gene	Forward	Reverse
AR	5'-TCAGACAGTCAAGAATTCAGAGC-3'	5'-CGCACAGGTACTTCTGTTTCC-3'
PSA	5'-CCCACTGCATCAGGAACAA-3'	5'-ATATCGTAGAGCGGGTGTGG-3'
β -Actin	5'-CTCCTCCACCTTTGACGCTG-3'	5'-CATACCAGGAAATGAGCTTGACAA-3'

Supplementary Methods:

1) qPCR reaction:

Amplification was performed using the following cycling conditions: 95°C for 5 min, followed by 35 amplification cycles at 94°C for 30 s, and at 55°C for 30 s, with a final extension at 72°C for 7 min.

2) Plasma Stability:

2.1. Test Compound

Compound Name	MW	Purity (%)
ASR603	242.23	96.00

2.2. Test Compound Stock Solution and Working Solution Preparation

10 mM stock solution with DMSO and dilute to 200 µM working solution.

2.3. Plasma Information

Species	Anticoagulant
Mouse	Heparin sodium
Human	Heparin sodium

2.4. Assay Procedure

1) Add test compound working solution into the test plasma to a final concentration of 2 µM. Mix thoroughly.

2) Split each incubation mixture into 2 aliquots and incubate in a 37°C water bath for 0, 10, 30, 60, 120 min. (For positive control, the incubation times are 0, 30, 60, 120, 240 min).

3) Take 20 µL of each sample and add 300 µL quenching solution. Centrifuge at 5500g for 10 min.

4) Mix 150 µL of the supernatant with 150 µL water for LC-MS/MS analysis.

2.5. Data Analysis

The % remaining of test compound after incubation in plasma was calculated using following equation: % Remaining= 100 x (PAR at appointed incubation time / PAR at T0 time)
where PAR is the peak area ratio of analyte versus internal standard (IS)

2.6. LC-MS/MS Method

Mobile Phase

Mobile Phase A: 0.1%FA-H₂O

Mobile Phase B: Acetonitrile

Column

AQ-C18, (2.1 × 50 mm, 5 µm)

Compound	Ion Transition	
	Q1 Ion (m/z)	Q3 Ion (m/z)
ASR603	243.2	183.9

3) Ubiquitination analysis

3.1 Chemicals and Instrumentation

DL-dithiothreitol (DTT), iodoacetamide (IAA), formic acid (FA), acetonitrile (ACN) was purchased from Sigma (St. Louis, MO, USA). Trypsin from bovine pancreas was purchased from Promega

(Madison, WI, USA). Ultrapure water was prepared from a Millipore purification system (Billerica, MA, USA). An Ultimate 3000 nano UHPLC system coupled with a Q Exactive HF mass spectrometer (Thermo Fisher Scientific, USA) with an ESI nanospray source.

3.2 SDS-PAGE

- 1) Loading samples and protein marker into SDS-PAGE gel (12% separating gel) and make sure not to overflow. Then cover the top and connect the anodes.
- 2) Run the gel at 80 kV for 30 min. Then increase the voltage to 120 kV and run for 1 h.
- 3) Stain the SDS-PAGE gel with silver staining.

3.3 In-gel Digestion

- 1) Cut the gel slice from each gel into 1 mm³ cubes and transfer the gel cubes to a 1.5 mL microcentrifuge tube. Centrifuge the tube for 1-2 sec to spin the gel slice to the bottom of the tube. Add 1 mL 30 mM K₃Fe(CN)₆ : 100 mM Na₂S₂O₃=50:50. Remove the supernatant until the brown disappears. Stop the reaction by adding 200 µL of water. Discard the supernatant after 10 min. Add 1 mL of NH₄HCO₃ standing 30 min, and then remove the supernatant.
- 2) Add 500 µL of ACN and incubate for 30 min. The gel pieces should become opaque and stick together.
- 3) Remove the ACN and rehydrate the gel slice in 10 mM DTT. Add enough solution to completely cover the gel slice. Incubate at 56°C for 1 h.
- 4) Carefully remove the DTT and add 500 µL of ACN. Incubate for 10 min at room temperature.
- 5) Remove the ACN and add 50 mM IAA to cover the gel slice. Incubate for 30 min at room temperature in the dark.
- 6) Remove the IAA and add 500 µL of ACN to the gel slices. Incubate for 10 min at room temperature. Carefully remove the ACN solution.
- 7) Add enough trypsin digestion solution to cover the gel slices. Incubate the gel pieces on ice for 45 min. Add more digestion solution if all the initial solution is absorbed by the gel pieces. Then incubate overnight at 37°C.
- 8) Recover the supernatant and transfer into a fresh 1.5 mL microcentrifuge tube. Add 50 mM NH₄HCO₃/ACN (1:2, v/v) to cover gel slices. Incubate for 1 h at 37°C. Transfer the solution to the 1.5 mL microcentrifuge tube. Add 0.1% TFA and incubate for 30 min, and then add 50 mM NH₄HCO₃/ACN (1: 2, v/v) to cover the gel sections.
- 9) Combine the extracts and lyophilize the extracted peptides to near dryness.
- 10) Resuspend peptides in 20 µL of 0.1% formic acid before LC-MS/MS analysis.

3.4 Nano LC-MS/MS Analysis

3.4.1 NanoLC

Nanoflow UPLC: Ultimate 3000 nano UHPLC system (ThermoFisher Scientific, USA)

Nanocolumn: trapping column (PepMap C18, 100Å, 100 µm × 2 cm, 5 µm) and an analytical column (PepMap C18, 100Å, 75 µm × 50 cm, 2 µm)

Loaded sample volume: 1 µg

Mobile phase: A: 0.1% formic acid in water; B: 0.1% formic acid in 80% acetonitrile.

Total flow rate: 250 nL/min

LC linear gradient: from 2 to 8% buffer B in 3 min, from 8% to 20% buffer B in 56 min, from 20% to 40% buffer B in 37 min, then from 40% to 90% buffer B in 4 min.

3.4.2 Mass Spectrometry

The full scan was performed between 300-1,650 m/z at the resolution 60,000 at 200 m/z, the automatic gain control target for the full scan was set to 3e6. The MS/MS scan was operated in Top 20 mode using the following settings: resolution 15,000 at 200 m/z; automatic gain control target 1e5; maximum injection time 19ms; normalized collision energy at 28%; isolation window of 1.4 Th; charge state exclusion: unassigned, 1, > 6; dynamic exclusion 30 s.

3.5 Data Analysis

Three raw MS files were analyzed and searched against AR_NTD reference sequence (provided by customers) using PEAKS STUDIO 8.5. The parameters were set as follows: the protein modifications were carbamidomethylation (C) (fixed), oxidation (M) (variable), Ubiquitin (variable); the enzyme specificity was set to trypsin; the maximum missed cleavages were set to 2; the precursor ion mass tolerance was set to 10 ppm, and MS/MS tolerance was 0.5 Da.

4) Generation of AR-NTD Mutants

Synthetic gene was cloned into pcDNA3.1(-) vector by EcoRI/BamHI with a N-terminal 8xHis tag. Vector pcDNA3.1(-) is a mammalian expression vector with the CMV promoter. The MCS is in the reverse (-) orientation

4.1. Sequence of AR_NTD Mutant_1 (K301):

HHHHHHHHMEVQLGLGRVYPRPPSKTYRGAFQNLFSVREVIQNPGPRHPEAASAAPPGASL
LLLQQQQQQQQQQQQQQQQQQQQQQQQQQQETSPRQQQQQQGGEDGSPQAHRRGPTGYLVLDE
EQQPSQPQSALECHPERGCVPEPGAAVAASKGLPQQLPAPPDEDDSAAPSTLSLLGPTFPGLS
SCSADLKDILSEASTMQLLQQQQQEAVSEGSSSGRAREASGAPTSSKDNYLGGTSTISDNAKE
LCKAVSVSMGLGVEALEHLSPGEQLRGDCMYAPLLGVPPAVRPTPCAPLAECKGSLLDDDSAGR

STEDTAEYSPFKGGYTKGLEGESLGCSGSAAAGSSGTLELPSTLSLYRSGALDEAAAYQSRDY
YNFPLALAGPPPPPPPPHAPHARIKLENPLDYGSAAAAAAQCRYGDLASLHGAGAAGPGSGS
PSAAASSSWHTLFTAEEGQLYGPCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGEAGAVAPYGYTR
PPQGLAGQESDFTAPDVWYPGGMVSRVPYPSPCTCVKSEMGPWMDSYSGPYGDMRLETARD
HVLPIIDYFPPQKTCLICGDEASGCHYGALTGSGCKVFFKRAAEGKQKYLCASTRNDCTIDKFRR
KNCPSCRLRKCYEAGMTLGARKLKKLGNLKLQEEGEASSTTSPTTEETTQKLTVSHIEGYECQPI
FLNVLEAIEPGVVCAGHDNNQPDFAALLSSLNELGERQLVHVVKWAKALPGFRNLHVDDQMA
VIQYSWMGLMVFAMGWSFTNVNSRMLYFAPDLVFNEYRMHKSRIYSQCVRMRHLSQEFGW
LQITPQEFLCMKALLLSIIPVDGLKNQKFFDELRMNYIKELDRIIACKRKNPTSCSRRFYQLTKLL
DSVQPIARELHQFTFDLLIKSHMVSVDPEMMAEISVQVPKILSGKVKPIYFHTQ

4.2. Sequence of AR-NTD Mutant_2 (K311):

HHHHHHHHMEVQLGLGRVYPRPPSKTYRGAQNLFSVREVIQNPGPRHPEAASAAPPASL
LLLQQQQQQQQQQQQQQQQQQQQQQQQQQQQQETSPRQQQQQQGGEDGSPQAHRRGPTGYLVLDE
EQQPSQPQSALECHPERGCVPEPGAAVAASKGLPQQLPAPPDEDDSAAPSTLSLLGPTFPGLS
SCSADLKDILSEASTMQLLQQQQQEAQVSEGSSSGRAREASGAPTSSKDNLYLGGTSTISDNAKE
LCKAVSVSMGLGVEALEHLSPEQLRGDCMYAPLLGVPPAVRPTPCAPLAECKGSLLDDSAAGK
STEDTAEYSPF**R**GGYTKGLEGESLGCSGSAAAGSSGTLELPSTLSLYRSGALDEAAAYQSRDY
YNFPLALAGPPPPPPPPHAPHARIKLENPLDYGSAAAAAAQCRYGDLASLHGAGAAGPGSGS
PSAAASSSWHTLFTAEEGQLYGPCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGEAGAVAPYGYTR
PPQGLAGQESDFTAPDVWYPGGMVSRVPYPSPCTCVKSEMGPWMDSYSGPYGDMRLETARD
HVLPIIDYFPPQKTCLICGDEASGCHYGALTGSGCKVFFKRAAEGKQKYLCASTRNDCTIDKFRR
KNCPSCRLRKCYEAGMTLGARKLKKLGNLKLQEEGEASSTTSPTTEETTQKLTVSHIEGYECQPI
FLNVLEAIEPGVVCAGHDNNQPDFAALLSSLNELGERQLVHVVKWAKALPGFRNLHVDDQMA
VIQYSWMGLMVFAMGWSFTNVNSRMLYFAPDLVFNEYRMHKSRIYSQCVRMRHLSQEFGW
LQITPQEFLCMKALLLSIIPVDGLKNQKFFDELRMNYIKELDRIIACKRKNPTSCSRRFYQLTKLL
DSVQPIARELHQFTFDLLIKSHMVSVDPEMMAEISVQVPKILSGKVKPIYFHTQ

5) Molecular Docking and MM/GBSA

The computational study was conducted at the Penn State Institute for Computational and Data Sciences (ICDS) using an RHEL8 cluster computer. For this study, the structure of the full-length androgen receptor protein (PDB ID: AF-P10275-F1-model_v4) was obtained from alphafold. Prior to docking, the protein was prepared using the Protein Preparation Workflow in the Maestro (Schrödinger suite release 2025.1) to correct any issue [1]. The structure was preprocessed by assigning bond orders, adding hydrogens, identifying disulfide bonds, and completing missing loops and side chains. Water molecules beyond a 5 Å cutoff were removed,

and the added hydrogens were optimized using PROPKA at a set pH. The structure was minimized with the OPLS3e force field to achieve its likely biological conformation [2]. The protein's binding site at N-terminal domain was identified using sitemap and binding docking grid was assigned by selecting the site entry in the Grid Generation Panel with default settings. The LigPrep module was used to create molecular configurations of ASR603, employing the OPLS3e force field to explore tautomeric and ionization states, resulting in 3D molecular structures [3]. Induced fit docking and MM/GBSA calculations for the ligands were conducted using the Glide and Prime modules with default parameters [4].

6) Molecular Dynamics Simulation (MDS)

The MD simulations of the selected molecules were conducted for 100 ns to investigate the conformational variability and stability of the complexes, using the Desmond package in the Schrödinger suite [5]. The molecule bound to NTD-AR was prepared by refining amino acid interactions with the OPLS3e force field. The protein was solvated in an orthorhombic water box with SPC water molecules, and Na⁺ counterions were added to neutralize the system. The box size was adjusted to fully encompass the protein-ligand complex. The system was then minimized and equilibrated following the default Desmond protocol in Schrödinger [6]. After equilibration, a temperature relaxation at 300 K and 1 bar pressure in the NPT ensemble was performed, followed by the final 100 ns MD simulation to assess complex stability using RMSD, and other profiles, analyzed via the Simulation Interaction Diagram.

7) Spatial Metabolomics and Glycan Analysis

Formalin fixed, paraffin embedded tissue sections were dewaxed by submerging for 2 x 3 minutes in fresh xylene. After drying, an optical image was acquired using an Epson Perfection V600 flatbed document scanner at 4800 dpi. An annotated serial section was co-registered to the section for MALDI imaging using GIMP and this co-registered image was used to define the regions of interest (ROIs) for mass spectrometry imaging data collection. Tissue sections for mass spectrometry imaging were first coated with 1,5-diaminonaphthalene (DAN, 10 mg/mL in 50% acetonitrile) for metabolite imaging using an HTX M5 Robotic Reagent Sprayer over 5 passes. Spray parameters were as follows: a nozzle temperature of 60°C, a nozzle height of 40 mm, a flow rate of 0.1 mL/min, a track speed of 1200 mm/min, a track spacing of 3 mm, and a track pattern of CC.

Metabolite data was collected in negative ion mode at 20 µm resolution using a Bruker timsTOF fleX QTOF mass spectrometer over the m/z range 50-600. A total of 200 laser shots were summed per pixel. Instrument acquisition parameters were as follows: Funnel 1 RF of 75.0

VPP, Funnel 2 RF of 100.0 Vpp, Multipole RF of 150.0 Vpp, Collision Energy of 10.0 eV, Collision RF of 500.0 Vpp, Transfer time of 50.0 μ s, and a Prepulse Storage of 5.0 μ s. FlexImaging 7.0 was used for imaging acquisition from the defined ROIs from the co-registered image. After metabolite imaging was performed, the DAN matrix was removed by submerging the slide in 100% ethanol for 1 min before being rehydrated with graded ethanol. Sections were then subjected to heat-induced antigen retrieval for 20 minutes at 95°C in 100 mM Tris, pH 9.0 using a BioCare Medical NexGen Decloaking Chamber. After cooling for 15 minutes, the buffer was exchanged to water over 5 changes and the sections were allowed to dry completely. The sections were coated with PNGaseF using the HTX Sprayer as follows: 0.1 mg/mL PNGaseF in 20 mM ammonium bicarbonate, pH 7.8, over 15 passes with a nozzle temperature of 45°C, a nozzle height of 40 mm, a flow rate of 0.025 mL/min, a track speed of 1200 mm/min, a track spacing of 3 mm, and a track pattern of CC. The sections were incubated in a humidity chamber at 37°C for 2 hours. Sections were then coated with 10 mg/mL α -cyano-4-hydroxycinnamic acid (CHCA) matrix in 70% ACN with 10 mM ammonium phosphate over 3 passes using the sprayer with the following parameters: a nozzle temperature of 75°C, a nozzle height of 40 mm, a flow rate of 0.12 mL/min, a track speed of 1200 mm/min, a track spacing of 3 mm, and a track pattern of HH.

Glycan image data were collected from the same ROIs in positive ion mode on the timsTOF at 20 μ m resolution over the m/z range 700-3500 with 200 laser shots summed per pixel. Instrument acquisition parameters were as follows: Funnel 1 RF of 450.0 VPP, Funnel 2 RF of 500.0 Vpp, Multipole RF of 500.0 Vpp, Collision Energy of 10.0 eV, Collision RF of 2700.0 Vpp, Transfer time of 140.0 μ s, and a Prepulse Storage of 14.0 μ s. Images were loaded into SCiLS Lab 2024b for visualization and manual peak selection. Putative identifications of metabolites and glycans were generated using the MetaboScape 2024 plugin for SCiLS. Metabolites were considered as [M-H]⁻, [M]⁻, and [M+Cl]⁻ ions, while glycans were considered as [M+Na]⁺ ions. Regions for statistical analysis were generated as .MLD files using VisioPharm. Using customs scripts provided by SCiLS Lab, the .MLD files were converted to .SEF files for use within the SCiLS Lab software. The .SEF files were imported into SCiLS and co-registered to the appropriate regions within the imaging data for both the metabolite and glycan datasets. All small regions of the same regions type for the same tissue were combined to a single region per tissue for analysis. Wilcoxon rank sum tests were performed to compare the same region type between samples.

References

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