

**ATLAS OF TISSUE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN HUMAN:  
A TRANSCRIPTOMIC META-ANALYSIS**

**Supplemental data**

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## **Supplementary Table S1: Extended renin-angiotensin-aldosterone system (ExtRAAS) gene**

**Supplementary Table S1: Extended renin-angiotensin-aldosterone system (ExtRAAS) gene.**

ExtRAAS constitute 37 genes; 25 encode for the renin-angiotensin system (RAS) components corresponding to angiotensinogen (AGT) 17 enzymes and 7 receptors; and 12 genes encode for corticosteroid system (COS) proteins corresponding to 9 enzymes and 3 receptors. Classical RAAS genes are annotated by an asterisk. RAS, renin-angiotensin system; COS, corticosteroid system; GeneID, gene refseq ID.

System	Gene Symbol	Gene Description	GeneID
RAS	ACE*	angiotensin I converting enzyme (peptidyl-dipeptidase A) 1	1636
RAS	ACE2	angiotensin I converting enzyme (peptidyl-dipeptidase A) 2	59272
RAS	AGT*	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	183
RAS	AGTR1*	angiotensin II receptor, type 1	185
RAS	AGTR2	angiotensin II receptor, type 2	186
RAS	ANPEP	alanyl (membrane) aminopeptidase	290
RAS	ATP6AP2	ATPase, H+ transporting, lysosomal accessory protein 2	10159
RAS	CMA1	chymase 1, mast cell	1215
RAS	CPA3	carboxypeptidase A3 (mast cell)	1359
RAS	CTSA	cathepsin A	5476
RAS	CTSD	cathepsin D	1509
RAS	CTSG	cathepsin G	1511
RAS	DPP3	dipeptidyl-peptidase 3	10072
RAS	EGFR	epidermal growth factor receptor	1956
RAS	ENPEP	glutamyl aminopeptidase (aminopeptidase A)	2028
RAS	IGF2R	insulin-like growth factor 2 receptor	3482
RAS	KLK1	kallikrein 1	3816
RAS	LNPEP	leucyl/cystinyl aminopeptidase	4012
RAS	MAS1	MAS1 oncogene	4142
RAS	MME	membrane metallo-endopeptidase	4311
RAS	NLN	neurolysin (metallopeptidase M3 family)	57486
RAS	PREP	prolyl endopeptidase	5550
RAS	REN*	renin	5972
RAS	RNPEP	arginyl aminopeptidase (aminopeptidase B)	6051
RAS	THOP1	thimet oligopeptidase 1	7064
COS	AKR1C4	aldo-keto reductase family 1, member C4	1109
COS	AKR1D1	aldo-keto reductase family 1, member D1	6718
COS	CYP11A1	cytochrome P450, family 11, subfamily A, polypeptide 1	1583
COS	CYP11B1	cytochrome P450, family 11, subfamily B, polypeptide 1	1584
COS	CYP11B2*	cytochrome P450, family 11, subfamily B, polypeptide 2	1585
COS	CYP17A1	cytochrome P450, family 17, subfamily A, polypeptide 1	1586
COS	CYP21A2	cytochrome P450, family 21, subfamily A, polypeptide 2	1589
COS	GPER	G protein-coupled estrogen receptor 1	2852
COS	HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	3290
COS	HSD11B2*	hydroxysteroid (11-beta) dehydrogenase 2	3291
COS	NR3C1	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	2908
COS	NR3C2*	nuclear receptor subfamily 3, group C, member 2	4306

## Supplementary Table S2: Detailed Inventory of Studied Datasets

**Supplementary Table S2: Detailed inventory of studied datasets.** Dataset ID: data set accession number in Gene expression omnibus (GEO) database; Platform ID: GEO accession number of platform; species: species from which tissues where obtained; Normal: number of normal samples in the dataset; Algorithm: normalization method used by authors; Cut height: the level at which the dendrogram was cut; MAC: mean agglomerative coefficient of dendrogram.

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Dataset ID	Platform ID	Species	Tissue	Normal	algorithm	Cut height	MAC
GSE18723	GPL96	Homo Sapiens	B cells	40	MAS 5	0.9	0.47
GSE16028	GPL570	Homo Sapiens	Blood	109	Quantile	0.82	0.48
GSE46480	GPL570	Homo Sapiens	Blood	98	Quantile	0.767	0.74
GSE10041	GPL570	Homo Sapiens	Blood	72	Global scaling	0.8	0.66
GSE19743	GPL570	Homo Sapiens	Blood	63	MBEI	0.8	0.63
GSE33580	GPL570	Homo Sapiens	Blood	43	MAS 5	0.89	0.57
GSE26049	GPL570	Homo Sapiens	Blood	42	RMA	0.9	0.67
GSE27263	GPL570	Homo Sapiens	Blood	26	RMA	0.82	0.79
GSE45536	GPL570	Homo Sapiens	Blood	24	RMA	0.987	0.71
GSE19314	GPL570	Homo sapiens	Blood	21	RMA	0.88	0.68
GSE22255	GPL570	Homo sapiens	Blood	20	RMA	0.93	0.71
GSE28750	GPL570	Homo Sapiens	Blood	20	RMA	0.9	0.8
GSE37171	GPL570	Homo Sapiens	Blood	20	RMA	0.8	0.8
GSE33341	GPL571	Homo sapiens	Blood	43	RMA	1	0.73
GSE21592	GPL571	Homo sapiens	Blood	20	RMA	1	0.83
GSE47199	GPL6244	Homo Sapiens	Blood	21	RMA	0.76	0.85
GSE12288	GPL96	Homo sapiens	Blood	112	MAS 5.0	0.785	0.56
GSE14795	GPL96	Homo Sapiens	Blood	20	MAS 5.0	0.94	0.62
GSE45460	GPL6244	Homo Sapiens	BM cells	31	RMA	1	0.84
GSE11504	GPL570	Homo Sapiens	BM cells	25	RMA	1	0.79
GSE16334	GPL96	Homo Sapiens	BM cells	11	RMA	1.02	0.84
GSE32719	GPL570	Homo Sapiens	BM cells	27	RMA	0.88	0.58
GSE24870	GPL571	Homo Sapiens	BM cells	20	MAS 5	1.033	0.75
GSE35010	GPL6244	Homo Sapiens	BM cells	16	RMA	0.875	0.86
GSE19429	GPL570	Homo Sapiens	BM cells	17	RMA	1	0.81
GSE39540	GPL571	Homo Sapiens	BM cells	61	Quantile	1	0.74
GSE29431	GPL570	Homo Sapiens	Breast	12	RMA	1	0.86
GSE42568	GPL570	Homo Sapiens	Breast	17	gcRMA	1	0.78
GSE5364	GPL96	Homo sapiens	Breast	13	Global scaling	1	0.8

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Dataset ID	Platform ID	Species	Tissue	Normal	algorithm	Cut height	MAC
GSE20437	GPL96	Homo sapiens	Breast	24	MAS 5,0	0.8	0.74
GSE21947	GPL96	Homo Sapiens	Breast	30	Mean expression	1.03	0.75
GSE10780	GPL570	Homo Sapiens	Breast	143	RMA	0.83	0.65
GSE31773	GPL570	Homo Sapiens	CD8 & CD4	17	RMA	1	0.85
GSE41328	GPL570	Homo sapiens	colon	10	PLIER	1	0.82
GSE13367	GPL570	Homo sapiens	colonic mucosa	38	RMA	1	0.77
GSE37364	GPL570	Homo sapiens	colonic mucosa	38	MAS 5,0	0.91	0.63
GSE24514	GPL96	Homo sapiens	colonic mucosa	15	Quantile	0.92	0.77
GSE22598	GPL570	Homo Sapiens	Colorectal	17	RMA	1	0.8
GSE23878	GPL570	Homo sapiens	Colorectal	24	PLIER	1	0.75
GSE32323	GPL570	Homo Sapiens	Colorectal	17	RMA	1	0.8
GSE9348	GPL570	Homo Sapiens	Colorectal	12	Global scaling	1.12	0.79
GSE15744	GPL570	Homo sapiens	Embryo	18	Global scaling	1	0.72
GSE18290	GPL570	Homo sapiens	Embryo	18	dChip signal intensity	0.81	0.79
GSE18887	GPL96	Homo sapiens	Embryo	18	RMA	1	0.79
GSE20347	GPL571	Homo Sapiens	Esophagus	17	RMA	1	0.8
GSE23400	GPL96	Homo Sapiens	Esophagus	53	RMA	0.92	0.75
GSE5364	GPL96	Homo sapiens	Esophagus	13	Global scaling	1	0.83
GSE16134	GPL570	Homo Sapiens	Gingiva	70	RMA	0.93	0.71
GSE10334	GPL570	Homo Sapiens	Gingiva	64	RMA	1	0.71
GSE22253	GPL6244	Homo Sapiens	Heart	108	gcRMA	1	0.65
GSE22459	GPL570	Homo Sapiens	Kidney	25	MAS 5	1.08	0.75
GSE9489	GPL570	Homo Sapiens	Kidney	13	Global scaling	1.08	0.78
GSE15641	GPL96	Homo Sapiens	Kidney	23	dChip	1	0.8
GSE11906	GPL570	Homo Sapiens	Large airway epithelium	21	RMA	1	0.6
GSE10135	GPL570	Homo Sapiens	Large airway epithelium	21	Global scaling	1	0.6
GSE16696	GPL570	Homo sapiens	Large airway epithelium	20	Global scaling	1	0.64
GSE18637	GPL570	Homo sapiens	Large airway epithelium	20	Global scaling	1	0.67
GSE22047	GPL570	Homo sapiens	Large airway epithelium	19	Global scaling	1.01	0.64

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Dataset ID	Platform ID	Species	Tissue	Normal	algorithm	Cut height	MAC
GSE11375	GPL570	Homo Sapiens	Leukocytes	26	Global scaling	0.85	0.75
GSE38941	GPL570	Homo sapiens	Liver	10	Median normalization	0.9	0.77
GSE45267	GPL570	Homo Sapiens	Liver	41	gcRMA	1	0.73
GSE29721	GPL570	Homo Sapiens	Liver	10	RMA	1	0.85
GSE14323	GPL571	Homo Sapiens	Liver	19	RMA	1.08	0.8
GSE41258	GPL96	Homo sapiens	Liver	13	LOWSESS	0.92	0.77
GSE19804	GPL570	Homo sapiens	Lung tissue	60	RMA	1	0.68
GSE18842	GPL570	Homo sapiens	Lung tissue	45	RMA	1	0.69
GSE31552	GPL6244	Homo sapiens	Lung tissue	36	RMA	1	0.83
GSE31547	GPL96	Homo sapiens	Lung tissue	20	Quantile	1	0.74
GSE10072	GPL96	Homo Sapiens	Lung tissue	49	RMA	0.785	0.75
GSE29819	GPL570	Homo sapiens	Myocardial	12	MAS 5.0	1	0.7
GSE12485	GPL570	Homo sapiens	Myocardial	10	RMA	1.09	0.78
GSE12486	GPL570	Homo sapiens	Myocardial	10	RMA	1	0.83
GSE20950	GPL570	Homo Sapiens	Omental adipose	11	RMA	0.567	0.84
GSE41168	GPL570	Homo Sapiens	Omental adipose	35	RMA	0.965	0.66
GSE20571	GPL6244	Homo Sapiens	Omental adipose	14	Global Median	1	0.84
GSE25401	GPL6244	Homo Sapiens	Omental adipose	26	Global Median	0.8	0.71
GSE17913	GPL570	Homo Sapiens	Oral mucosa	40	RMA	0.9	0.68
GSE37265	GPL570	Homo Sapiens	Oral mucosa	19	RMA	0.85	0.76
GSE14407	GPL570	Homo Sapiens	Ovary surface epithelium	12	MAS 5	1.06	0.74
GSE38666	GPL570	Homo Sapiens	Ovary surface epithelium	12	MAS 5	1.06	0.74
GSE29220	GPL570	Homo Sapiens	Ovary surface epithelium	11	gcRMA	1.154	0.81
GSE29450	GPL570	Homo Sapiens	Ovary surface epithelium	10	RMA	1.09	0.81
GSE26712	GPL96	Homo Sapiens	Ovary surface epithelium	10	RMA	1.16	0.76
GSE16515	GPL570	Homo Sapiens	Pancreatic tissue	16	gcRMA	0.8	0.86
GSE15471	GPL570	Homo Sapiens	Pancreatic tissue	39	RMA	1	0.82
GSE28735	GPL6244	Homo sapiens	pancreatic tissue	45	RMA	1	0.79
GSE27562	GPL570	Homo sapiens	PBMC	46	RMA	0.93	0.71



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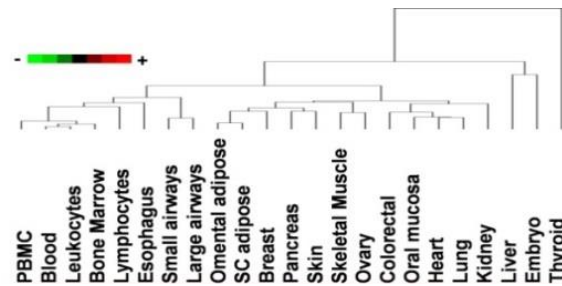
Dataset ID	Platform ID	Species	Tissue	Normal	algorithm	Cut height	MAC
GSE11761	GPL570	Homo Sapiens	PBMC	40	gcRMA	1.05	0.79
GSE14642	GPL570	Homo Sapiens	PBMC	40	gcRMA	0.93	0.78
GSE15932	GPL570	Homo sapiens	PBMC	32	VSN	0.84	0.6
GSE21942	GPL570	Homo Sapiens	PBMC	15	gcRMA	0.99	0.7
GSE17114	GPL570	Homo sapiens	PBMC	14	RMA	0.875	0.73
GSE43553	GPL571	Homo Sapiens	PBMC	34	Global scaling	0.9	0.79
GSE41890	GPL6244	Homo Sapiens	PBMC	24	gcRMA	0.91	0.77
GSE28686	GPL6244	Homo Sapiens	PBMC	20	gcRMA	0.78	0.82
GSE12585	GPL96	Homo Sapiens	PBMC	23	RMA	1	0.74
GSE14577	GPL96	Homo Sapiens	PBMC	15	RMA	1	0.75
GSE25507	GPL570	Homo sapiens	Periheral lymphocytes	64	RMA	0.85	0.66
GSE7638	GPL571	Homo sapiens	Peripheral monocytes	160	NUSE	0.86	0.72
GSE36895	GPL570	Homo Sapiens	Renal cortex	23	RMA	1	0.72
GSE20950	GPL570	Homo Sapiens	Subcutaneous adipose	12	RMA	0.6	0.84
GSE26339	GPL570	Homo Sapiens	Subcutaneous adipose	11	Mas 5	1.1	0.83
GSE27916	GPL570	Homo Sapiens	Subcutaneous adipose	255	PLIER	0.93	0.72
GSE27916	GPL570	Homo Sapiens	Subcutaneous adipose	120	PLIER	0.94	0.69
GSE27949	GPL570	Homo Sapiens	Subcutaneous adipose	11	MAS5	1	0.82
GSE28005	GPL570	Homo Sapiens	Subcutaneous adipose	13	RMA	1	0.8
GSE29718	GPL6244	Homo Sapiens	Subcutaneous adipose	15	RMA	1	0.78
GSE19811	GPL96	Homo Sapiens	Subcutaneous adipose	13	RMA	1.1	0.81
GSE35710	GPL96	Homo Sapiens	Subcutaneous adipose	24	PLIER	1	0.78
GSE18206	GPL570	Homo sapiens	Skin	21	VSN	1	0.74
GSE30999	GPL570	Homo sapiens	Skin	85	gcRMA	1	0.77
GSE34248	GPL570	Homo sapiens	Skin	14	Rosetta resolver	0.92	0.76
GSE36842	GPL570	Homo sapiens	Skin	23	fRMA	0.88	0.75
GSE41662	GPL570	Homo sapiens	Skin	24	Rosetta resolver	0.8	0.69
GSE41663	GPL570	Homo sapiens	Skin	15	Rosetta resolver	0.86	0.76
GSE32407	GPL571	Homo sapiens	Skin	40	gcRMA	1.088	0.78

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Dataset ID	Platform ID	Species	Tissue	Normal	algorithm	Cut height	MAC
GSE11784	GPL570	Homo sapiens	small airway epithelium	63	MAS 5,0	0.93	0.72
GSE22047	GPL570	Homo sapiens	small airway epithelium	60	Global scaling	0.93	0.62
GSE30063	GPL570	Homo sapiens	small airway epithelium	60	Global scaling	0.93	0.62
GSE19667	GPL570	Homo sapiens	small airway epithelium	48	MAS 5,0	0.84	0.58
GSE19407	GPL570	Homo Sapiens	small airway epithelium	47	MAS 5	0.86	0.72
GSE11906	GPL570	Homo Sapiens	small airway epithelium	35	RMA	1	0.74
GSE13933	GPL570	Homo sapiens	small airway epithelium	23	MAS 5,0	1.05	0.66
GSE27681	GPL570	Homo sapiens	small airway epithelium	21	Global scaling	1	0.7
GSE14924	GPL570	Homo Sapiens	T cells	21	MAS 5	1	0.62
GSE29265	GPL570	Homo Sapiens	Thyroid	20	RMA	0.71	0.71
GSE33630	GPL570	Homo Sapiens	Thyroid	46	RMA	0.69	0.69
GSE13601	GPL8300	Homo Sapiens	Tongue	27	MAS 5	0.88	0.72
GSE13070	GPL570	Homo Sapiens	Vastus lateralis	87	MAS 5.0	0.82	0.65
GSE13070	GPL570	Homo Sapiens	Vastus lateralis	53	MAS 5.0	0.85	0.67
GSE14901	GPL570	Homo Sapiens	Vastus lateralis	72	MAS 5	1.04	0.61
GSE17674	GPL570	Homo Sapiens	Vastus lateralis	18	RMA	0.925	0.8
GSE19420	GPL570	Homo sapiens	Vastus lateralis	24	MAS 5,0	1	0.63
GSE25462	GPL570	Homo sapiens	Vastus lateralis	50	MAS 5,0	1	0.6
GSE25941	GPL570	Homo Sapiens	Vastus lateralis	36	Global scaling	0.9	0.54
GSE38718	GPL570	Homo Sapiens	Vastus lateralis	22	RMA	1	0.73
GSE41168	GPL570	Homo Sapiens	Vastus lateralis	47	RMA	0.79	0.54
GSE8157	GPL570	Homo sapiens	Vastus lateralis	43	RMA	1.16	0.78
GSE9419	GPL570	Homo Sapiens	Vastus lateralis	66	MAS 5	0.803	0.52
GSE11681	GPL96	Homo sapiens	Vastus lateralis	10	RMA	1	0.78
GSE11686	GPL96	Homo Sapiens	Vastus lateralis	16	MAS5	1	0.68
GSE17371	GPL96	Homo sapiens	Vastus lateralis	12	MAS 5,0	0.9	0.72
GSE13985	GPL570	Homo sapiens	WBC	10	RMA	0.82	0.8
GSE28498	GPL6244	Homo Sapiens	WBC	26	RMA	0.6	0.82

### Supplementary Table S3: Tissue Expression Profiles of ExtRAAS Genes

**Supplementary Table S3: Tissue expression profiles of extRAAS genes.** Tissues are arranged according to the tissue dendrogram of figure 5 in the article (see dendrogram below). PBMC, peripheral blood mononuclear cells; small airways, small airways epithelium; large airways, large airways epithelium; SC adipose, sub-cutaneous adipose tissue.



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Gene symbol	PBMC	Blood	Leukocytes	Bone Marrow	Lymphocytes	Esophagus	Small airways	Large airways
ACE	31 ± 5	35 ± 4	36 ± 7	43 ± 6	37 ± 7	14 ± 3	50 ± 1	55 ± 0
ACE2	20 ± 4	24 ± 4	19 ± 5	23 ± 5	40 ± 4	36 ± 11	54 ± 0	59 ± 0
AGT	41 ± 3	47 ± 4	42 ± 9	39 ± 5	49 ± 4	43 ± 5	47 ± 0	51 ± 0
AGTR1	24 ± 4	28 ± 5	25 ± 6	31 ± 4	42 ± 5	32 ± 13	33 ± 1	36 ± 1
AGTR2	30 ± 4	26 ± 4	21 ± 7	20 ± 4	37 ± 3	21 ± 3	26 ± 1	35 ± 1
AKR1C4	16 ± 4	17 ± 3	10 ± 2	11 ± 2	23 ± 5	13 ± 5	38 ± 1	44 ± 0
AKR1D1	13 ± 4	11 ± 3	6 ± 3	6 ± 3	18 ± 5	8 ± 6	16 ± 1	15 ± 0
ANPEP	86 ± 4	94 ± 1	96 ± 2	71 ± 7	57 ± 10	21 ± 6	84 ± 0	75 ± 0
ATP6AP2	98 ± 1	97 ± 1	98 ± 1	94 ± 3	99 ± 1	95 ± 2	99 ± 0	99 ± 0
CMA1	18 ± 2	23 ± 2	22 ± 3	22 ± 3	26 ± 3	26 ± 7	21 ± 1	13 ± 1
CPA3	58 ± 5	67 ± 3	46 ± 12	76 ± 11	62 ± 5	72 ± 6	89 ± 0	82 ± 0
CTSA	98 ± 1	96 ± 1	98 ± 1	87 ± 4	90 ± 4	91 ± 3	93 ± 0	92 ± 0
CTSD	85 ± 3	82 ± 2	91 ± 4	71 ± 4	70 ± 6	78 ± 3	93 ± 0	93 ± 0
CTSG	48 ± 3	53 ± 3	56 ± 10	87 ± 7	62 ± 4	57 ± 5	35 ± 1	30 ± 0
CYP11A1	20 ± 3	29 ± 2	23 ± 4	25 ± 3	36 ± 6	39 ± 5	21 ± 2	11 ± 1
CYP11B1	25 ± 6	32 ± 6	26 ± 13	26 ± 7	34 ± 7	22 ± 10	15 ± 1	14 ± 1
CYP11B2	47 ± 6	45 ± 5	58 ± 10	47 ± 6	29 ± 13	39 ± 9	21 ± 2	27 ± 0
CYP17A1	27 ± 4	36 ± 4	36 ± 7	33 ± 6	43 ± 2	40 ± 8	33 ± 1	32 ± 1
CYP21A2	34 ± 5	37 ± 4	42 ± 5	37 ± 4	31 ± 9	30 ± 9	24 ± 1	21 ± 1
DPP3	78 ± 3	74 ± 4	75 ± 3	72 ± 5	71 ± 9	56 ± 8	79 ± 1	82 ± 0
EGFR	28 ± 7	43 ± 5	43 ± 7	51 ± 8	49 ± 9	62 ± 16	35 ± 1	33 ± 0
ENPEP	15 ± 5	7 ± 3	8 ± 3	11 ± 3	3 ± 1	11 ± 6	4 ± 1	18 ± 1
GPFR	41 ± 6	49 ± 4	56 ± 1	40 ± 7	34 ± 8	34 ± 7	21 ± 1	17 ± 0
HSD11B1	34 ± 3	44 ± 3	34 ± 6	29 ± 5	50 ± 2	34 ± 8	41 ± 1	38 ± 1
HSD11B2	23 ± 5	23 ± 4	31 ± 7	31 ± 7	16 ± 6	38 ± 3	32 ± 1	35 ± 1
IGF2R	93 ± 2	96 ± 1	95 ± 3	72 ± 6	91 ± 5	84 ± 1	89 ± 0	89 ± 0
KLK1	62 ± 3	64 ± 3	64 ± 6	58 ± 6	65 ± 3	57 ± 2	55 ± 1	47 ± 0
LNPEP	66 ± 8	48 ± 5	53 ± 15	55 ± 10	56 ± 7	28 ± 2	49 ± 0	54 ± 0
MAS1	21 ± 5	27 ± 4	19 ± 5	23 ± 5	35 ± 3	48 ± 8	22 ± 1	19 ± 1
MME	66 ± 8	95 ± 3	88 ± 10	72 ± 9	43 ± 16	42 ± 14	45 ± 1	36 ± 1
NR3C1	94 ± 2	94 ± 2	95 ± 2	89 ± 3	95 ± 1	82 ± 6	93 ± 0	93 ± 0
NR3C2	71 ± 3	57 ± 4	50 ± 13	32 ± 6	80 ± 5	30 ± 10	85 ± 0	85 ± 0
PREP	79 ± 2	79 ± 2	78 ± 2	74 ± 4	79 ± 5	75 ± 5	77 ± 0	79 ± 0
REN	30 ± 5	33 ± 4	30 ± 5	36 ± 5	30 ± 4	33 ± 12	34 ± 1	25 ± 1
RNPEP	91 ± 1	91 ± 2	94 ± 2	82 ± 5	87 ± 2	92 ± 1	96 ± 0	96 ± 0
THOP1	55 ± 3	51 ± 4	55 ± 5	59 ± 7	58 ± 5	48 ± 7	68 ± 0	68 ± 0

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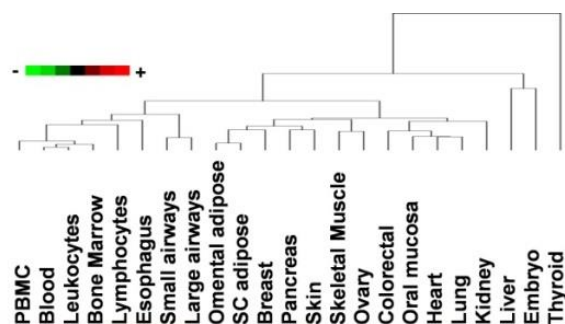
Gene symbol	Omental adipose	SC adipose	Breast	Pancreas	Skin	Skeletal Muscle	Ovary	Colorectal
ACE	67 ± 1	68 ± 2	38 ± 12	58 ± 6	44 ± 5	50 ± 4	23 ± 5	61 ± 7
ACE2	38 ± 1	35 ± 1	44 ± 3	56 ± 1	28 ± 4	36 ± 4	37 ± 8	84 ± 4
AGT	51 ± 5	63 ± 1	58 ± 7	70 ± 8	60 ± 3	89 ± 1	60 ± 4	66 ± 4
AGTR1	93 ± 1	94 ± 1	82 ± 5	63 ± 4	84 ± 5	80 ± 2	76 ± 5	51 ± 6
AGTR2	18 ± 3	27 ± 1	31 ± 3	25 ± 5	20 ± 4	37 ± 3	36 ± 2	34 ± 3
AKR1C4	49 ± 12	25 ± 3	22 ± 5	28 ± 8	18 ± 3	19 ± 2	20 ± 6	18 ± 4
AKR1D1	9 ± 2	2 ± 0	23 ± 9	15 ± 6	14 ± 4	15 ± 3	13 ± 4	9 ± 4
ANPEP	67 ± 2	70 ± 2	79 ± 3	99 ± 1	73 ± 6	33 ± 2	31 ± 5	96 ± 1
ATP6AP2	96 ± 1	98 ± 0	98 ± 1	98 ± 1	98 ± 1	88 ± 1	100 ± 0	98 ± 2
CMA1	51 ± 1	45 ± 2	45 ± 6	33 ± 4	60 ± 7	36 ± 2	28 ± 5	41 ± 5
CPA3	75 ± 3	76 ± 1	65 ± 9	94 ± 2	78 ± 6	57 ± 2	34 ± 12	80 ± 5
CTSA	95 ± 0	95 ± 0	85 ± 4	95 ± 2	94 ± 1	85 ± 2	79 ± 3	99 ± 1
CTSD	89 ± 2	87 ± 1	74 ± 6	90 ± 5	83 ± 3	78 ± 2	53 ± 9	91 ± 2
CTSG	65 ± 1	75 ± 1	57 ± 9	56 ± 7	70 ± 5	69 ± 2	52 ± 1	67 ± 3
CYP11A1	37 ± 2	37 ± 1	38 ± 3	21 ± 10	20 ± 6	33 ± 2	37 ± 7	27 ± 4
CYP11B1	33 ± 7	26 ± 2	31 ± 9	22 ± 11	14 ± 1	31 ± 4	30 ± 6	22 ± 7
CYP11B2	46 ± 4	64 ± 1	37 ± 9	44 ± 15	16 ± 6	46 ± 6	28 ± 7	48 ± 7
CYP17A1	36 ± 1	39 ± 1	31 ± 7	25 ± 12	14 ± 5	49 ± 3	33 ± 8	38 ± 4
CYP21A2	44 ± 3	49 ± 1	38 ± 9	30 ± 11	74 ± 11	39 ± 4	50 ± 7	34 ± 7
DPP3	72 ± 2	81 ± 1	66 ± 9	74 ± 8	72 ± 3	59 ± 3	70 ± 3	92 ± 2
EGFR	67 ± 5	58 ± 3	75 ± 3	54 ± 21	44 ± 4	61 ± 4	86 ± 5	55 ± 9
ENPEP	88 ± 1	66 ± 3	56 ± 8	72 ± 3	46 ± 6	57 ± 4	43 ± 9	37 ± 9
GPFR	75 ± 2	83 ± 1	54 ± 12	44 ± 5	54 ± 5	48 ± 3	57 ± 4	63 ± 5
HSD11B1	77 ± 5	91 ± 0	64 ± 8	61 ± 7	82 ± 2	61 ± 2	78 ± 2	46 ± 2
HSD11B2	37 ± 0	31 ± 1	34 ± 4	45 ± 1	73 ± 4	34 ± 1	37 ± 5	98 ± 1
IGF2R	93 ± 1	91 ± 1	81 ± 5	92 ± 2	87 ± 2	93 ± 1	77 ± 4	92 ± 3
KLK1	57 ± 2	61 ± 1	58 ± 4	98 ± 1	83 ± 3	67 ± 2	69 ± 2	91 ± 2
LNPEP	72 ± 7	29 ± 2	31 ± 9	59 ± 17	44 ± 4	46 ± 4	30 ± 7	43 ± 5
MAS1	20 ± 3	37 ± 1	35 ± 7	16 ± 10	18 ± 4	45 ± 3	35 ± 8	45 ± 2
MME	96 ± 1	95 ± 0	91 ± 3	62 ± 8	62 ± 4	79 ± 2	43 ± 11	50 ± 7
NR3C1	97 ± 1	97 ± 1	94 ± 3	93 ± 2	96 ± 1	98 ± 0	97 ± 2	82 ± 7
NR3C2	73 ± 3	71 ± 1	78 ± 3	83 ± 3	75 ± 2	87 ± 1	83 ± 8	95 ± 2
PREP	74 ± 3	75 ± 1	74 ± 5	80 ± 3	79 ± 2	94 ± 0	76 ± 1	92 ± 2
REN	24 ± 1	27 ± 1	25 ± 8	24 ± 10	24 ± 6	27 ± 3	29 ± 6	38 ± 4
RNPEP	86 ± 1	85 ± 1	87 ± 2	93 ± 2	81 ± 3	83 ± 1	78 ± 5	96 ± 1
THOP1	62 ± 2	53 ± 2	52 ± 5	59 ± 3	44 ± 8	64 ± 3	47 ± 4	75 ± 3

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Gene symbol	Oral Mucosa	Heart	Lung	Kidney	Liver	Embryo	Thyroid
ACE	53 ± 3	57 ± 5	65 ± 11	56 ± 12	35 ± 11	32 ± 9	58 ± 5
ACE2	50 ± 4	79 ± 2	36 ± 4	92 ± 3	48 ± 8	44 ± 15	40 ± 7
AGT	51 ± 2	94 ± 4	51 ± 4	90 ± 4	100 ± 1	84 ± 4	66 ± 2
AGTR1	38 ± 6	63 ± 4	71 ± 4	82 ± 8	98 ± 1	53 ± 7	98 ± 1
AGTR2	24 ± 4	36 ± 8	60 ± 6	39 ± 5	28 ± 3	49 ± 5	50 ± 7
AKR1C4	7 ± 2	11 ± 3	10 ± 2	19 ± 6	96 ± 2	23 ± 5	36 ± 4
AKR1D1	3 ± 0	8 ± 3	5 ± 3	11 ± 6	97 ± 2	33 ± 8	91 ± 0
ANPEP	69 ± 3	48 ± 4	65 ± 11	98 ± 1	98 ± 1	48 ± 9	58 ± 4
ATP6AP2	99 ± 0	95 ± 1	97 ± 1	99 ± 1	96 ± 2	95 ± 1	82 ± 5
CMA1	44 ± 4	41 ± 5	28 ± 5	26 ± 2	20 ± 3	16 ± 5	63 ± 4
CPA3	84 ± 7	59 ± 8	96 ± 1	60 ± 1	49 ± 6	18 ± 5	60 ± 12
CTSA	95 ± 1	94 ± 0	96 ± 1	99 ± 0	93 ± 2	78 ± 2	77 ± 11
CTSD	83 ± 1	88 ± 4	96 ± 1	92 ± 1	91 ± 2	60 ± 2	89 ± 3
CTSG	72 ± 2	64 ± 9	59 ± 6	59 ± 2	53 ± 11	43 ± 4	83 ± 2
CYP11A1	55 ± 2	32 ± 3	31 ± 5	21 ± 4	45 ± 8	39 ± 6	26 ± 6
CYP11B1	7 ± 1	20 ± 9	22 ± 7	27 ± 9	20 ± 12	17 ± 4	65 ± 0
CYP11B2	57 ± 4	57 ± 10	48 ± 4	34 ± 13	54 ± 7	39 ± 6	41 ± 12
CYP17A1	37 ± 3	47 ± 9	36 ± 4	85 ± 4	53 ± 6	41 ± 1	79 ± 7
CYP21A2	45 ± 4	47 ± 4	40 ± 4	32 ± 8	61 ± 9	33 ± 5	6 ± 0
DPP3	86 ± 2	74 ± 3	75 ± 5	77 ± 5	74 ± 5	66 ± 5	4 ± 1
EGFR	69 ± 3	54 ± 9	63 ± 7	70 ± 11	68 ± 7	47 ± 9	45 ± 6
ENPEP	43 ± 9	69 ± 4	49 ± 9	97 ± 1	93 ± 2	30 ± 8	92 ± 4
GPFR	57 ± 2	56 ± 2	61 ± 4	63 ± 9	73 ± 9	35 ± 5	56 ± 3
HSD11B1	44 ± 6	59 ± 10	70 ± 7	54 ± 9	99 ± 1	36 ± 6	56 ± 6
HSD11B2	49 ± 3	35 ± 7	40 ± 3	98 ± 0	36 ± 5	36 ± 2	83 ± 2
IGF2R	94 ± 1	93 ± 1	90 ± 2	92 ± 4	94 ± 1	83 ± 3	100 ± 0
KLK1	66 ± 3	68 ± 6	55 ± 5	84 ± 2	56 ± 7	54 ± 5	30 ± 3
LNPEP	40 ± 3	72 ± 8	47 ± 13	31 ± 7	29 ± 8	44 ± 8	49 ± 9
MAS1	31 ± 2	32 ± 8	33 ± 9	38 ± 4	42 ± 3	37 ± 6	25 ± 2
MME	66 ± 3	64 ± 7	89 ± 2	97 ± 1	71 ± 7	68 ± 3	93 ± 1
NR3C1	94 ± 1	92 ± 4	91 ± 2	90 ± 5	92 ± 3	45 ± 13	63 ± 2
NR3C2	48 ± 7	86 ± 3	73 ± 5	88 ± 3	69 ± 9	42 ± 12	36 ± 3
PREP	86 ± 1	82 ± 2	77 ± 3	74 ± 5	77 ± 7	88 ± 1	29 ± 8
REN	48 ± 4	33 ± 7	44 ± 4	79 ± 7	37 ± 3	28 ± 7	41 ± 8
RNPEP	95 ± 1	85 ± 1	91 ± 2	86 ± 5	87 ± 2	87 ± 0	48 ± 4
THOP1	71 ± 2	67 ± 3	51 ± 9	48 ± 11	69 ± 7	67 ± 2	12 ± 1

## Supplementary Table S4: ExtRAAS Co-expression Modules in All 23 Studied Tissues

**Supplementary Table S4: ExtRAAS co-expression modules in all 23 studied tissue.** Below each tissue the number of datasets and corresponding samples are represented as (datasets, samples). At the top of each module the average coordination rate is expressed in percentage (average percentage of genes within a module that are always coordinated across the different datasets of a specific tissue). Next to each gene symbol the abundance of the mRNA is expressed in mean MCR (Mean expression centile rank). Genes corresponding to core groups are colored; CTSA and CTSD in red; MR, GR and AGTR1 in blue; and CTSG, CPA3 and CMA1 in green. Tissues are arranged based on the tissue dendrogram of figure 5 in the article (see dendrogram below).



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Tissues (datasets, samples)	Module 1	Module 2	Module 3	Module 4	Module 5	Module 6	Module 7	Module 8	Non-clustered genes	
<b>Thyroid (2, 66)</b>	100%	100%	100%	100%	100%	100%	100%	100%		
	CTSD CYP17A1 RNPEP	89 ATP6AP2 79 GR 48 GPER ACE2	82 MME 63 CTSG 56 CMA1 40 CPA3 HSD11B1	93 CYP11B2 41 KLK1 83 63 60 56	41 AGTR1 30 ENPEP HSD11B2 ACE	98 AKR1D1 92 CYP11B1 83 AKR1C4 58	91 PREP 65 THOP1 36	29 LNPEP 12 REN	49 IGF2R 41 CTSA AGT ANPEP AGTR2 EGFR MR CYP11A1 MAS1 CYP21A2 DPP3	100 77 66 58 50 45 36 26 25 6 4
<b>Embryo (4, 66)</b>	83%	80%	83%	87%	87%	80%				
	ATP6AP2 RNPEP THOP1 DPP3	95 AGTR2 87 LNPEP 67 MR 66 GPER CYP21A2	49 CTSG 44 CYP17A1 42 MAS1 35 CYP11B1 33	43 ANPEP 41 GR 37 CYP11A1 17 ENPEP REN	48 PREP 45 KLK1 39 CYP11B2 30 HSD11B1 28 ACE	88 AGT 54 AGTR1 39 AKR1D1 36 AKR1C4 32 CPA3	84 53 33 23 18		IGF2R CTSA MME CTSD EGFR ACE2 HSD11B2 CMA1	83 78 68 60 47 44 36 16
<b>Liver (5, 93)</b>	83%	60%	87%	80%	80%	74%	74%	67%		
	ATP6AP2 IGF2R CTSA CTSD DPP3 CYP21A2 ACE	96 AGTR1 94 GR	98 HSD11B1 92 AKR1D1 AKR1C4	99 EGFR 97 REN 96 CYP11B1	68 ANPEP 37 KLK1 20 HSD11B2	98 MAS1 56 LNPEP 36 AGTR2	42 ENPEP 29 MME 28 MR	93 CYP11B2 71 CYP17A1 69 CYP11A1	54 AGT 53 RNPEP 45 PREP GPER THOP1 CTSG CPA3 ACE2 CMA1	100 87 77 73 69 53 49 48 20
<b>Kidney (4, 84)</b>	84%	88%	85%	94%	80%					
	CTSA ANPEP ENPEP MME ACE2 CTSD AGT CYP17A1 KLK1 REN ACE	99 ATP6AP2 98 GR 97 MR 97 AGTR1 92 92 90 85 84 75 56	99 CTSG 90 AGTR2 88 MAS1 82 AKR1C4 AKR1D1	59 THOP1 39 CYP11B2 38 CYP21A2 19 CMA1 11	48 PREP 34 CPA3 32 HSD11B1 26 LNPEP CYP11A1	74 60 54 31 21			HSD11B2 IGF2R RNPEP DPP3 EGFR GPER CYP11B1	98 92 86 77 70 63 27



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<b>Lung</b> (5, 210)	90%		85%		100%		80%		86%		93%		80%		100%			
	CTSD	96	CPA3	96	CTSG	59	KLK1	55	EGFR	63	ATP6AP2	97	CYP11B2	48	AKR1C4	10	ACE	65
	CTSA	96	GR	91	CMA1	28	HSD11B2	40	REN	44	IGF2R	90	CYP21A2	40	AKR1D1	5	GPER	61
	RNPEP	91	MME	89			CYP11A1	31	MAS1	33	PREP	77					AGTR2	60
	DPP3	75	MR	73			CYP11B1	22									AGT	51
	ANPEP	65	AGTR1	71													THOP1	51
	LNPEP	47	HSD11B1	70													ACE2	36
		ENPEP	49													CYP17A1	36	
<b>Heart</b> (4, 140)	77%		75%		80%		100%		81%		81%		75%					
	CTSA	94	GR	92	CTSG	64	EGFR	54	KLK1	68	IGF2R	93	ACE2	79			ATP6AP2	95
	AGT	94	ENPEP	69	AGTR1	63	REN	33	CMA1	41	MME	64	LNPEP	72			MR	86
	CTSD	88			CPA3	59	MAS1	32	HSD11B2	35	HSD11B1	59					RNPEP	85
	DPP3	74			ACE	57			CYP11B1	20	AKR1D1	8					PREP	82
	THOP1	67			AKR1C4	11											CYP11B2	57
																	GPER	56
																ANPEP	48	
																CYP21A2	47	
																CYP17A1	47	
																AGTR2	36	
																CYP11A1	32	
<b>Oral mucosa</b> (4, 193)	81%		71%		96%		75%		87%		75%		75%		83%			
	CTSA	95	GR	94	CPA3	84	REN	48	RNPEP	95	KLK1	66	ACE2	50	AGT	69	ATP6AP2	99
	DPP3	86	MR	48	CTSG	72	MAS1	31	IGF2R	94	HSD11B2	49	LNPEP	40	AKR1C4	51	CYP11B2	57
	THOP1	71			ANPEP	69	AGTR2	24	PREP	86					EGFR	7	GPER	57
	CYP11A1	55			MME	66	CYP11B1	7	CTSD	83							ACE	53
					HSD11B1	44	AKR1D1	3									CYP21A2	45
					CMA1	44											AGTR1	38
				ENPEP	43											CYP17A1	37	
<b>Colorectal</b> (8, 171)	82%		78%		96%		80%		83%		75%		75%		62%			
	CTSA	98	ATP6AP2	98	CPA3	80	RNPEP	96	ANPEP	96	AGT	66	EGFR	55	ACE	61	LNPEP	43
	HSD11B2	98	GR	82	CTSG	66	PREP	92	ACE2	84	CYP11B2	48	CYP17A1	37	MME	50	REN	37
	MR	95	GPER	63	CMA1	41	DPP3	91	MAS1	44	AGTR2	34					ENPEP	36
	IGF2R	91	AGTR1	50			KLK1	91	AKR1C4	18	CYP21A2	34					CYP11A1	26
	CTSD	91	HSD11B1	45			THOP1	74	AKR1D1	9	CYP11B1	21						
<b>Ovary Epithelium</b> (5, 55)	85%		80%		80%		88%		90%		84%		85%		85%			
	CTSA	79	GR	97	EGFR	86	CTSG	52	THOP1	47	ATP6AP2	100	KLK1	69	AGT	60	RNPEP	78
	IGF2R	77	MR	83	CYP17A1	33	ACE2	37	MME	43	HSD11B1	78	CYP21A2	50	CTSD	53	PREP	76
	DPP3	70	CYP11B1	30	REN	29	MAS1	35	HSD11B2	37	AGTR1	76	CYP11B2	28	AGTR2	36	LNPEP	30
	GPER	57			CMA1	28	AKR1C4	20	CYP11A1	37	ENPEP	43	ACE	23	ANPEP	31		
							AKR1D1	13			CPA3	34						
<b>Skeletal Muscle</b> (14, 556)	64%		76%		57%		74%		67%		57%							
	CTSA	85	GR	98	CPA3	57	KLK1	67	CYP11B2	46	ATP6AP2	88					PREP	94
	RNPEP	83	IGF2R	93	CMA1	36	CYP17A1	49	CYP21A2	39	AGTR1	80					AGT	89
	CTSD	78	MR	87			REN	27	AKR1C4	19							MME	79
																	CTSG	69
																	THOP1	64
																	HSD11B1	61
																EGFR	61	
																DPP3	59	
																ENPEP	57	

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																		ACE	50
																		GPER	48
																		LNPEP	46
																		MAS1	45
																		AGTR2	37
																		ACE2	36
																		HSD11B2	34
																		CYP11A1	33
																		ANPEP	33
																		CYP11B1	31
																		AKR1D1	15
<b>Skin (7, 222)</b>	81%		57%		90%		71%		57%		71%								
	GPER	54	AGTR1	84	CPA3	78	THOP1	44	GR	96	ATP6AP2	98						CTSA	94
	ACE	44	MR	75	CTSG	70	REN	24	HSD11B2	73	ACE2	28						IGF2R	87
	CYP11B2	16			CMA1	60												CTSD	83
																		KLK1	83
																		HSD11B1	82
																		RNPEP	81
																		PREP	79
																		CYP21A2	74
																		ANPEP	73
																		DPP3	72
																		MME	62
																		AGT	60
																		ENPEP	46
																		EGFR	44
																		LNPEP	44
																		CYP11A1	20
																		AGTR2	20
																		MAS1	18
																		AKR1C4	18
																		AKR1D1	14
																		CYP11B1	14
																		CYP17A1	14
<b>Pancreas (3, 100)</b>	100%		100%		100%		100%		100%		100%								
	ATP6AP2	98	DPP3	74	CPA3	94	RNPEP	93	CYP11B2	44	ANPEP	99						MR	83
	CTSA	95	THOP1	59	CTSG	56	PREP	80	CYP21A2	30	KLK1	98						AGT	70
	GR	93			CMA1	33	ACE	58	AGTR2	25	MAS1	16						AGTR1	63
	IGF2R	92					ACE2	56	CYP17A1	25								MME	62
	CTSD	90					HSD11B2	45	REN	24								EGFR	54
	ENPEP	72							CYP11B1	22								GPER	44
	HSD11B1	61							AKR1D1	15								AKR1C4	28
	LNPEP	59																CYP11A1	21
<b>Sub-cutaneous adipose (9, 474)</b>	81%		88%		96%		78%		85%		75%		78%		79%				
	CTSA	95	GR	97	CPA3	76	ATP6AP2	98	CYP11B2	64	ACE	68	CYP17A1	39	MME	95		HSD11B1	91
	IGF2R	91	AGTR1	94	CTSG	75	GPER	83	KLK1	61	THOP1	53	MAS1	37	AGT	63		EGFR	58
	CTSD	87	MR	71	CMA1	45	DPP3	81	CYP21A2	49	AKR1C4	25	REN	27	LNPEP	29		ACE2	35
	RNPEP	85	ENPEP	66			ANPEP	70	HSD11B2	31			CYP11B1	26					
	PREP	75							AGTR2	27									
	CYP11A1	37							AKR1D1	2									

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<b>Omental adipose (4, 86)</b>	91%		83%		83%		85%		75%											
	ATP6AP2	96	GR	97	ACE	67	AGT	51	PREP	74										
	CTSA	95	MME	96	KLK1	57	ACE2	38	LNPEP	72										
	CTSD	89	AGTR1	93	CYP11B2	46	REN	24												
	RNPEP	86	IGF2R	93	CYP21A2	44	MAS1	20												
	HSD11B1	77	ENPEP	88	CYP11A1	37	AKR1D1	9												
	CPA3	75	GPER	75	HSD11B2	37														
	DPP3	72	MR	73	CYP17A1	36														
	CTSG	65	ANPEP	67	CYP11B1	33														
	THOP1	62	EGFR	67	AGTR2	18														
CMA1	51																			
AKR1C4	49																			
<b>Breast (6, 239)</b>	86%		83%		73%		84%		83%		75%		83%							
	RNPEP	86	ATP6AP2	98	CPA3	65	EGFR	75	ACE2	43	AGT	57	ANPEP	79			MME	90		
	CTSA	85	GR	94	CTSG	57	MAS1	35	REN	25	ACE	38	HSD11B2	34			HSD11B1	63		
	CTSD	74	AGTR1	82	CMA1	45	AGTR2	31			CYP11A1	38					KLK1	57		
	PREP	73	IGF2R	81							CYP11B1	31					GPER	54		
	DPP3	66	MR	78													CYP21A2	38		
	THOP1	52	ENPEP	55													CYP11B2	36		
																	CYP17A1	31		
																	LNPEP	30		
																	AKR1D1	23		
<b>Large airways (5, 101)</b>	96%		93%		100%		96%		95%		93%		73%		80%					
	RNPEP	96	ATP6AP2	99	CPA3	82	ANPEP	75	EGFR	33	HSD11B1	38	IGF2R	89	CYP17A1	32	AGT	51		
	CTSD	93	GR	93	AKR1C4	44	ACE	55	REN	25	HSD11B2	35	DPP3	82	CMA1	13	KLK1	47		
	CTSA	92	MR	85	CTSG	30	MME	36	MAS1	19	CYP21A2	21	AKR1D1	15			CYP11B1	14		
	PREP	79	ACE2	59	CYP11A1	11	AGTR1	36	ENPEP	18										
	THOP1	68	LNPEP	54			CYP11B2	27												
			AGTR2	35			GPER	17												
<b>Small airways (8, 357)</b>	96%		100%		90%		88%		78%		91%		88%							
	RNPEP	96	GR	93	CPA3	89	REN	34	MME	45	ATP6AP2	99	CYP21A2	24			KLK1	55		
	CTSD	93	MR	85	EGFR	35	AGTR1	33	AGTR2	26	AGT	47	CYP11B2	21			ACE	50		
	CTSA	93			CTSG	35	CYP17A1	33	AKR1D1	16	HSD11B1	41					LNPEP	49		
	IGF2R	89			HSD11B2	32	CYP11A1	21	ENPEP	4	AKR1C4	38					MAS1	22		
	ANPEP	84					CMA1	21									GPER	21		
	DPP3	79					CYP11B1	15												
	PREP	77																		
	THOP1	68																		
	ACE2	54																		
<b>Esophagus (3, 83)</b>	92%		92%		92%		100%		92%		92%									
	RNPEP	91	GR	82	CPA3	72	AGT	42	CYP21A2	30	ATP6AP2	95					EGFR	62		
	CTSA	90	AGTR1	31	CTSG	57	GPER	34	ACE	14	IGF2R	83					KLK1	56		
	CTSD	78	MR	30	CMA1	26	HSD11B1	33	AKR1C4	13	LNPEP	28					MAS1	48		
	PREP	74	ENPEP	10													MME	42		
	DPP3	55															CYP17A1	40		
	THOP1	48															CYP11B2	39		
	CYP11A1	39															HSD11B2	38		
	ACE2	36															REN	33		
																	CYP11B1	22		
																ANPEP	21			

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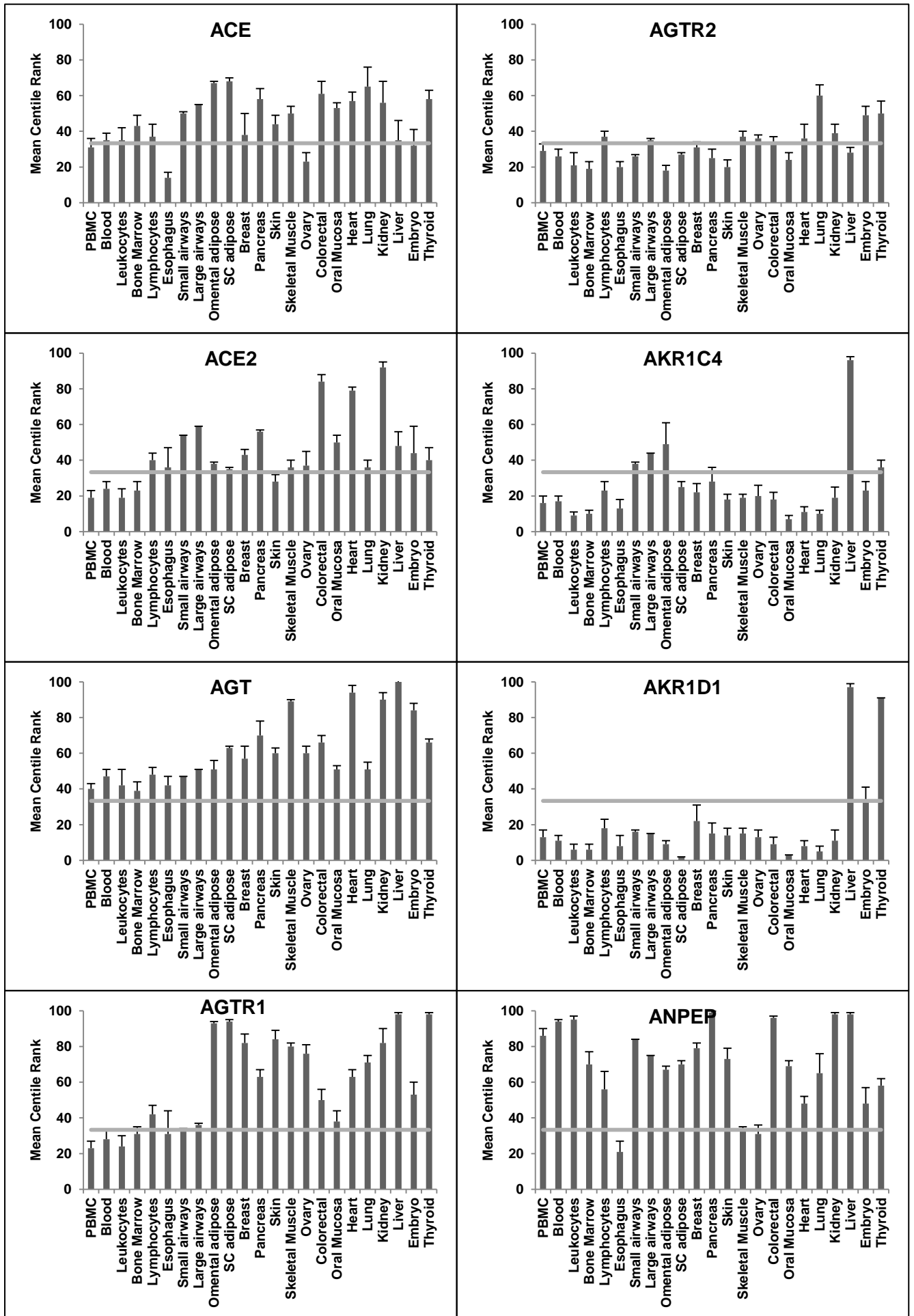
															AGTR2	20	
															AKR1D1	8	
<b>Lymphocytes (6, 184)</b>	77%		95%		83%		93%		83%		79%		75%				
	IGF2R	90	ATP6AP2	99	CTSG	61	EGFR	49	CYP17A1	43	KLK1	65	CTSD	70			
	CTSA	90	GR	95	ANPEP	56	AGT	48	ACE	37	CPA3	61	THOP1	58	HSD11B1	50	
	RNPEP	87	MR	90	MME	42	REN	30	AGTR2	37	LNPEP	56	GPPEP	33	HSD11B2	16	
	PREP	79			AGTR1	42	AKR1C4	23	CYP11A1	35	ACE2	40	CYP21A2	31			
	DPP3	70			MAS1	34	AKR1D1	18									
	CYP11B1	34			CMA1	26											
	CYP11B2	28															
ENPEP	3																
<b>Bone marrow (8, 208)</b>	72%		75%		71%		73%		78%		75%		72%		67%		
	CTSA	86	GR	89	CTSG	87	CYP21A2	36	EGFR	51	CYP17A1	33	ACE	43	KLK1	57	
	RNPEP	82	ANPEP	70	CPA3	76	MR	32	GPPEP	40	AGTR1	31	AGT	39	CYP11B2	47	
	PREP	74	LNPEP	55	DPP3	72	CYP11B1	26	HSD11B2	31	MAS1	22	REN	35	HSD11B1	29	
	IGF2R	71				CYP11A1	25	ENPEP	10	AKR1D1	6	ACE2	23				
	CTSD	70				AGTR2	19				CMA1	22					
						AKR1C4	10										
<b>Leukocytes (4, 222)</b>	83%		75%		75%		88%		79%		75%		75%		75%		
	ATP6AP2	98	MR	50	CTSG	56	CYP17A1	36	KLK1	64	AGT	42	CYP11B1	26	AGTR2	21	
	CTSA	97	CPA3	46	ENPEP	8	ACE	35	CYP11B2	58	AGTR1	24	AKR1D1	6	AKR1C4	9	
	RNPEP	93				HSD11B2	31	GPPEP	55								
	CTSD	91				REN	30	CYP21A2	41								
	PREP	78				CMA1	22	HSD11B1	34								
	DPP3	75				ACE2	19	CYP11A1	23								
<b>Total Blood (17, 774)</b>	76%		69%		65%		71%		69%								
	IGF2R	96	ATP6AP2	97	PREP	79	HSD11B1	44	REN	33						CPA3	
	CTSA	96	GR	94	DPP3	74	CYP17A1	36	CYP11B1	32						KLK1	
	MME	95	MR	57					AKR1D1	11						CTSG	
	ANPEP	94	LNPEP	48												THOP1	
	RNPEP	91														GPPEP	
	CTSD	82														AGT	
																	CYP11B2
																	EGFR
																	CYP21A2
																	ACE
																	CYP11A1
																	AGTR1
																	MAS1
																AGTR2	
																ACE2	
																CMA1	
																HSD11B2	
																AKR1C4	
																ENPEP	

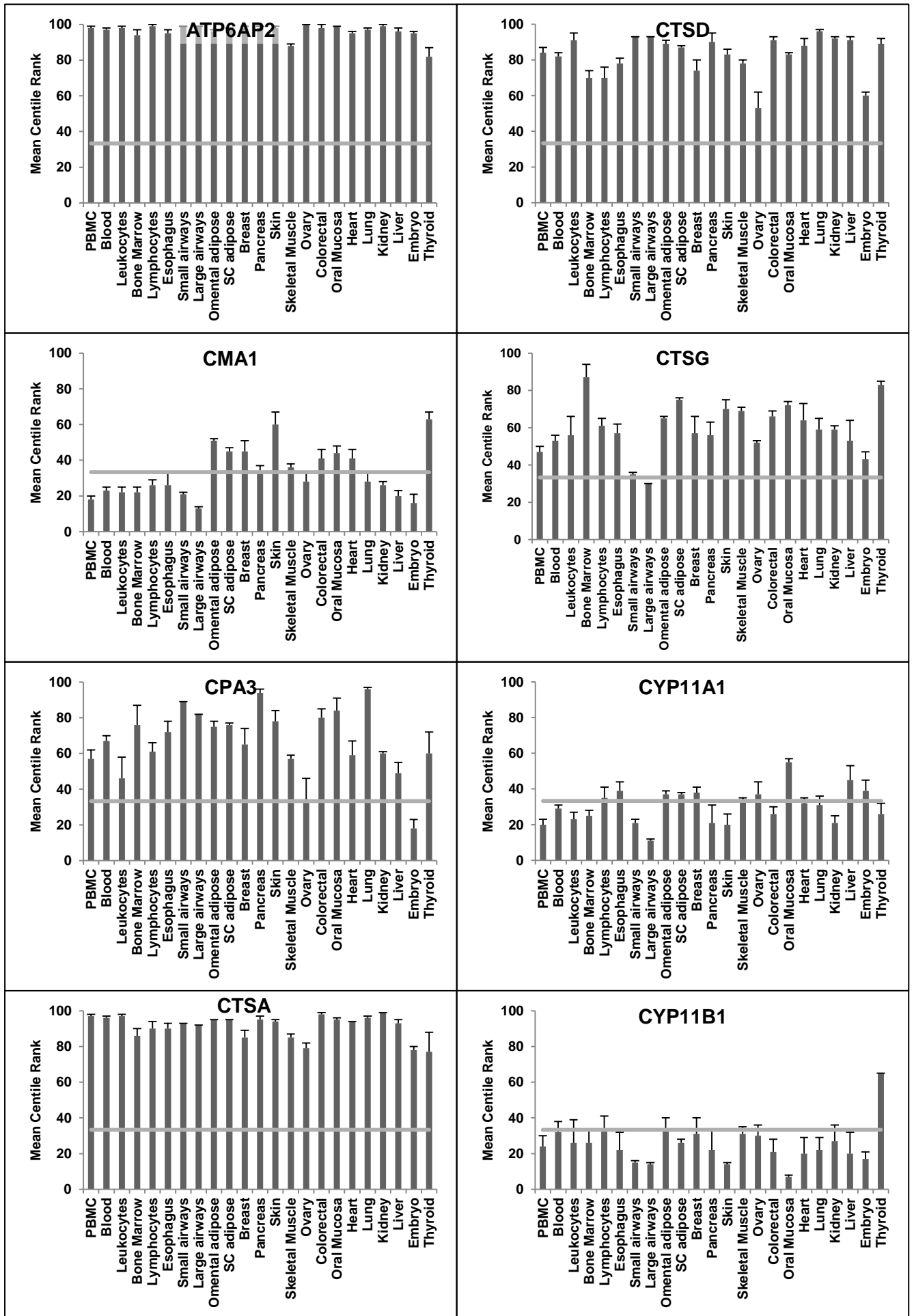
Nehme et al: Atlas of Tissue Renin-Angiotensin-Aldosterone System (RAAS) in Human

PBMC (11, 303)	71%		77%		70%		68%		79%		79%						
	CTSA	97	ATP6AP2	98	AGTR2	29	AGT	40	KLK1	61	CYP17A1	26					ANPEP
IGF2R	93	GR	94	AGTR1	23	ACE	31	CYP11B2	47	CYP11A1	20					PREP	79
RNPEP	91	MR	71	AKR1D1	13	REN	30	GPB	40	ENPEP	15					DPP3	78
CTSD	84	LNPEP	65			MAS1	21									MME	66
THOP1	54															CPA3	58
																CTSG	48
																CYP21A2	34
																HSD11B1	34
																EGFR	28
																CYP11B1	25
																HSD11B2	23
																ACE2	20
																CMA1	18
																AKR1C4	16

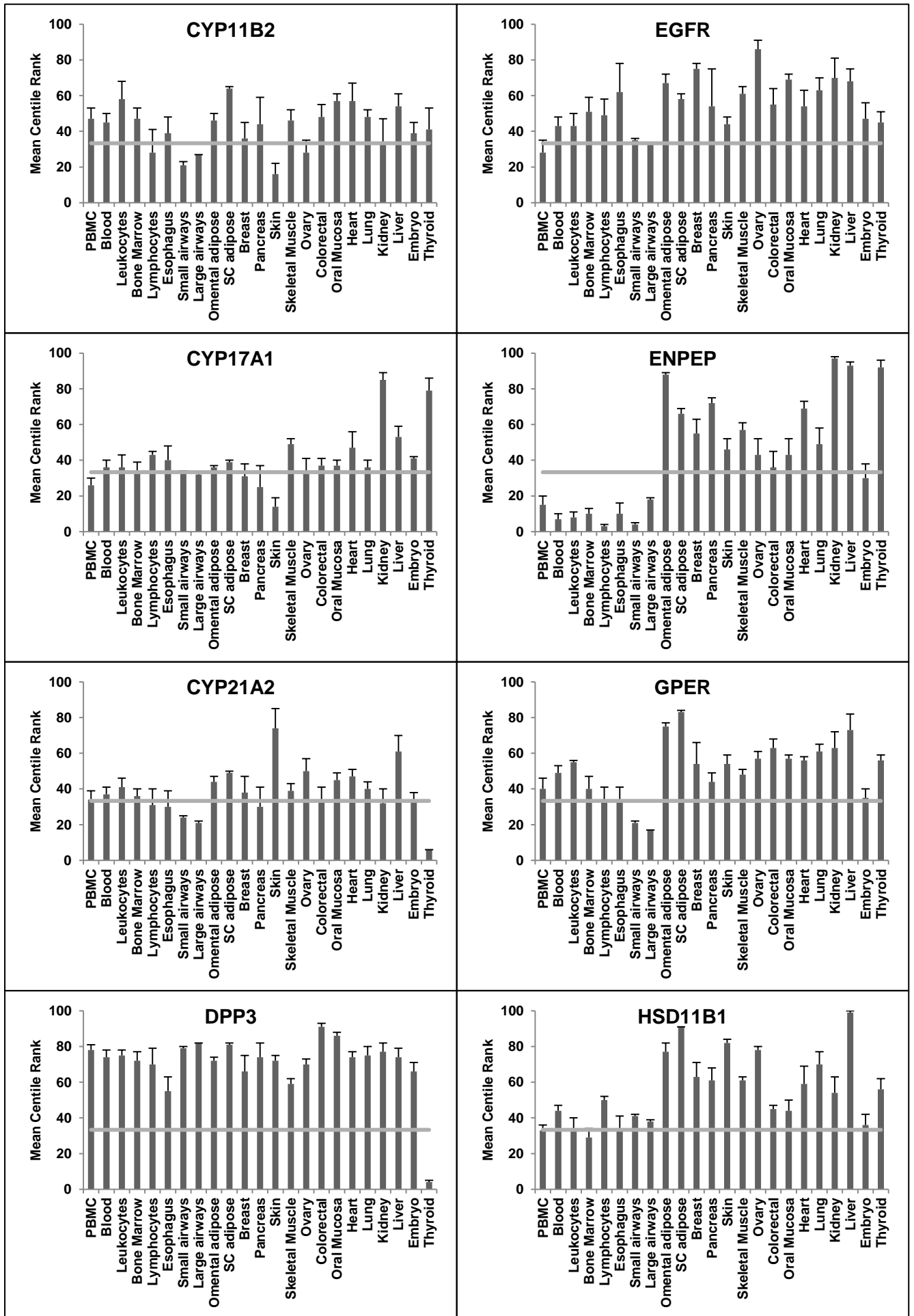
## **Supplementary Figure S1: ExtRAAS Gene Expression Profiles Across Studied Tissues**

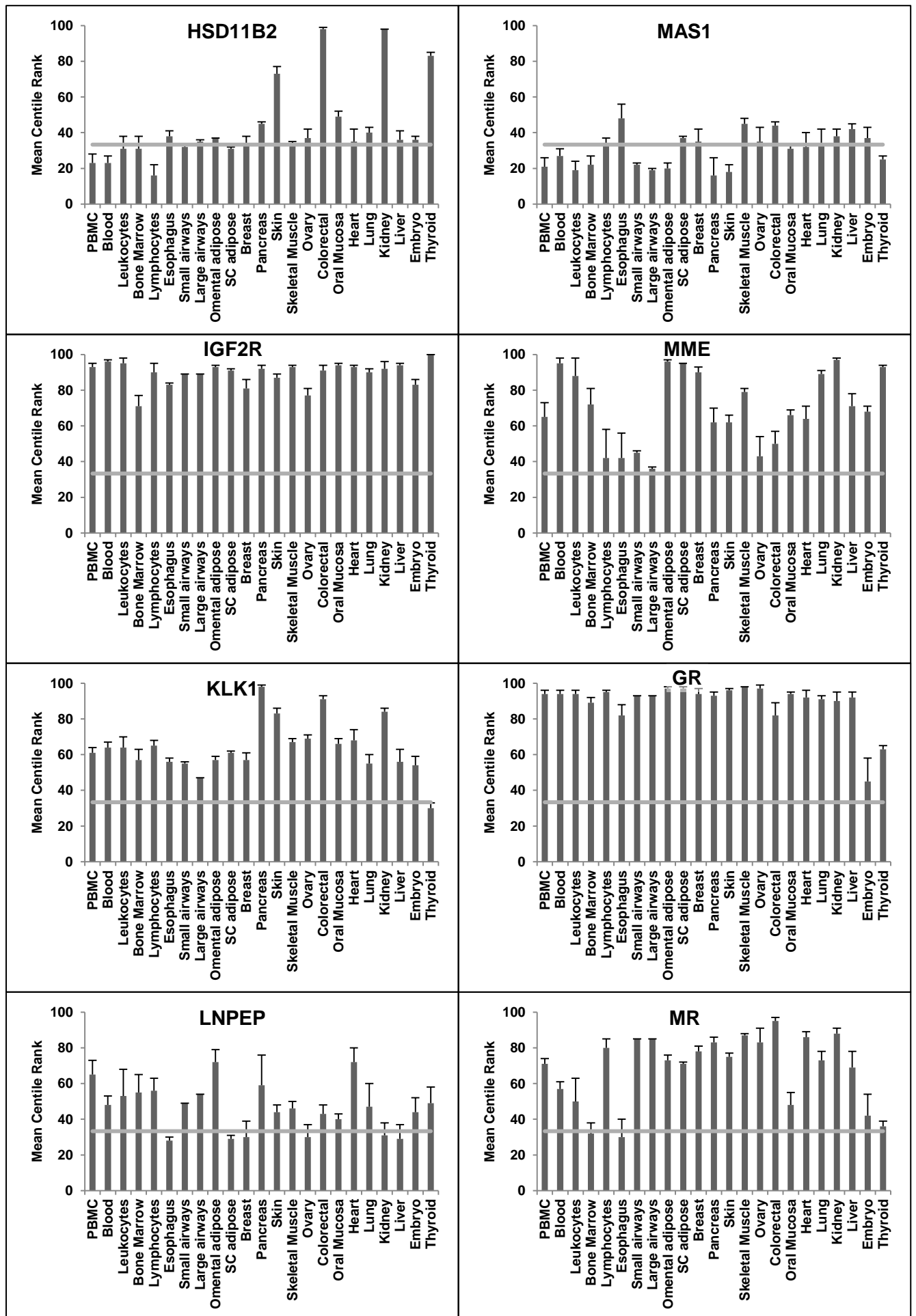
**Supplementary Figure S1: ExtRAAS gene expression profiles across studied tissues.** The expression profile of each of the extRAAS genes across all studied tissues represented in a bar-graph as mean expression centile rank (MCR)  $\pm$  SEM. A horizontal cut-off line was drawn at the MCR level 33.3.

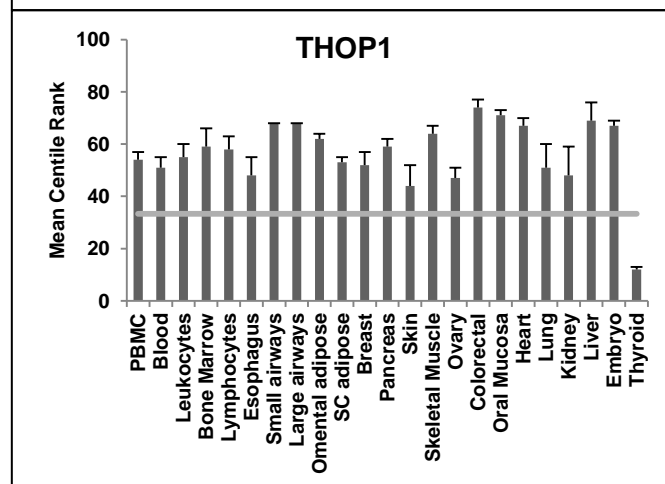
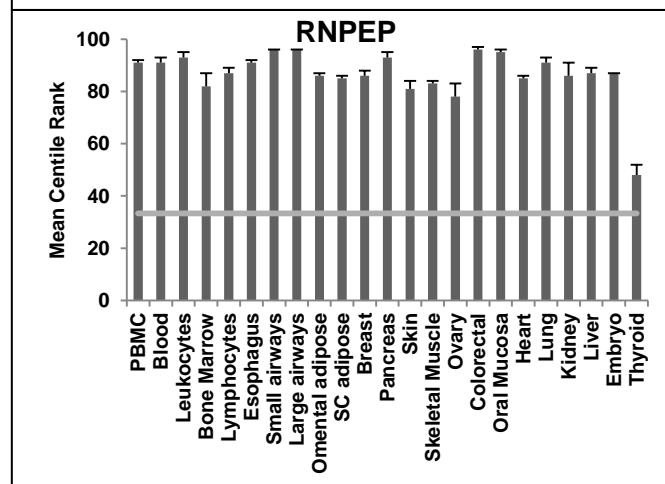
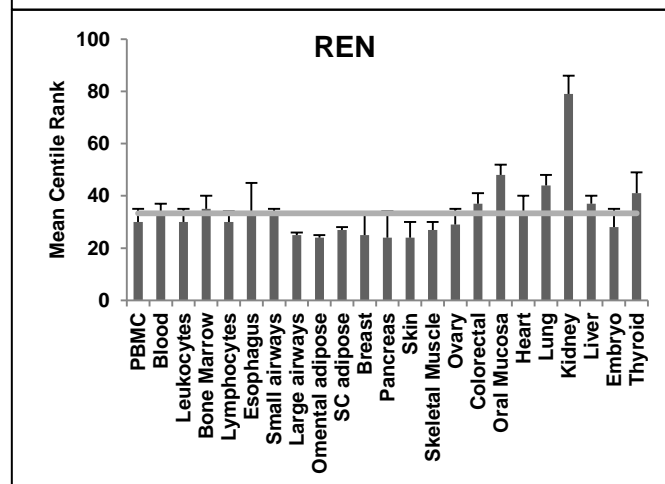
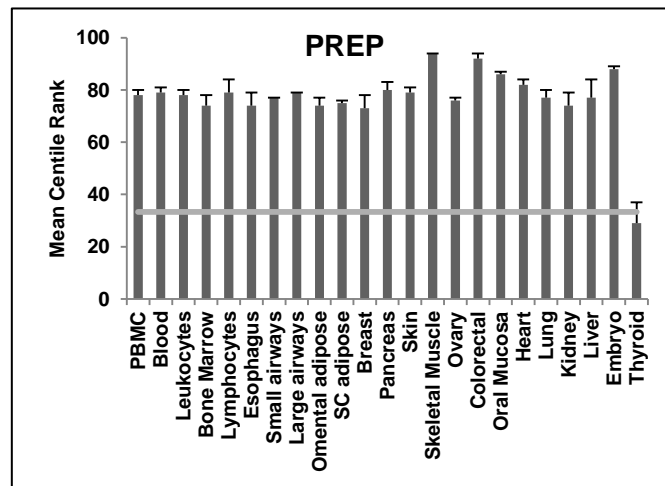






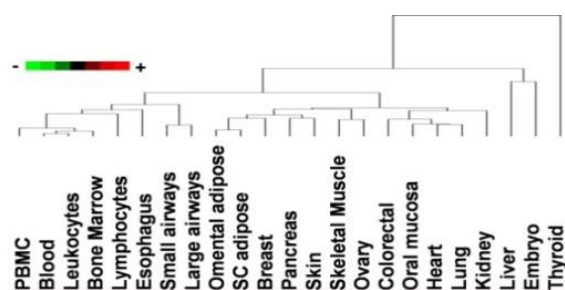




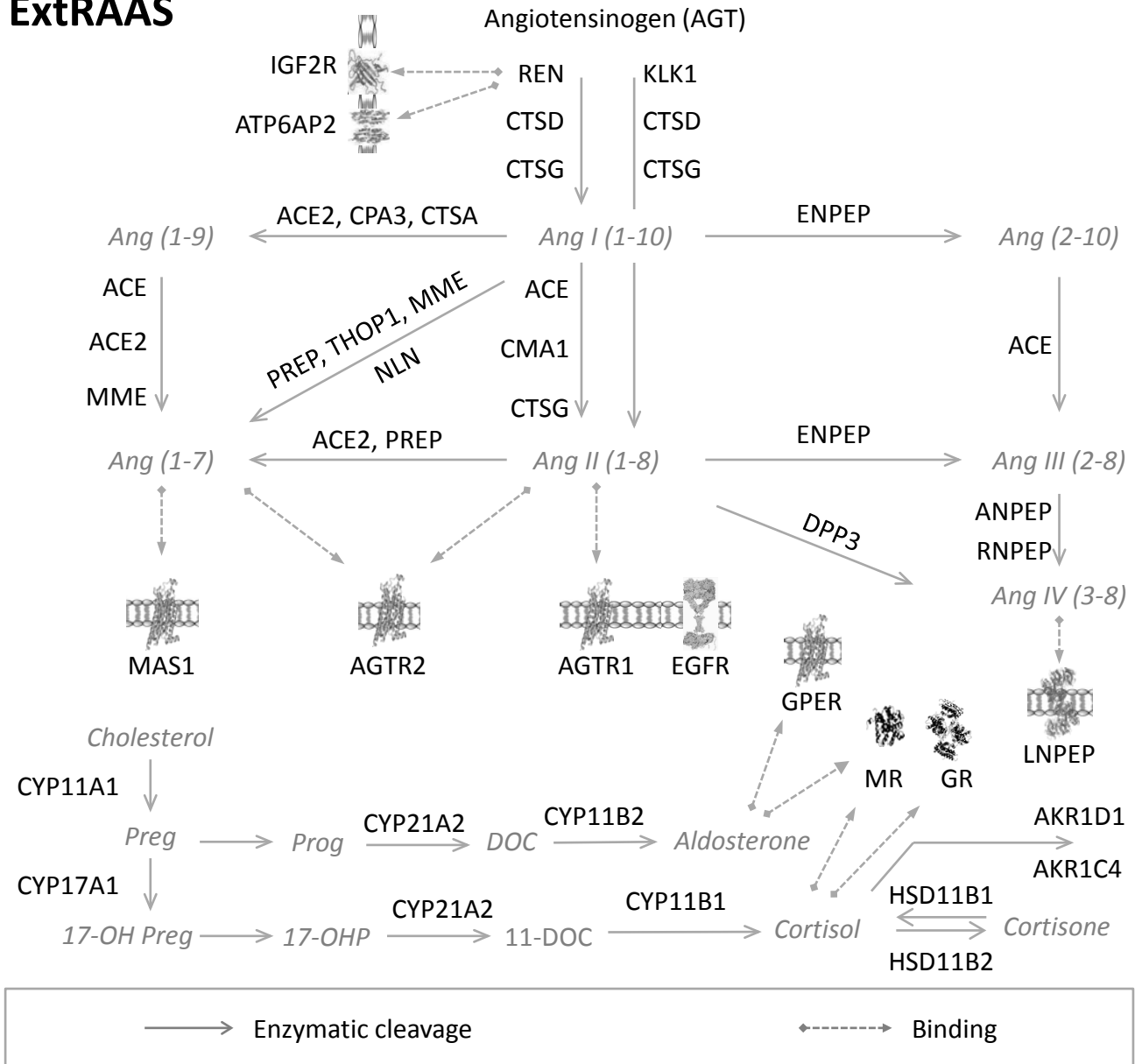


## Supplementary Atlas S1: ExtRAAS Maps in All Studied Tissues

**Supplementary Atlas S1: ExtRAAS maps in all studied tissues.** For each tissue, the number of datasets, samples and modules are represented as (datasets, samples, modules) below the tissue name. Gene transcripts are represented by the corresponding official symbols. The genes are represented in the map based on their coordination (same color = same cluster) and mean expression centile rank (MCR, 4 levels, larger font size= higher expression level). Genes below the first tertile (MCR  $\leq$  33) in each tissue were omitted for simplicity. Non-clustered genes are colored in black. Core group-based modules when present are colored similarly across tissue: CTSA-CTSD-based modules in red; CTSG-CPA3-CMA1-based modules in green; and GR-MR-AGTR1-based modules in dark blue. Angiotensin peptides and corticosteroid metabolites are represented in gray italics. Expression profiles of ExtRAAS genes in each tissue are represented using their MCR in a bar graph. Tissues are arranged based on the tissue dendrogram of figure 5 in the article (see dendrogram below).



# ExtRAAS



## MCR font size

≤ 33 → eliminated

34-40 → 9

41-60 → 11

61-80 → 14

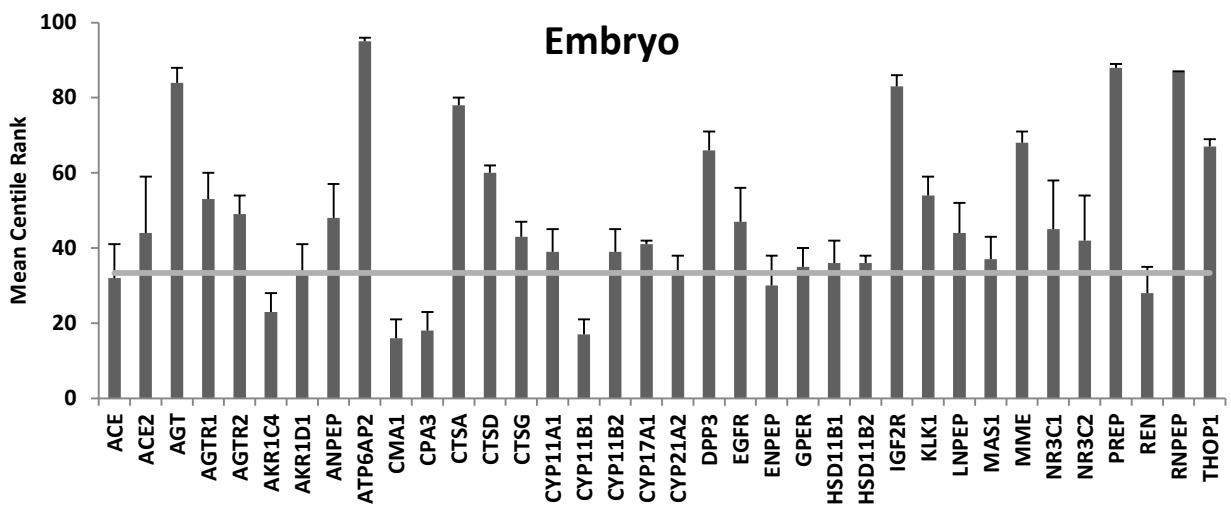
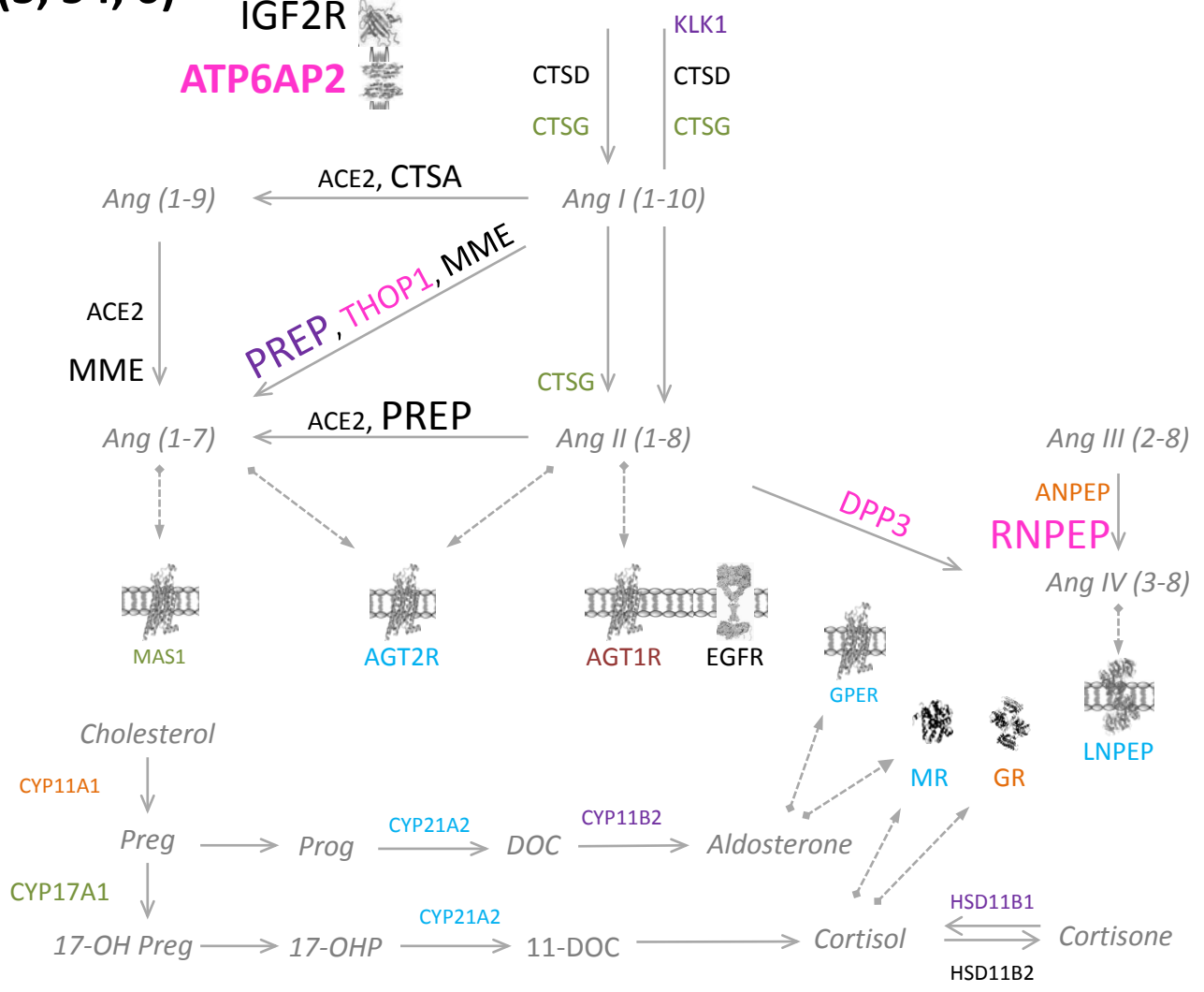
81-90 → 18

91-100 → 18



# Embryo (3, 54, 6)

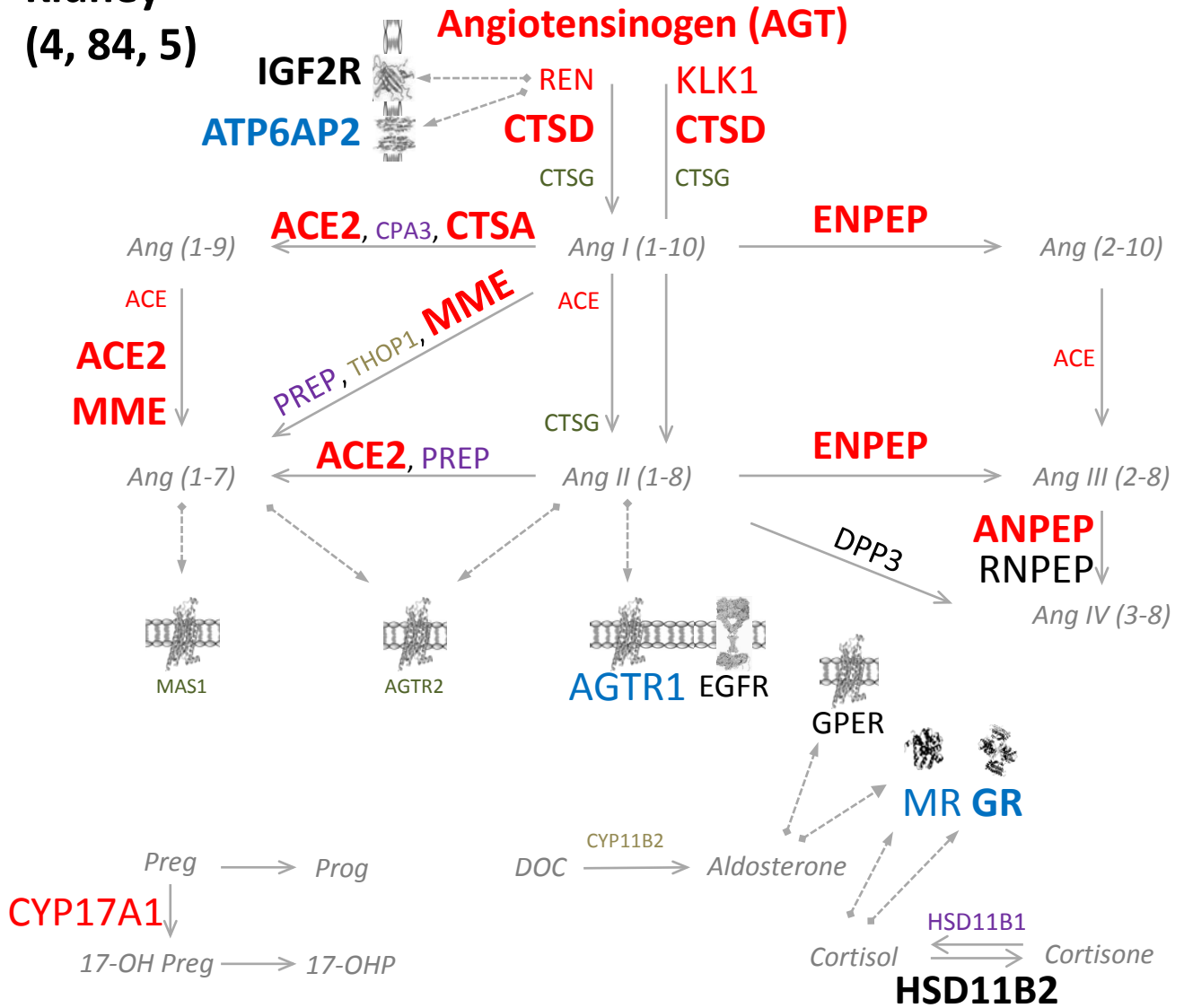
## Angiotensinogen (AGT)



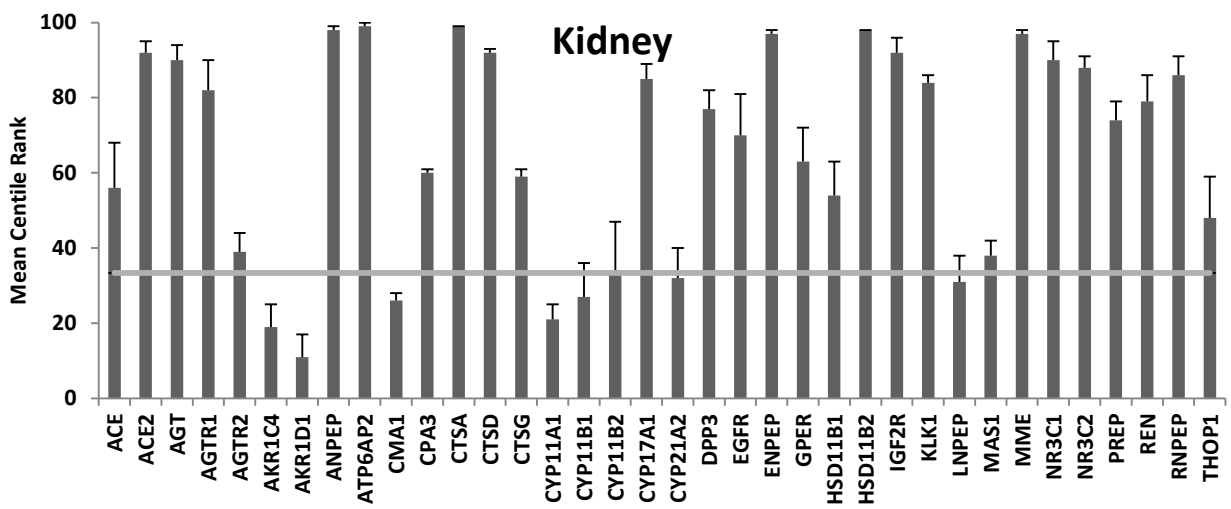




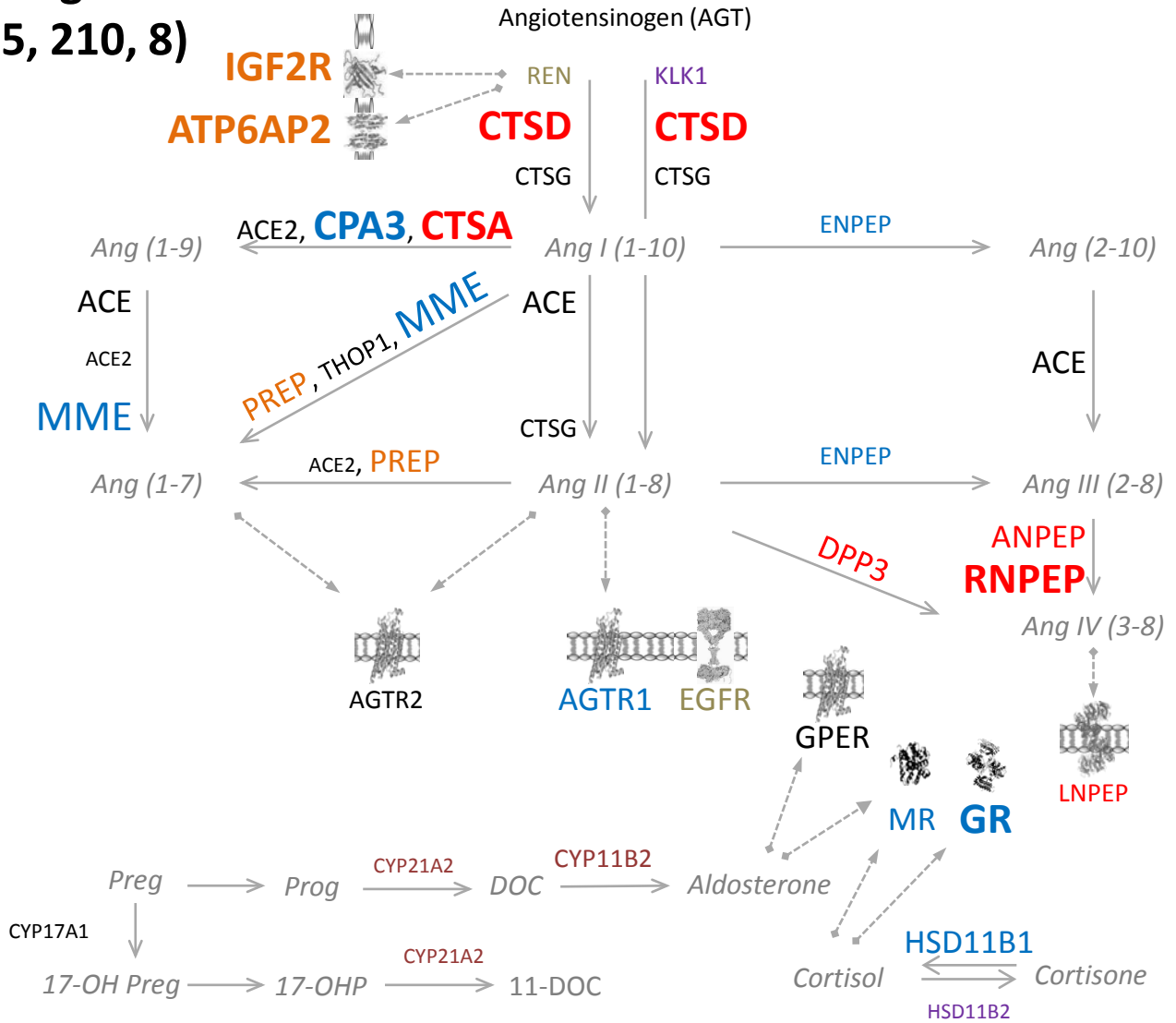
# Kidney (4, 84, 5)



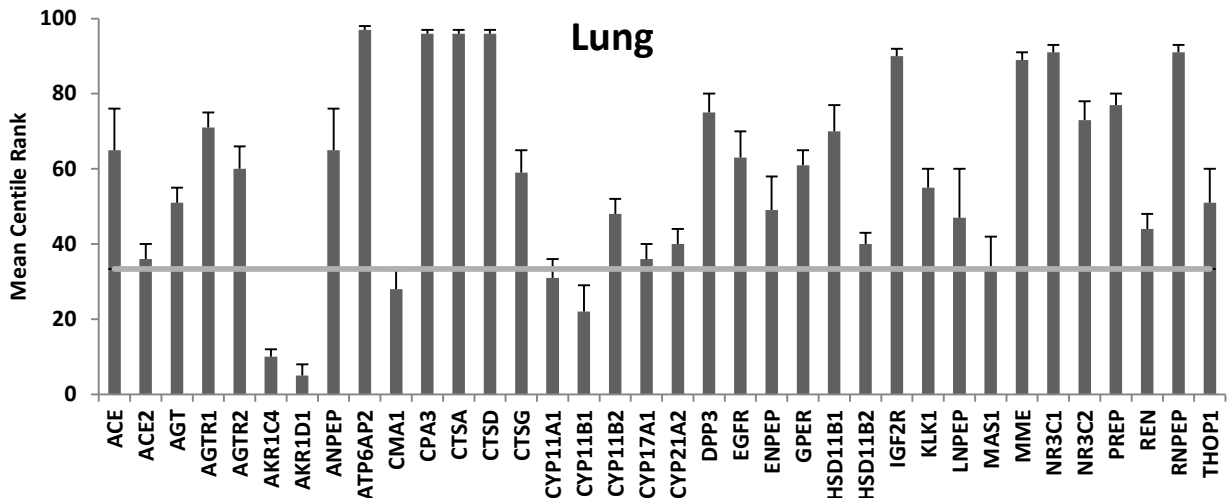
→ Enzymatic cleavage      ← Binding



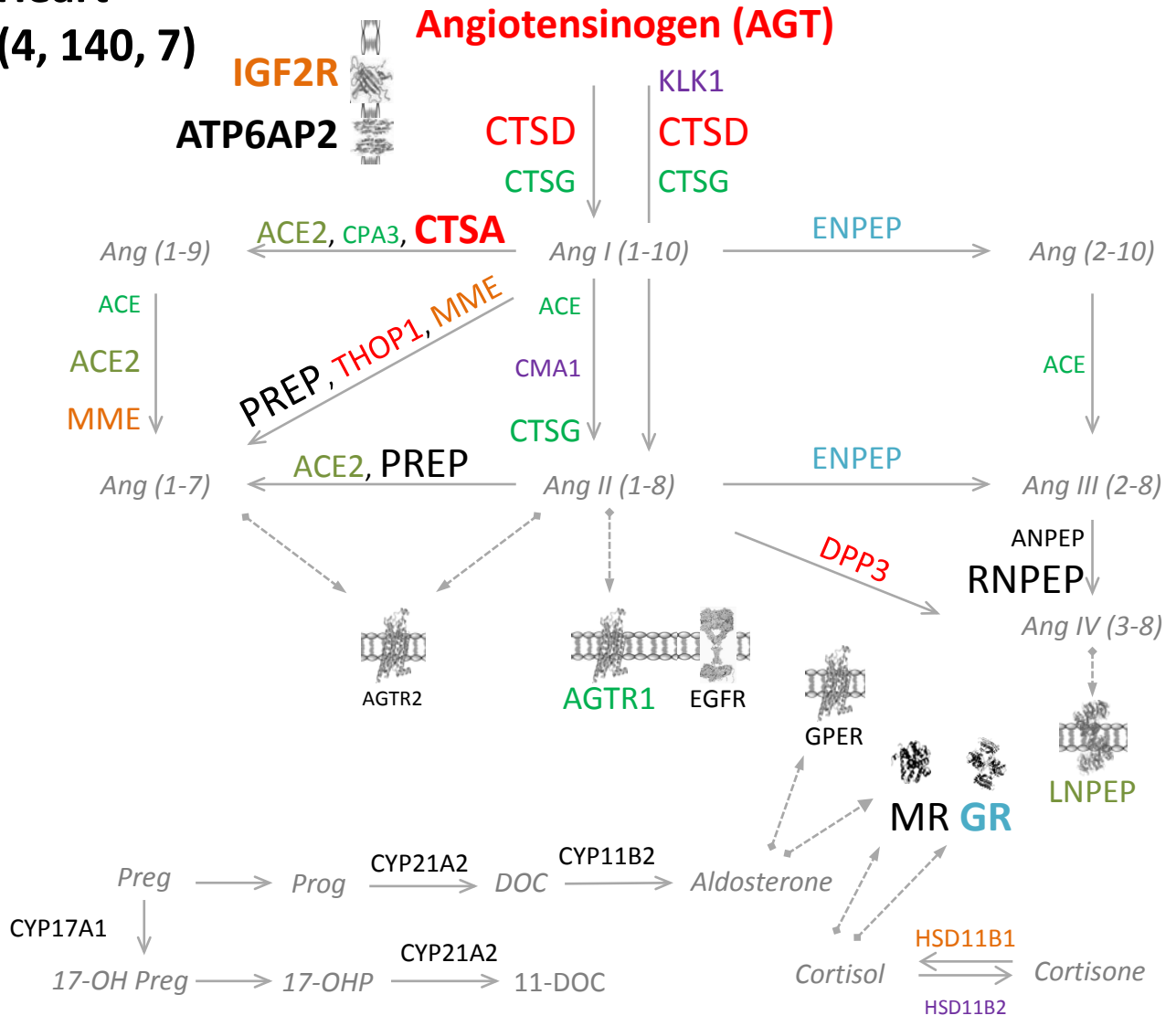
# Lung (5, 210, 8)



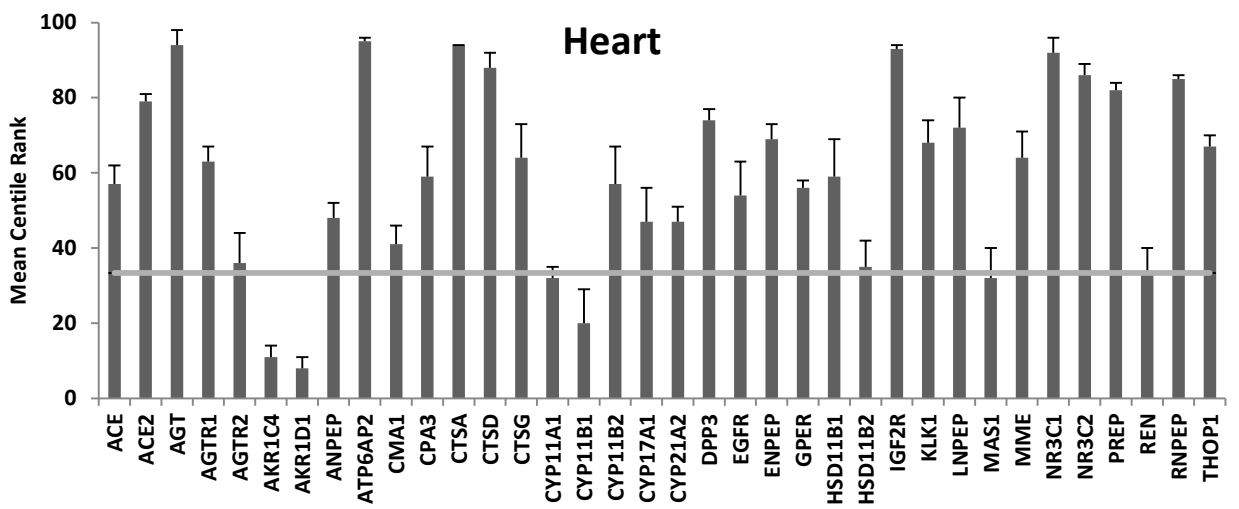
→ Enzymatic cleavage      ↔ Binding



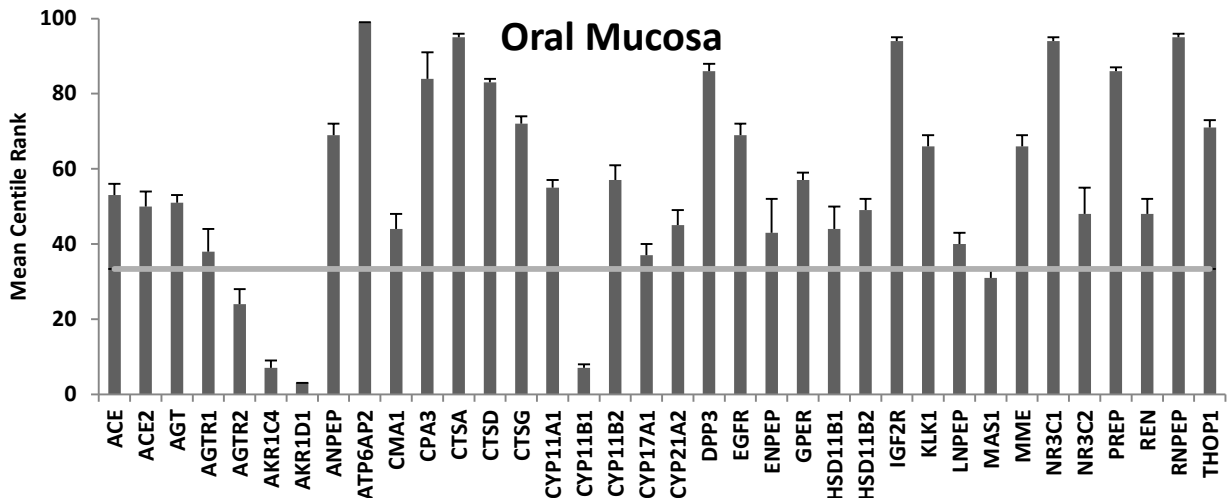
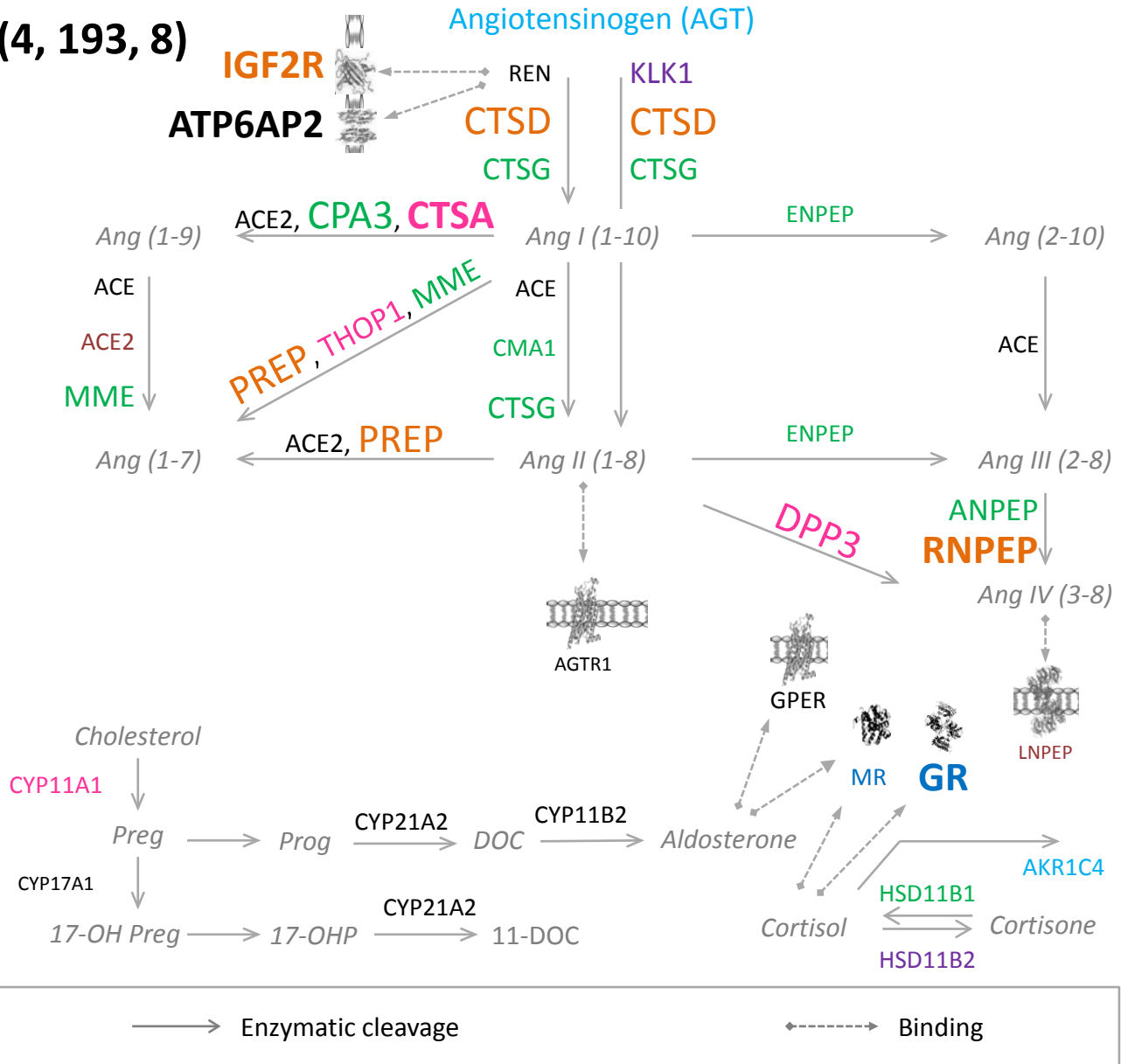
# Heart (4, 140, 7)



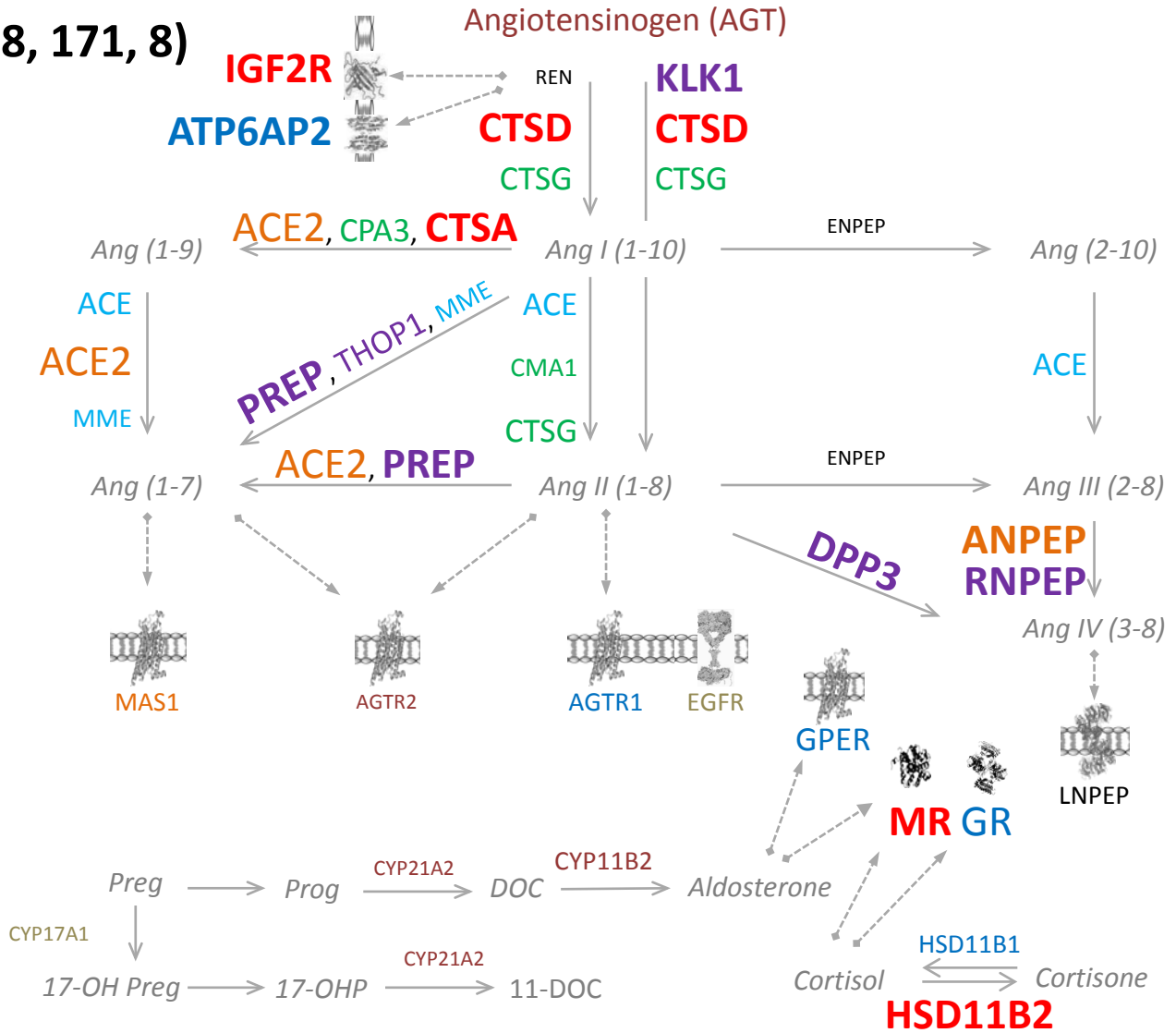
Enzymatic cleavage
  Binding



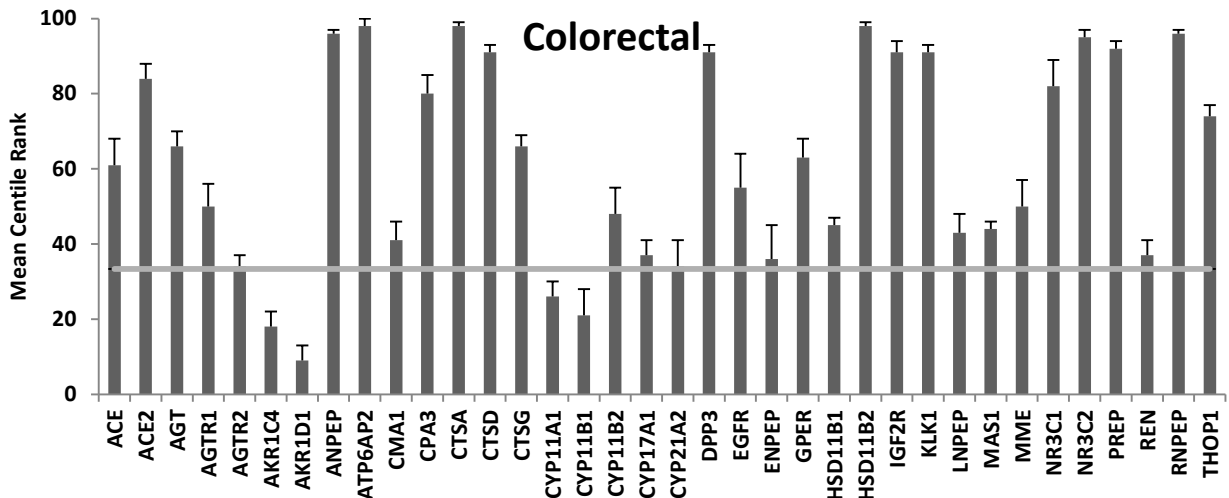
# Oral Mucosa (4, 193, 8)



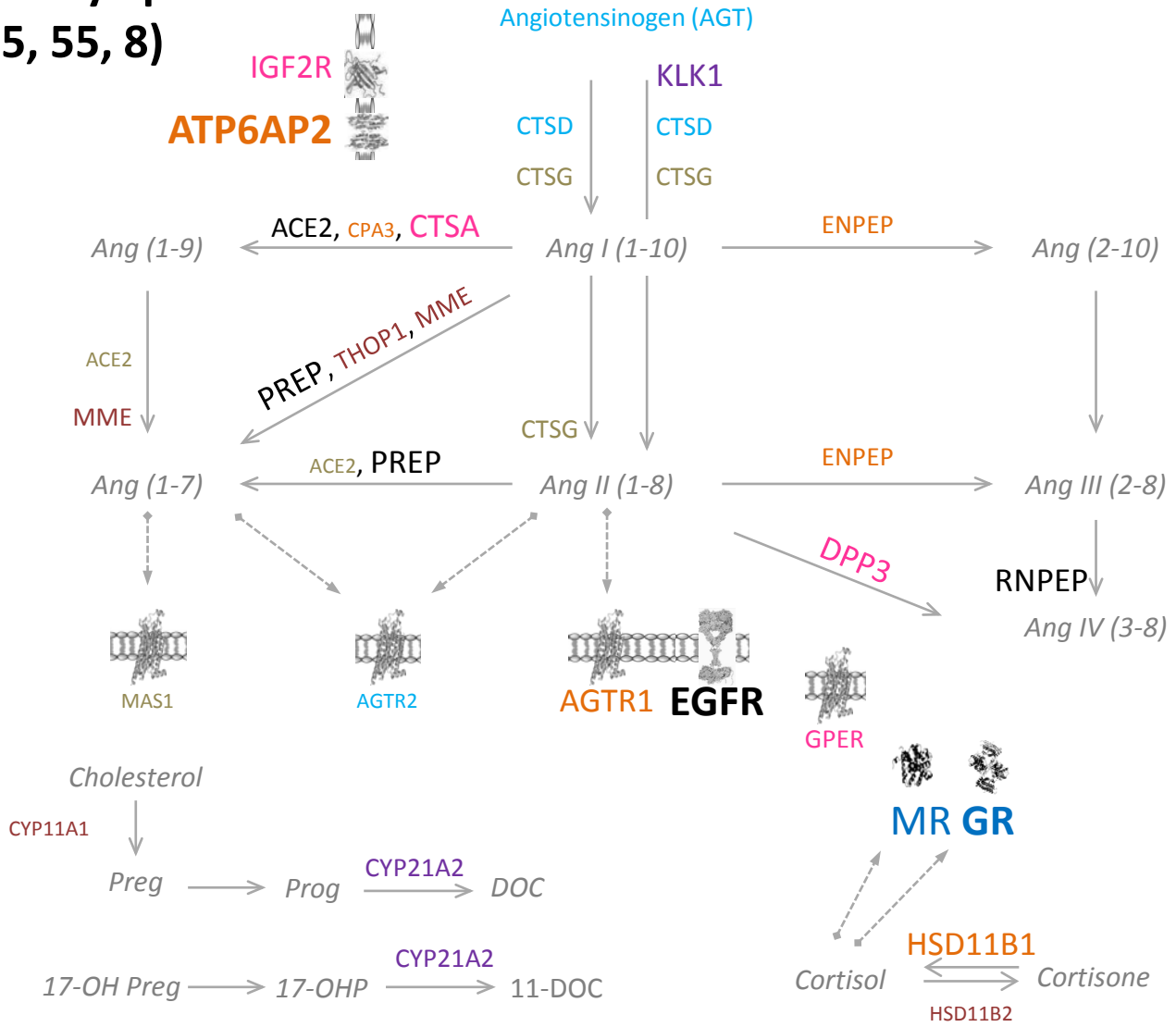
# Colorectal (8, 171, 8)



→ Enzymatic cleavage      ← Binding

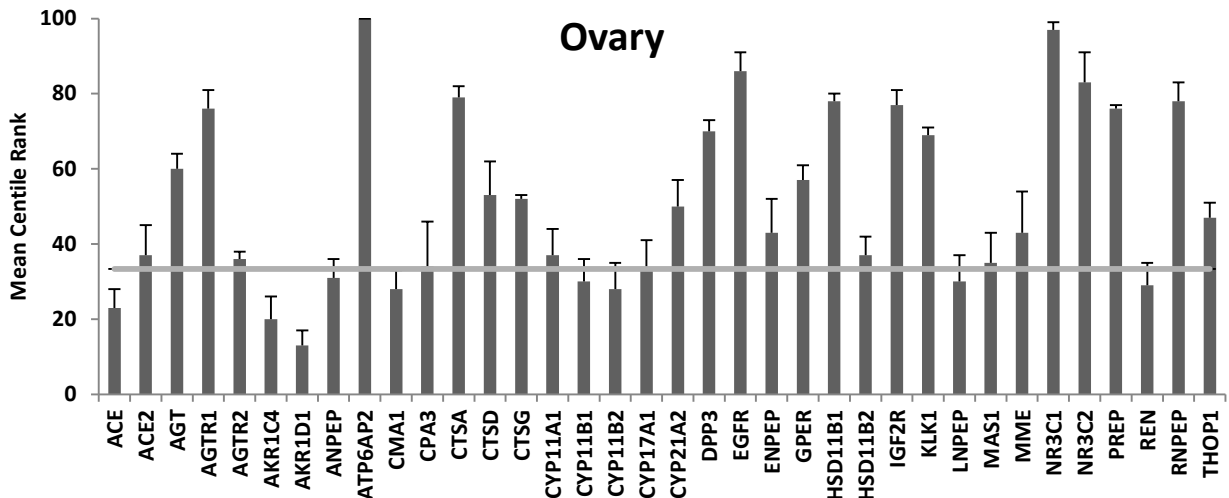


# Ovary Epithelium (5, 55, 8)

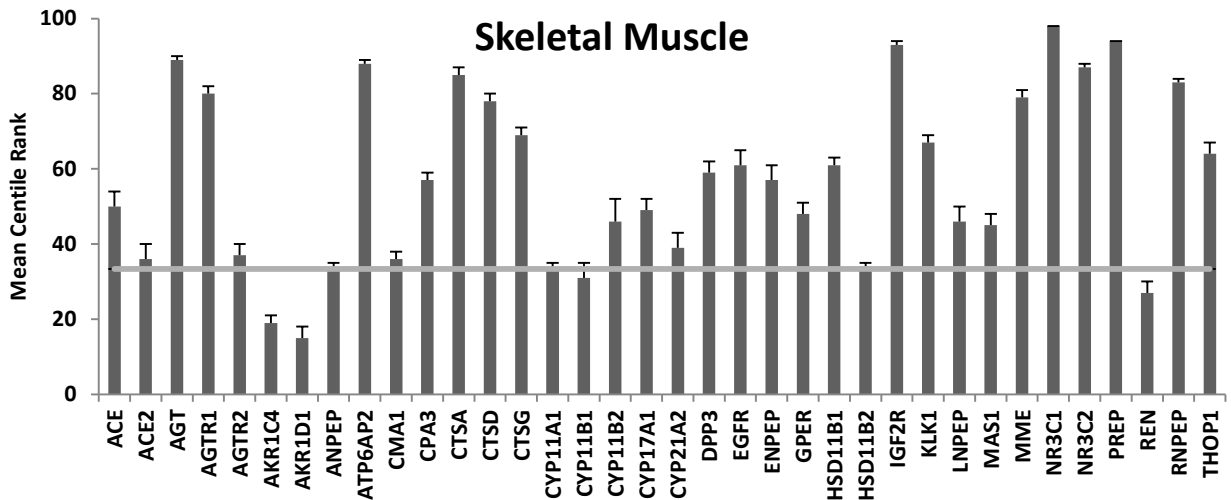
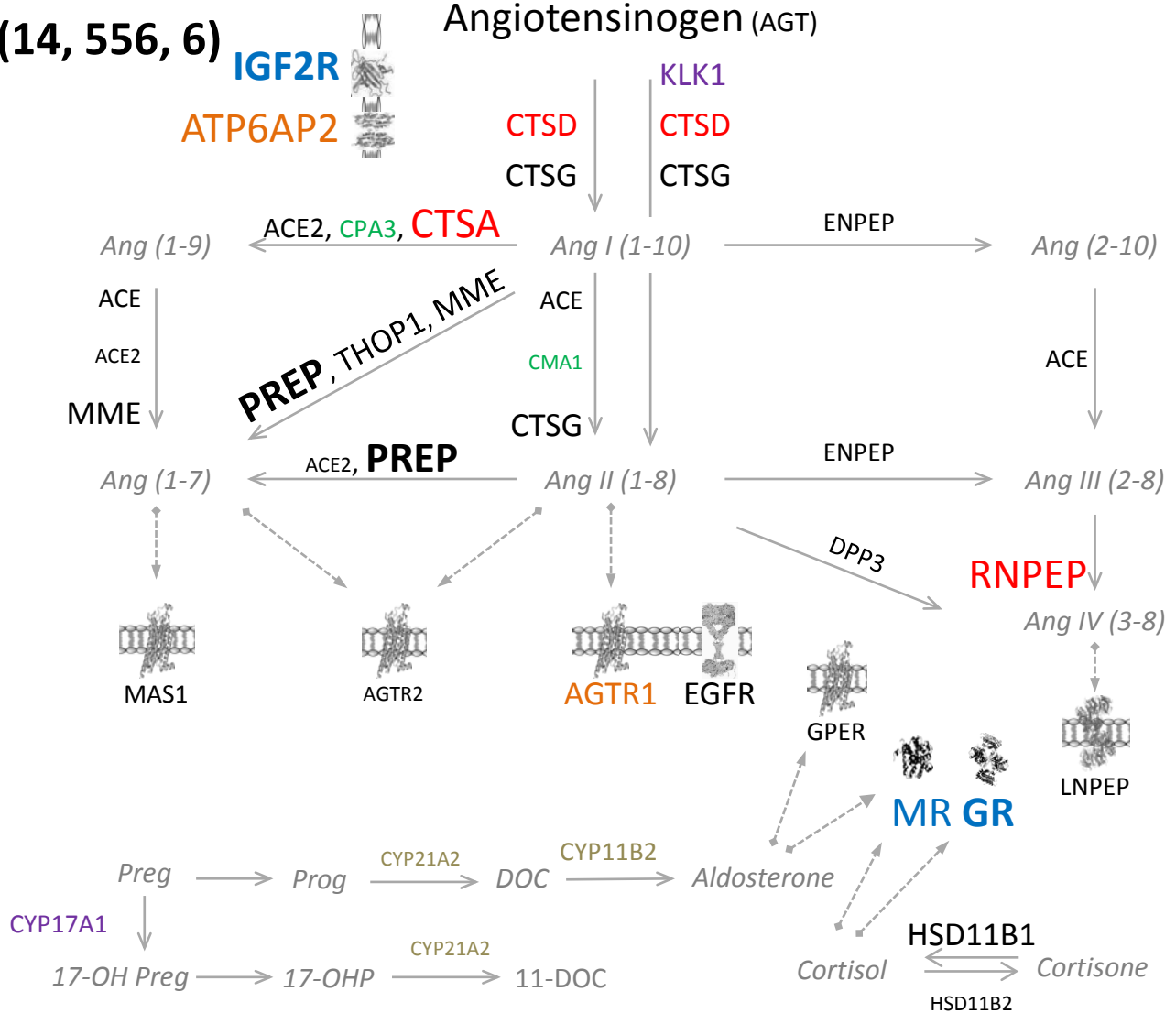


→ Enzymatic cleavage

◊ Binding

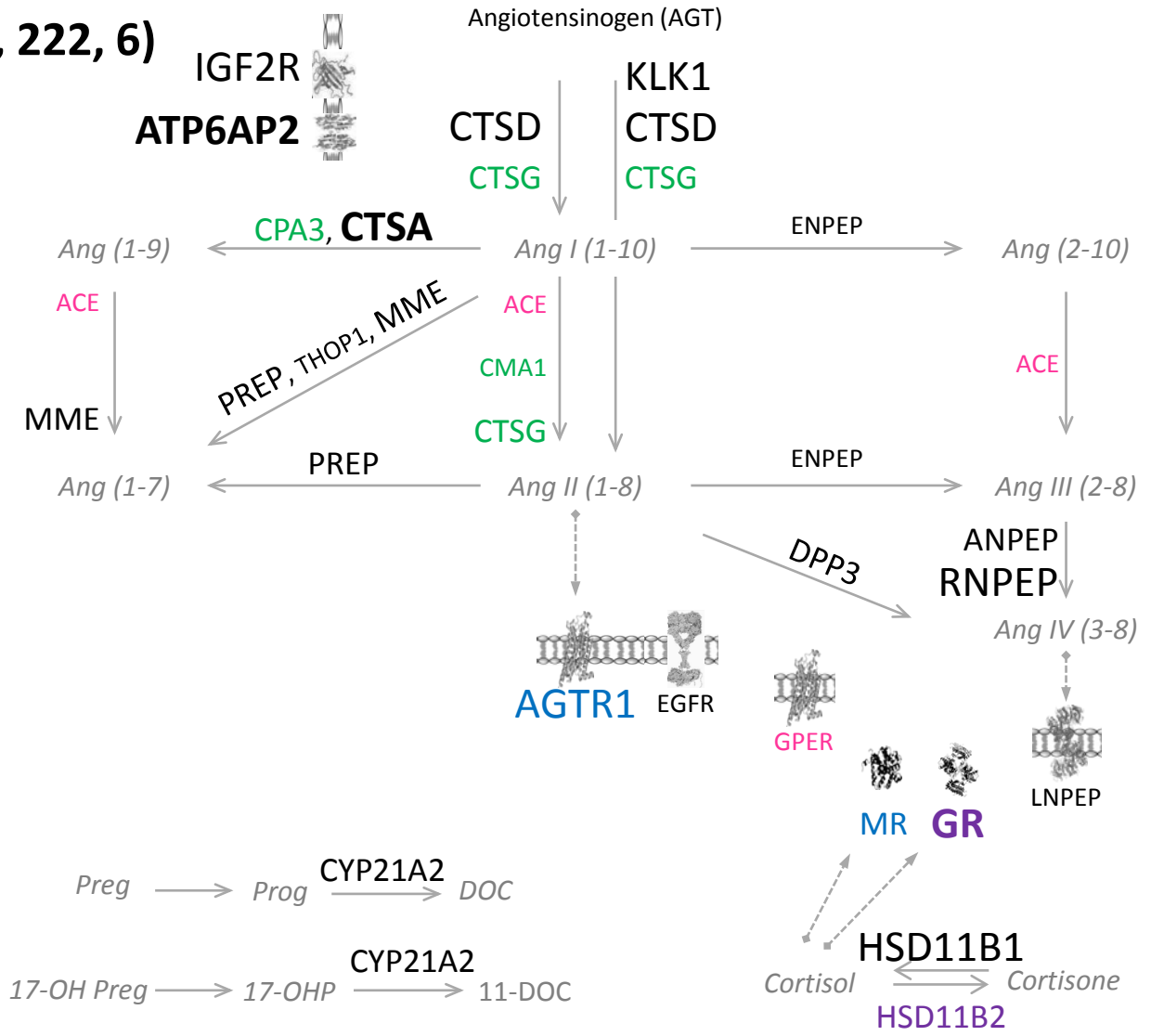


# Skeletal Muscle (14, 556, 6)

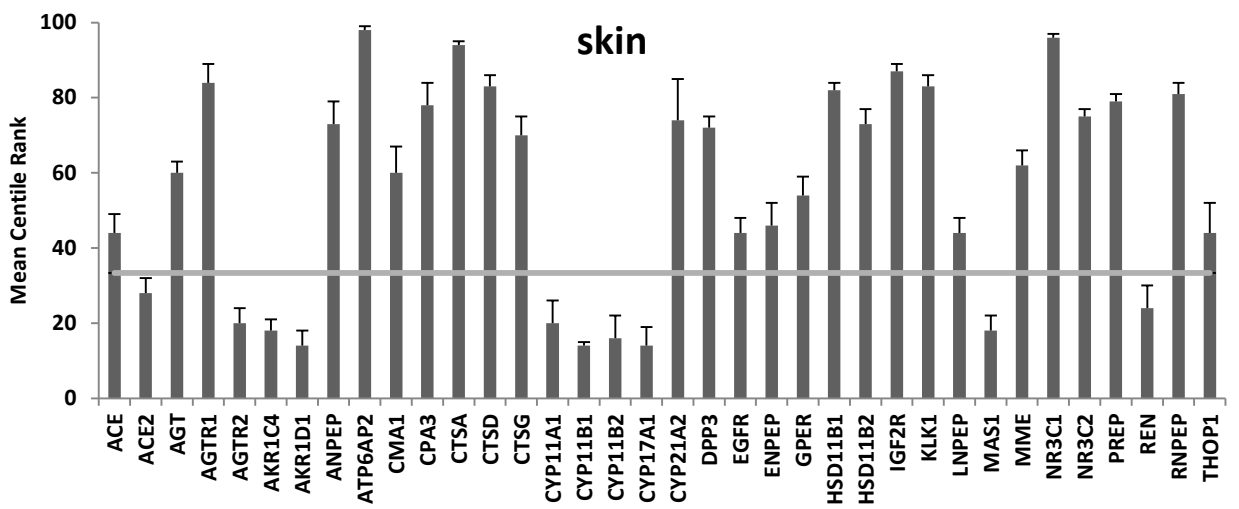


# Skin

(7, 222, 6)

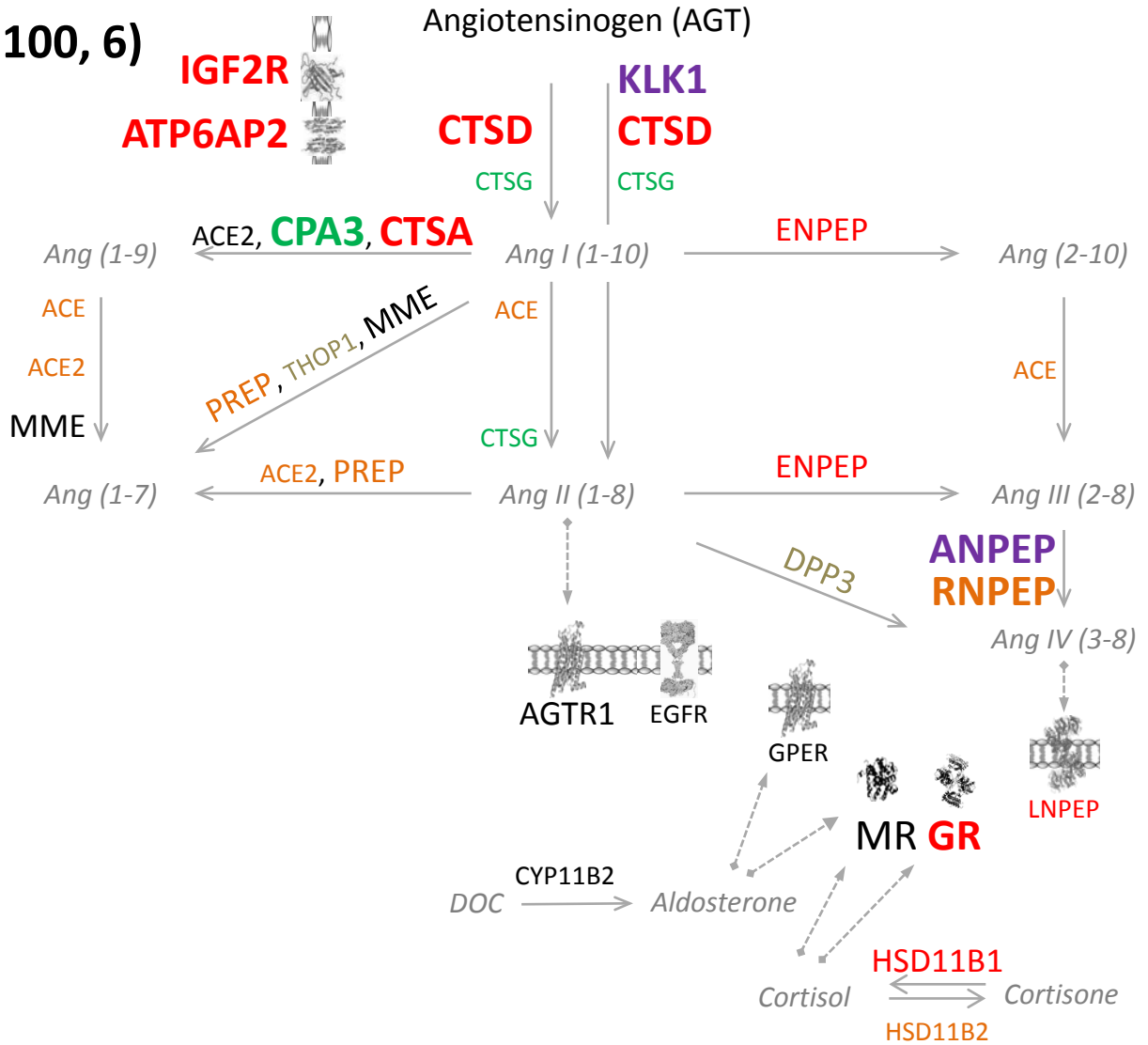


→ Enzymatic cleavage      ◀--- Binding

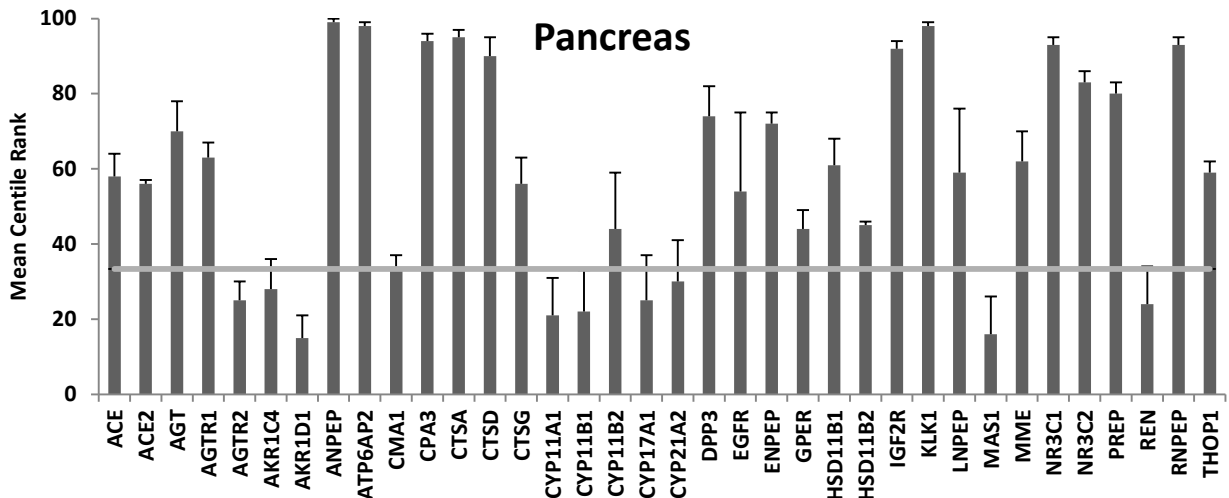




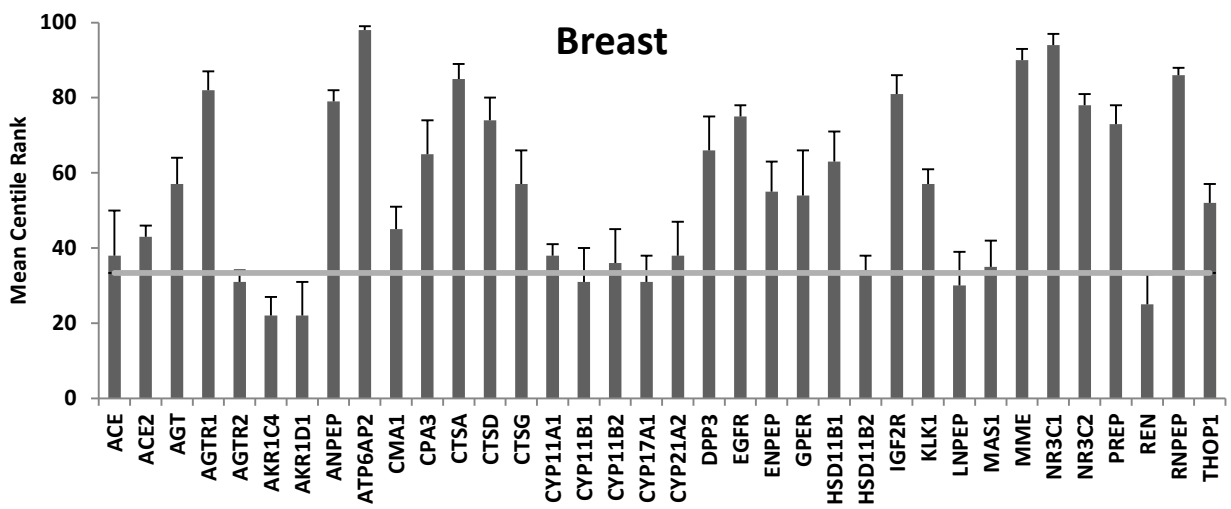
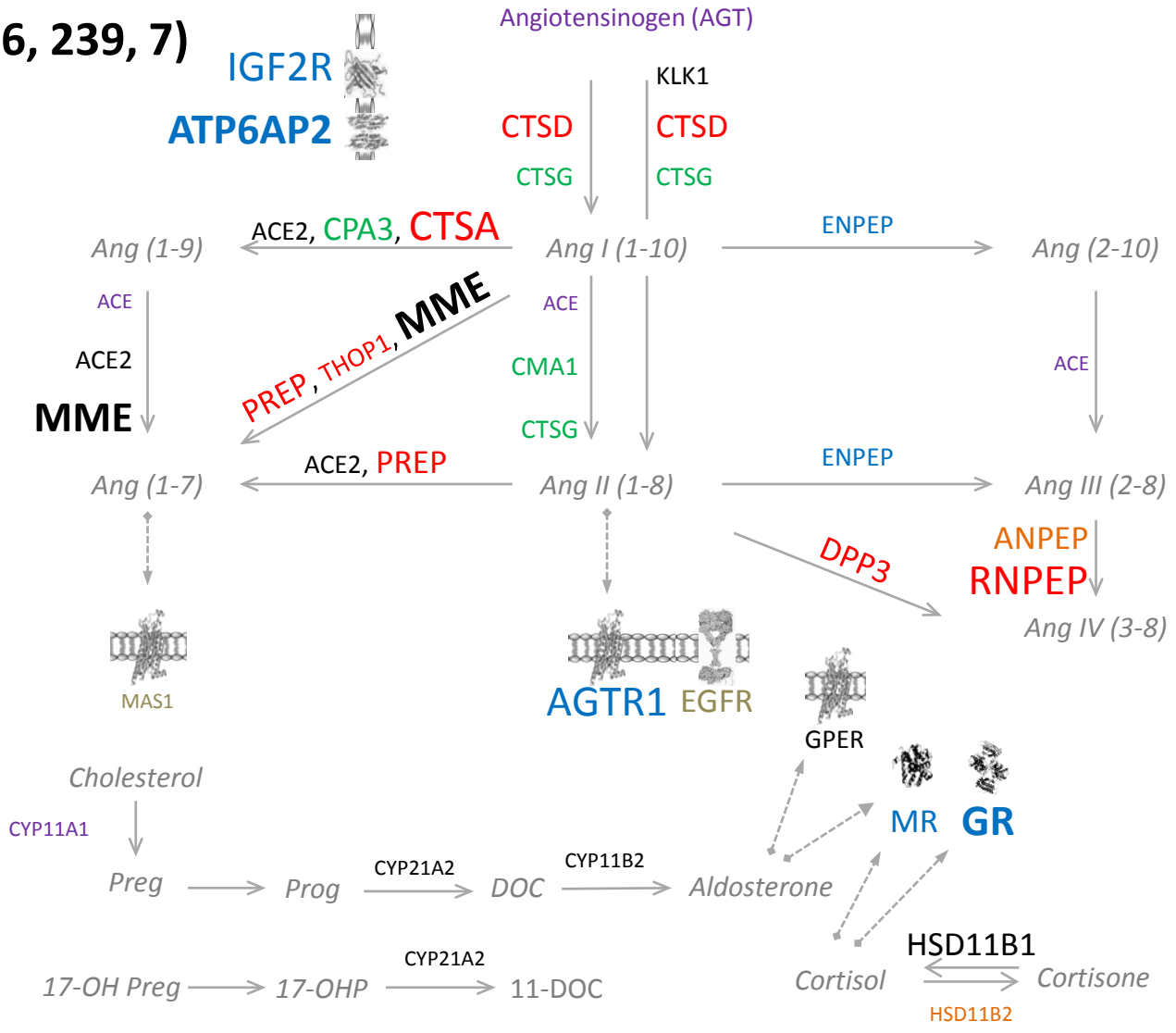
# Pancreas (3, 100, 6)



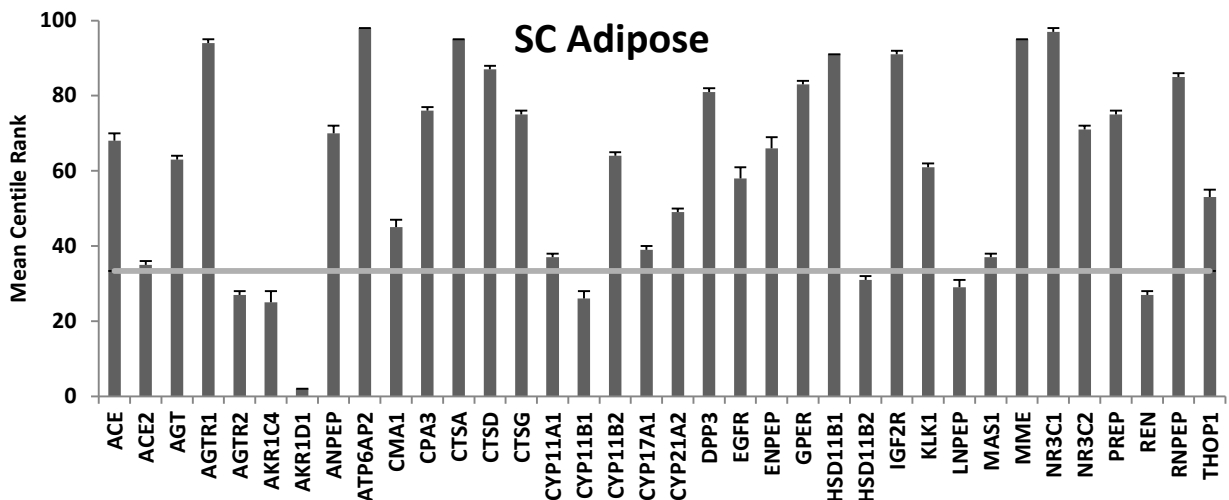
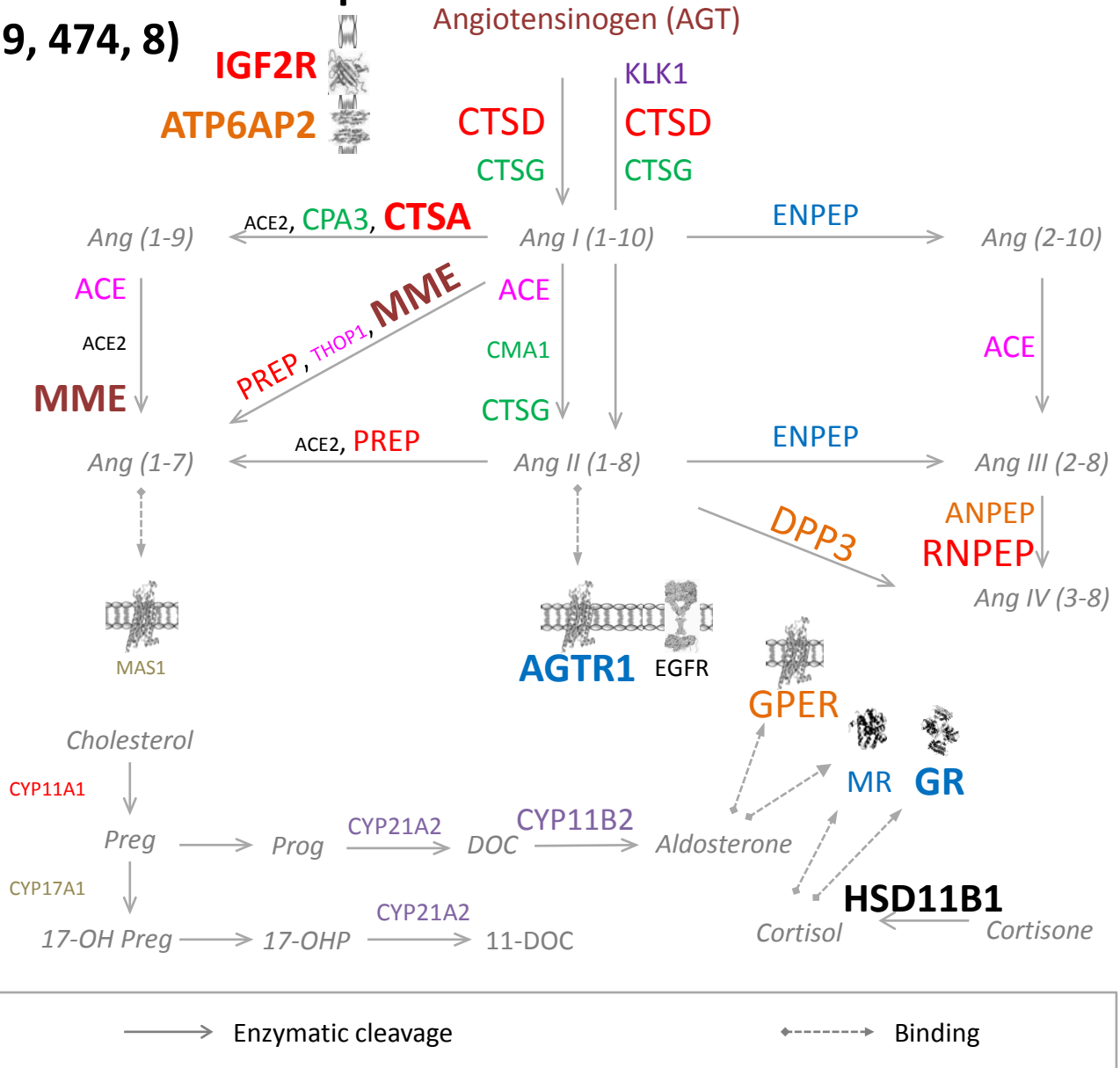
→ Enzymatic cleavage      ⇌ Binding



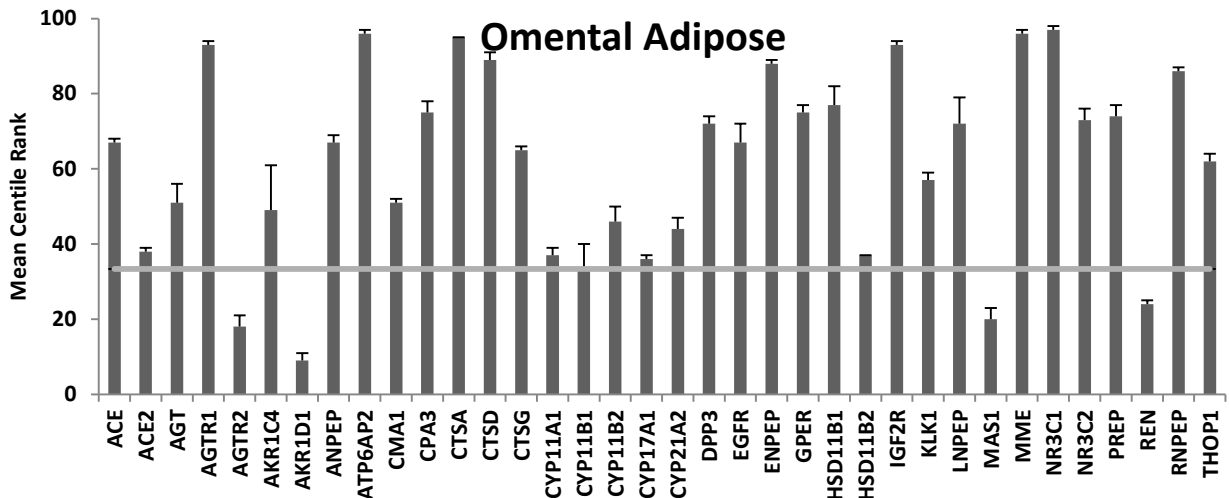
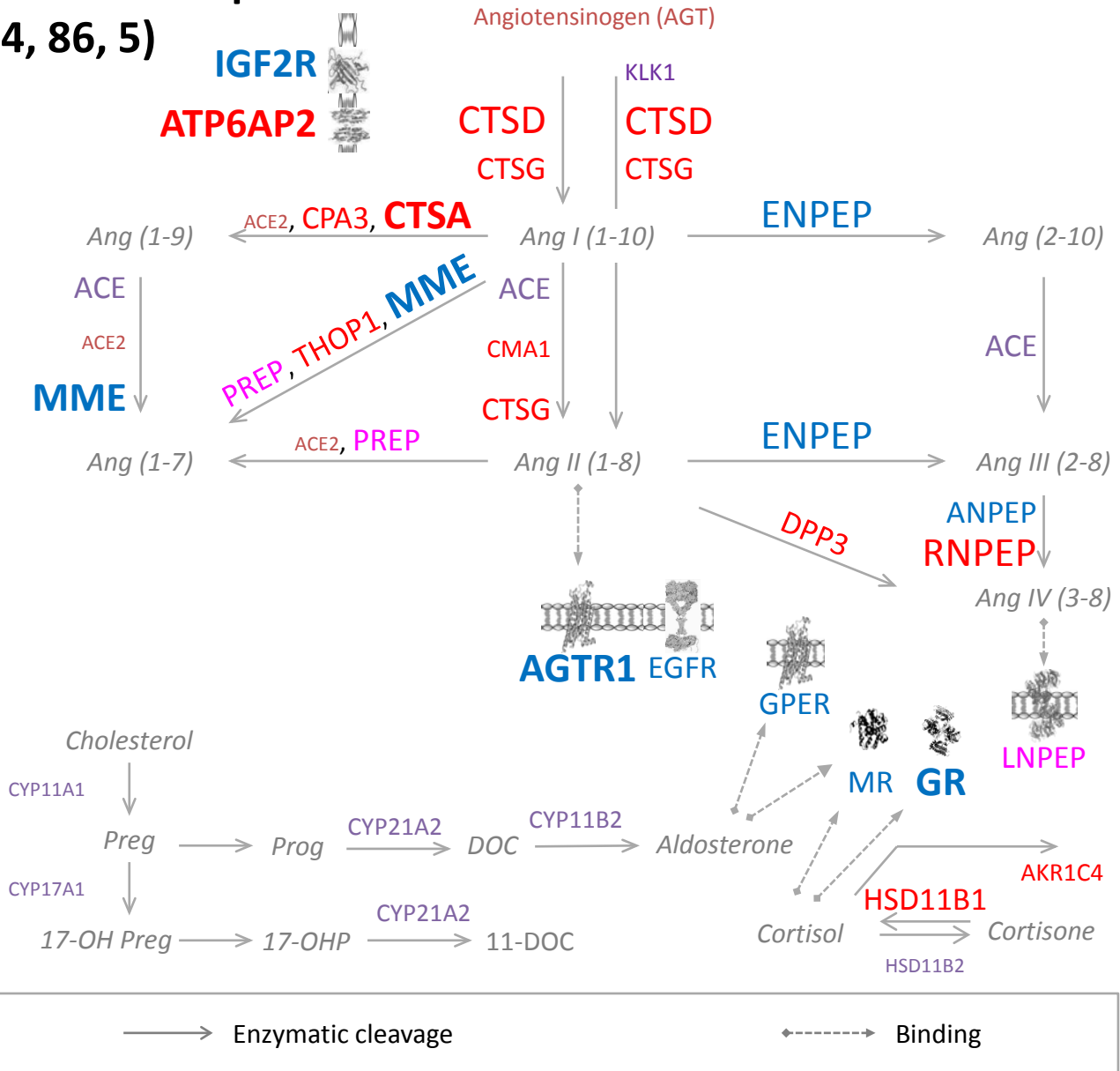
# Breast (6, 239, 7)



# Subcutaneous Adipose (9, 474, 8)

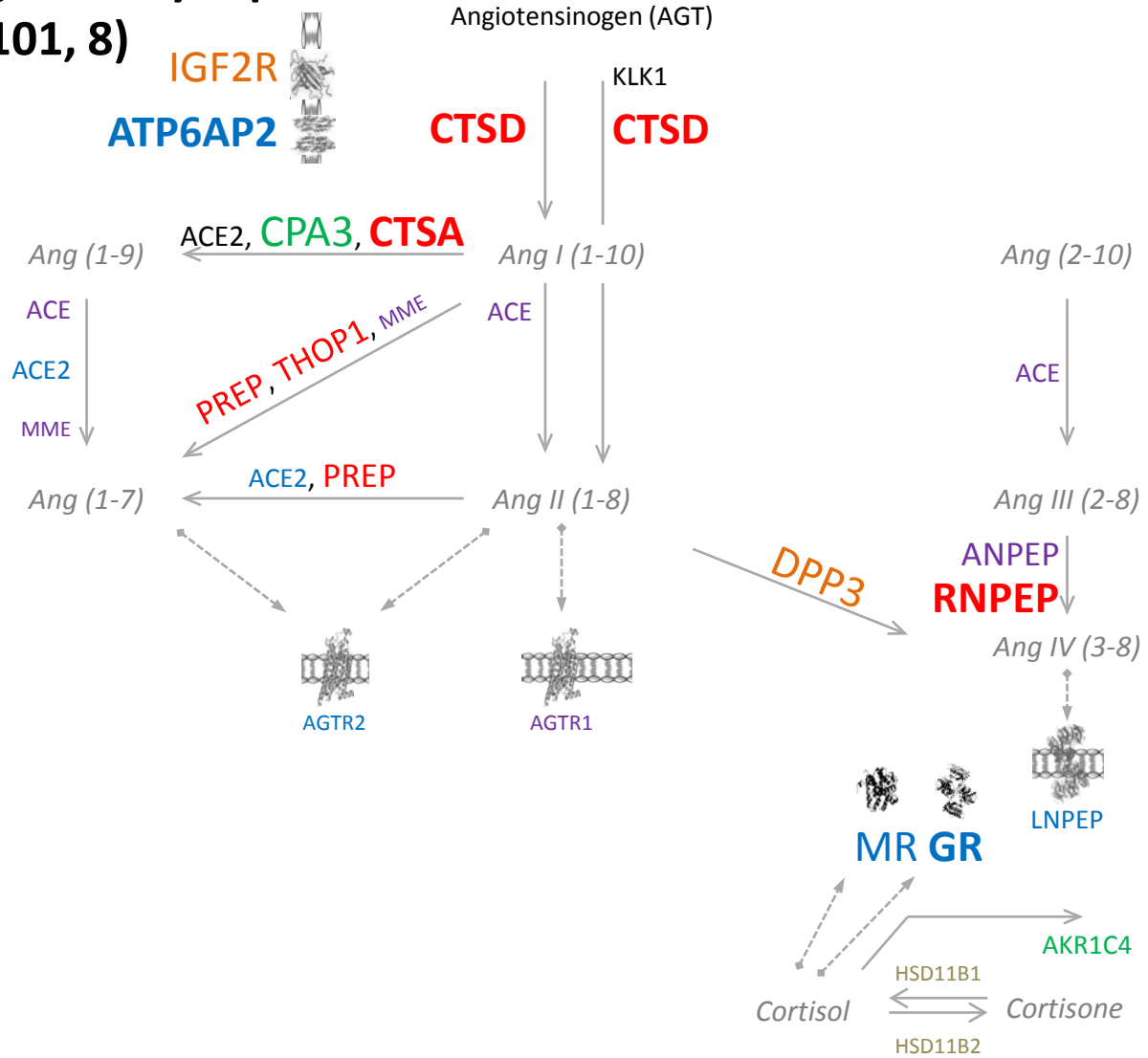


# Omental Adipose (4, 86, 5)



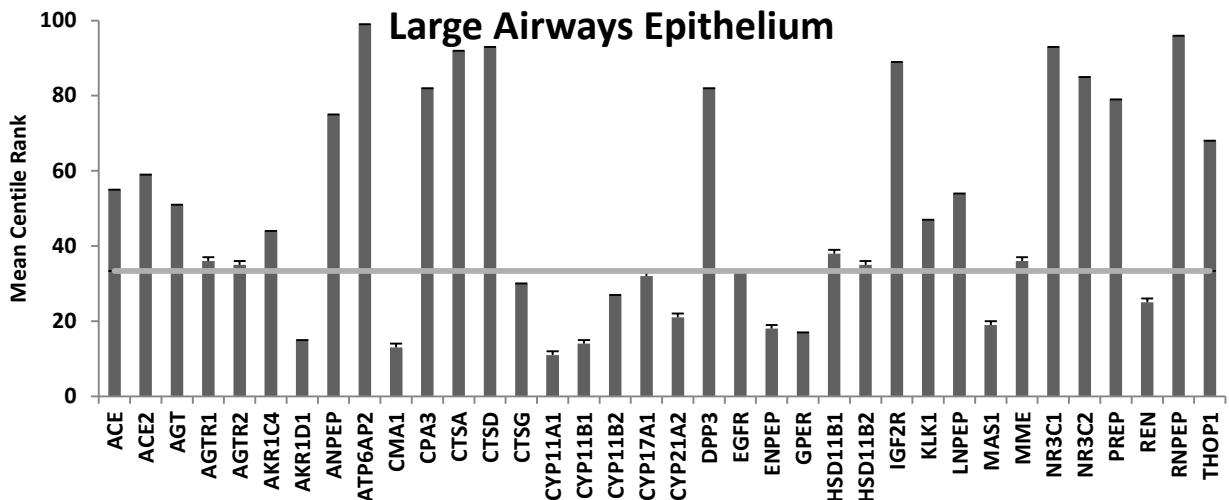
# Large Airways Epithelium

(5, 101, 8)

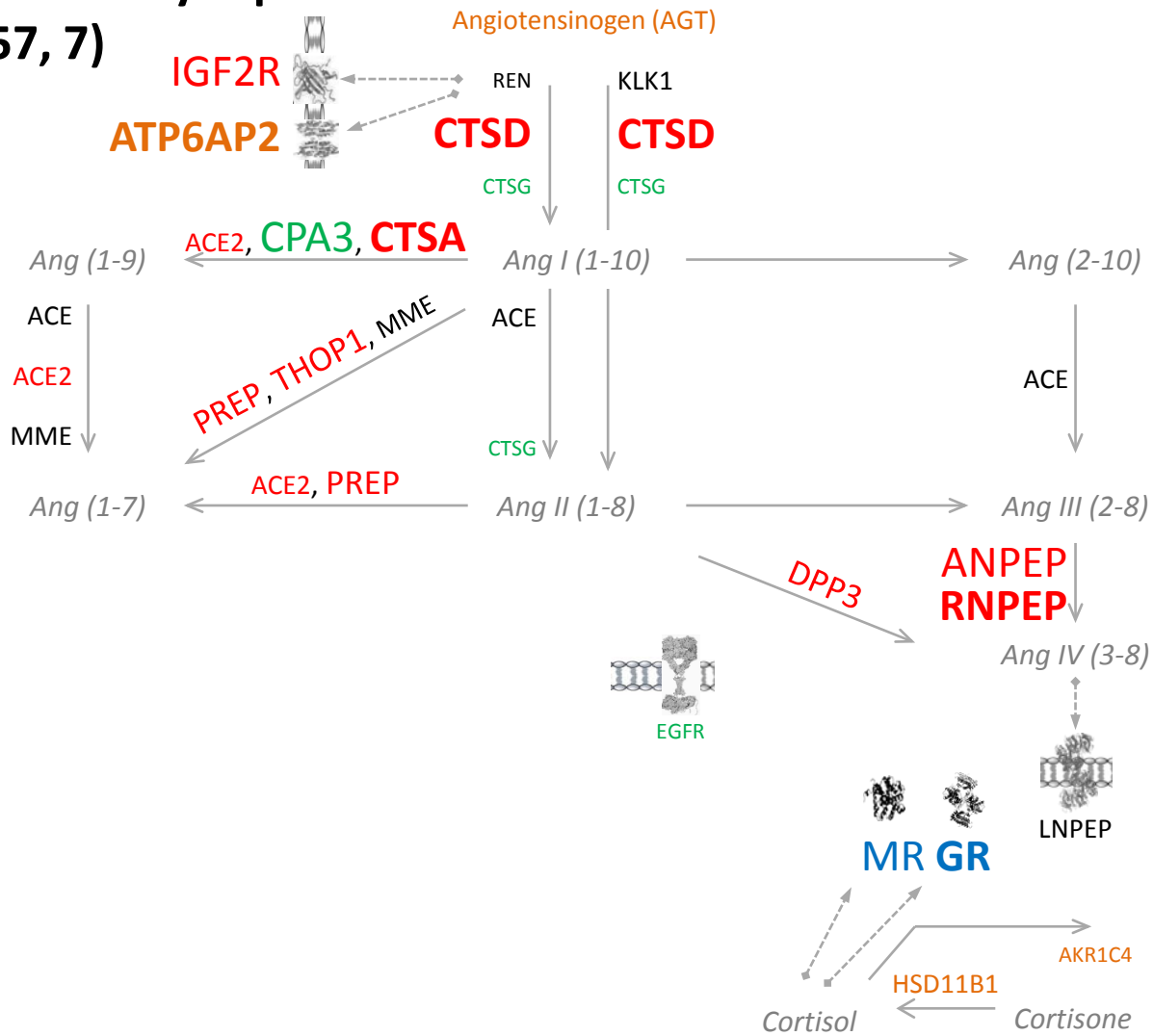


→ Enzymatic cleavage

⇌ Binding

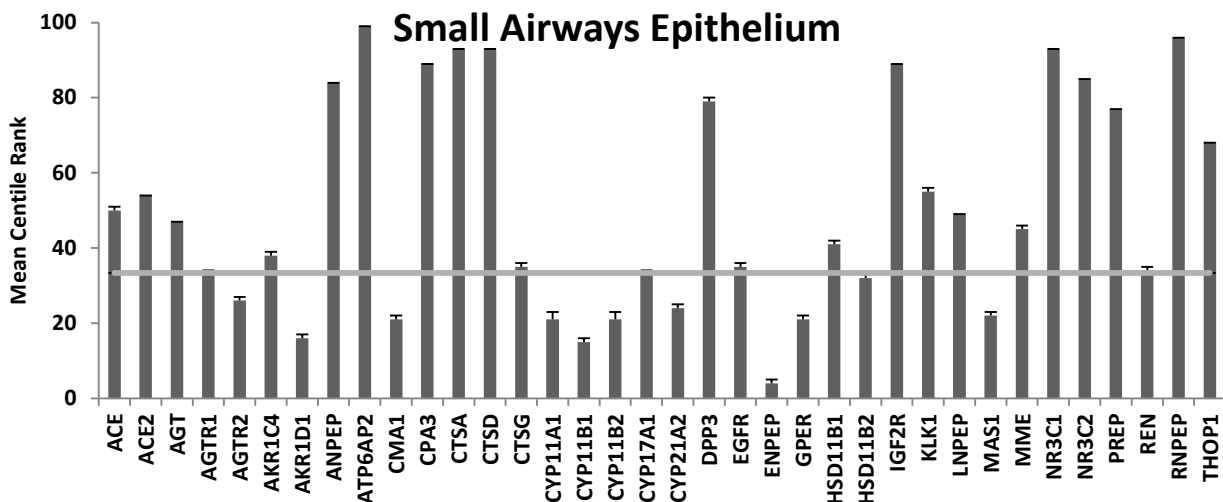


# Small Airways Epithelium (8, 57, 7)

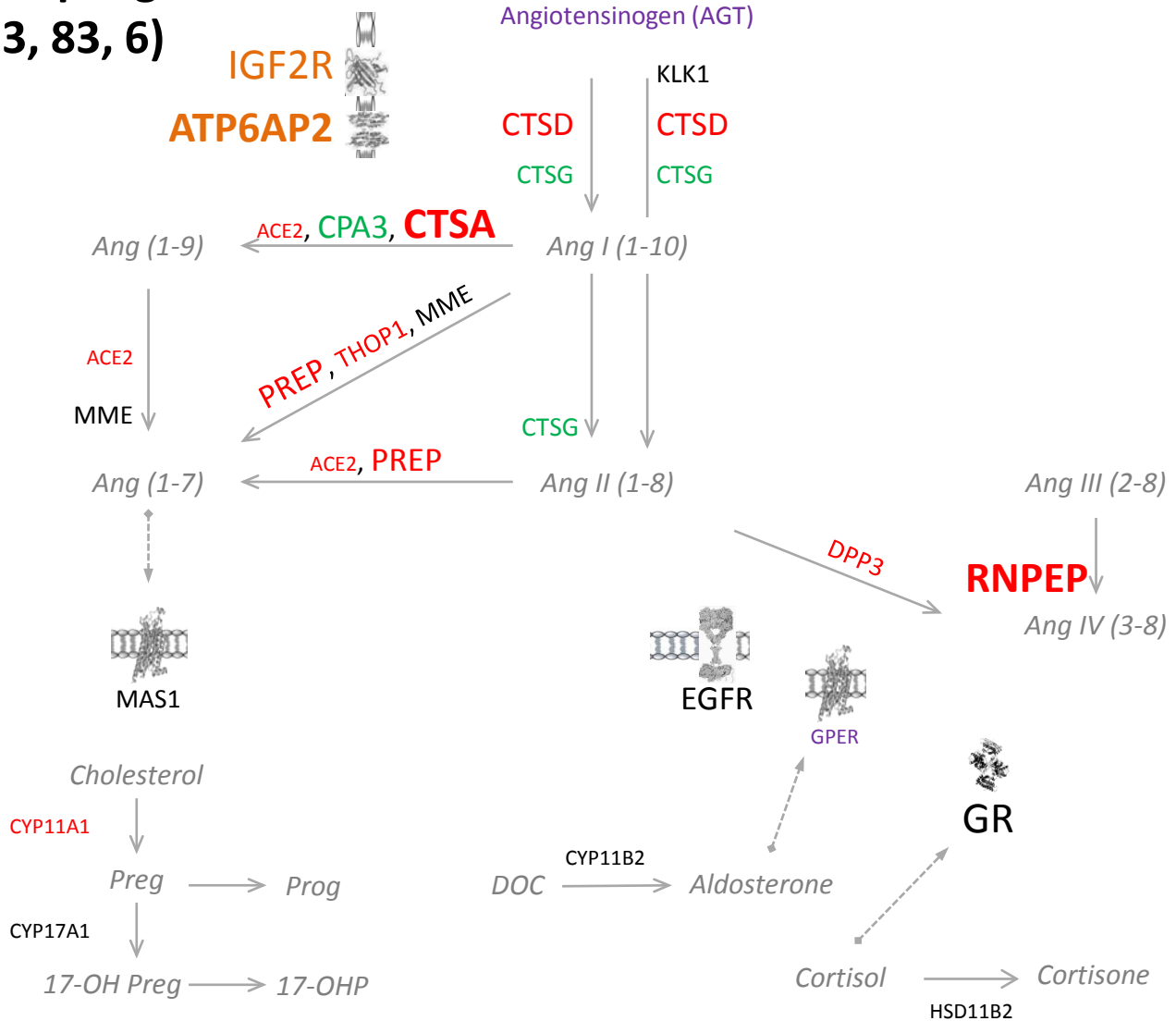


→ Enzymatic cleavage

⇌ Binding

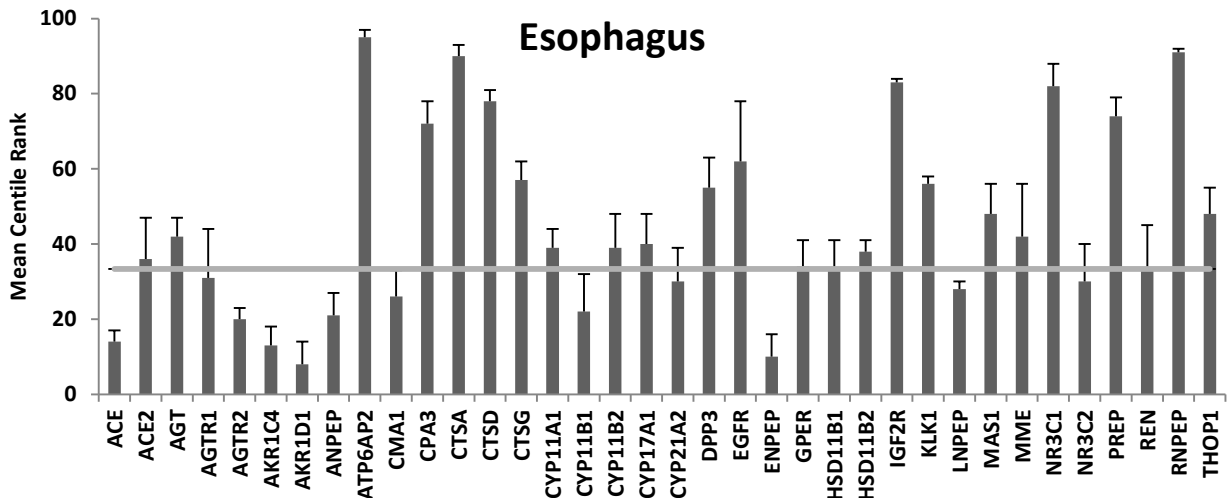


# Esophagus (3, 83, 6)

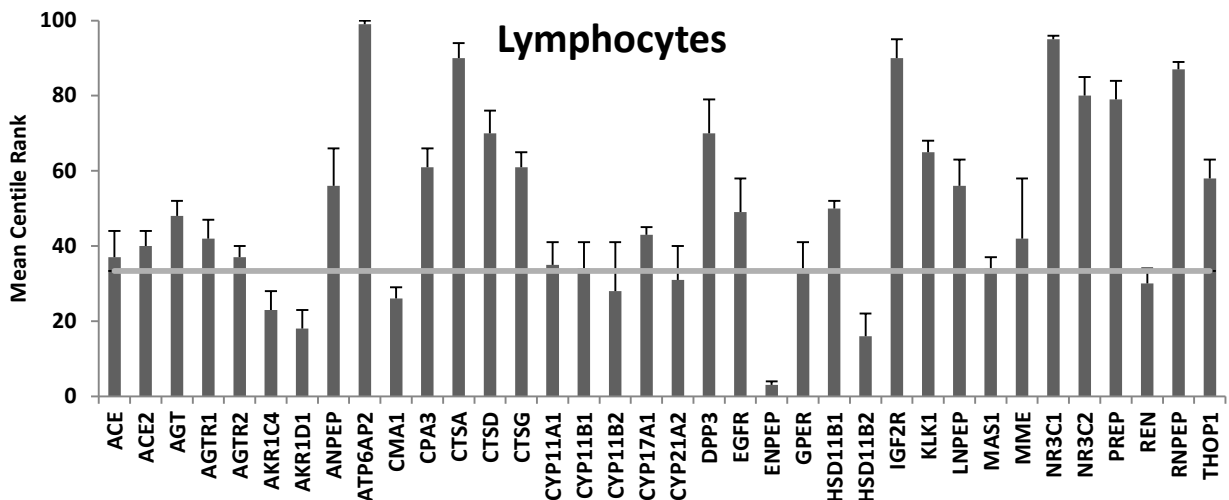
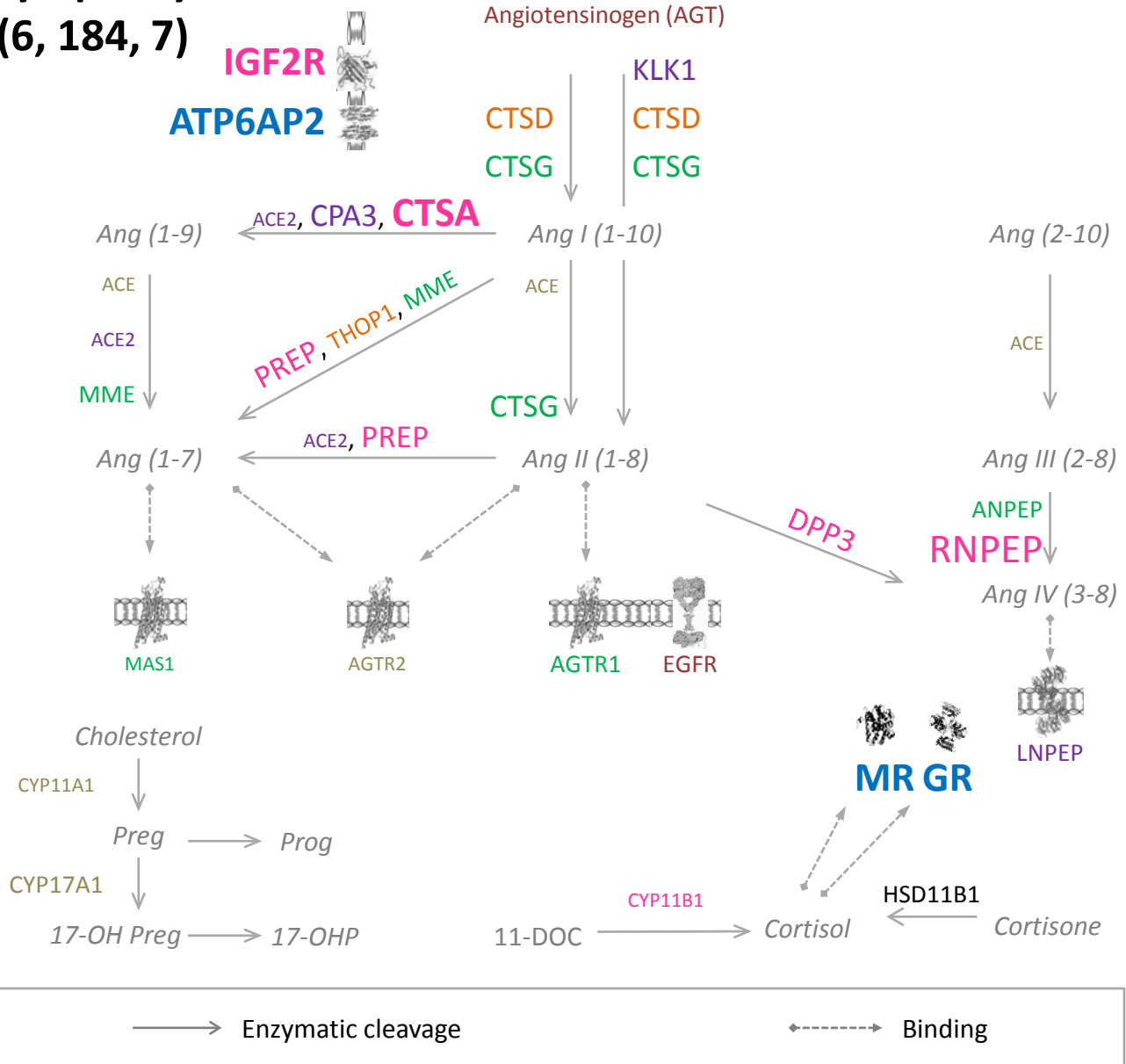


→ Enzymatic cleavage

◊ Binding

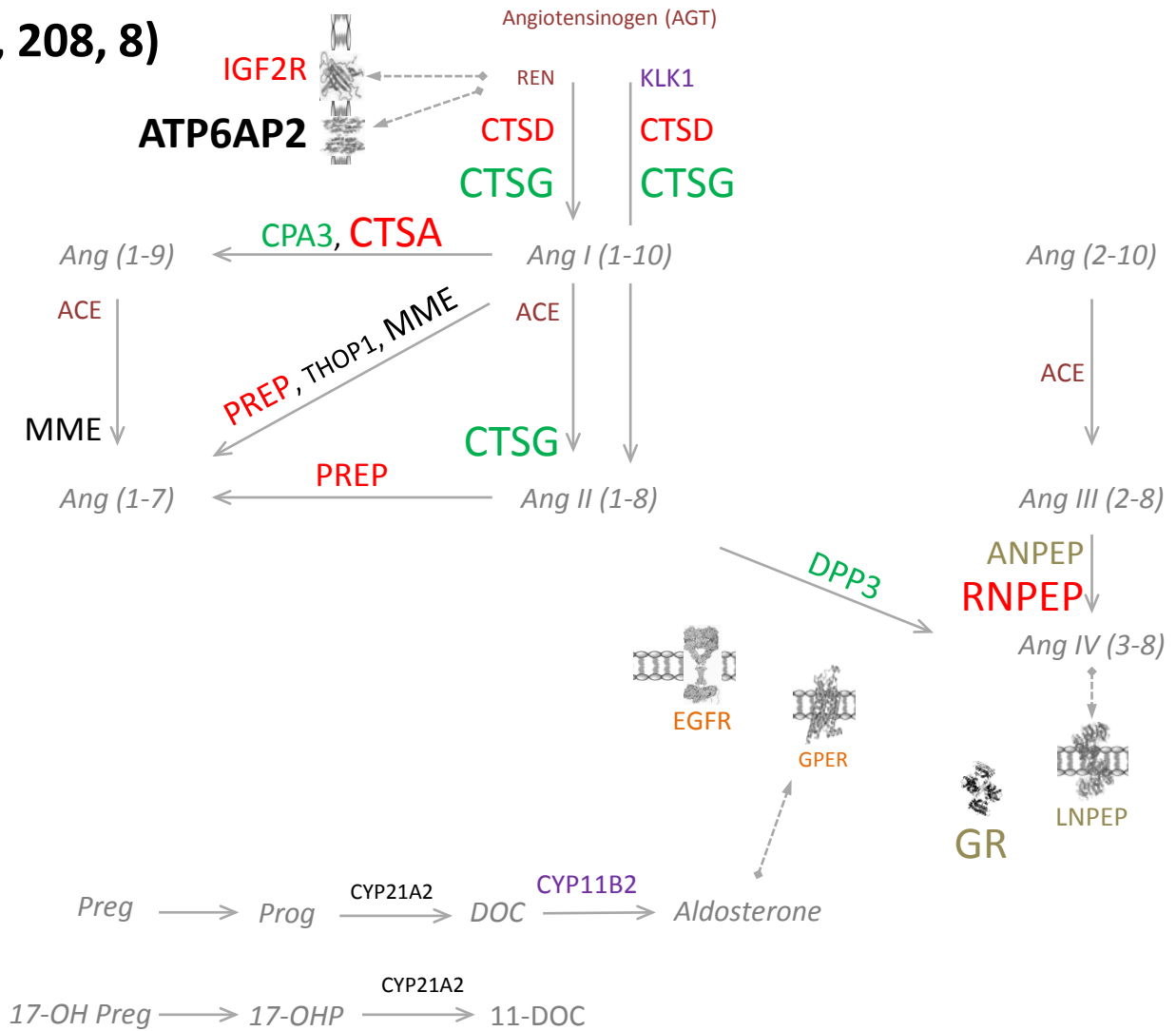


# Lymphocytes (6, 184, 7)

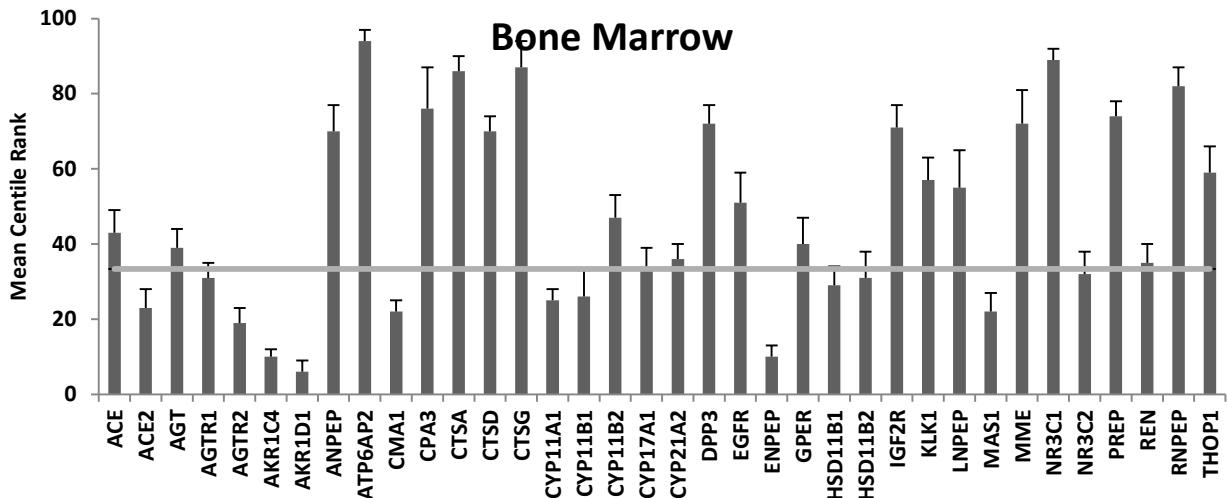




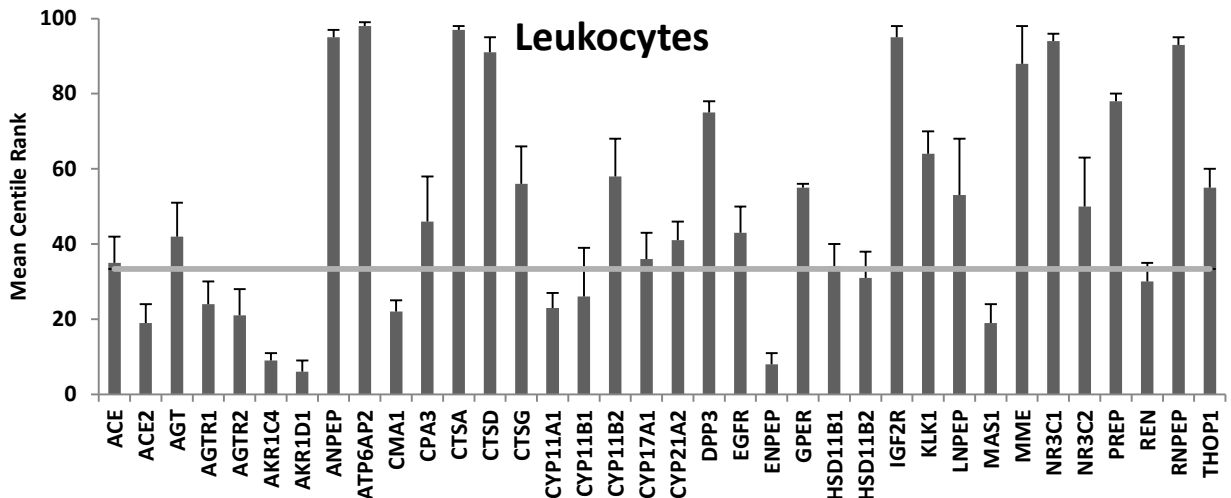
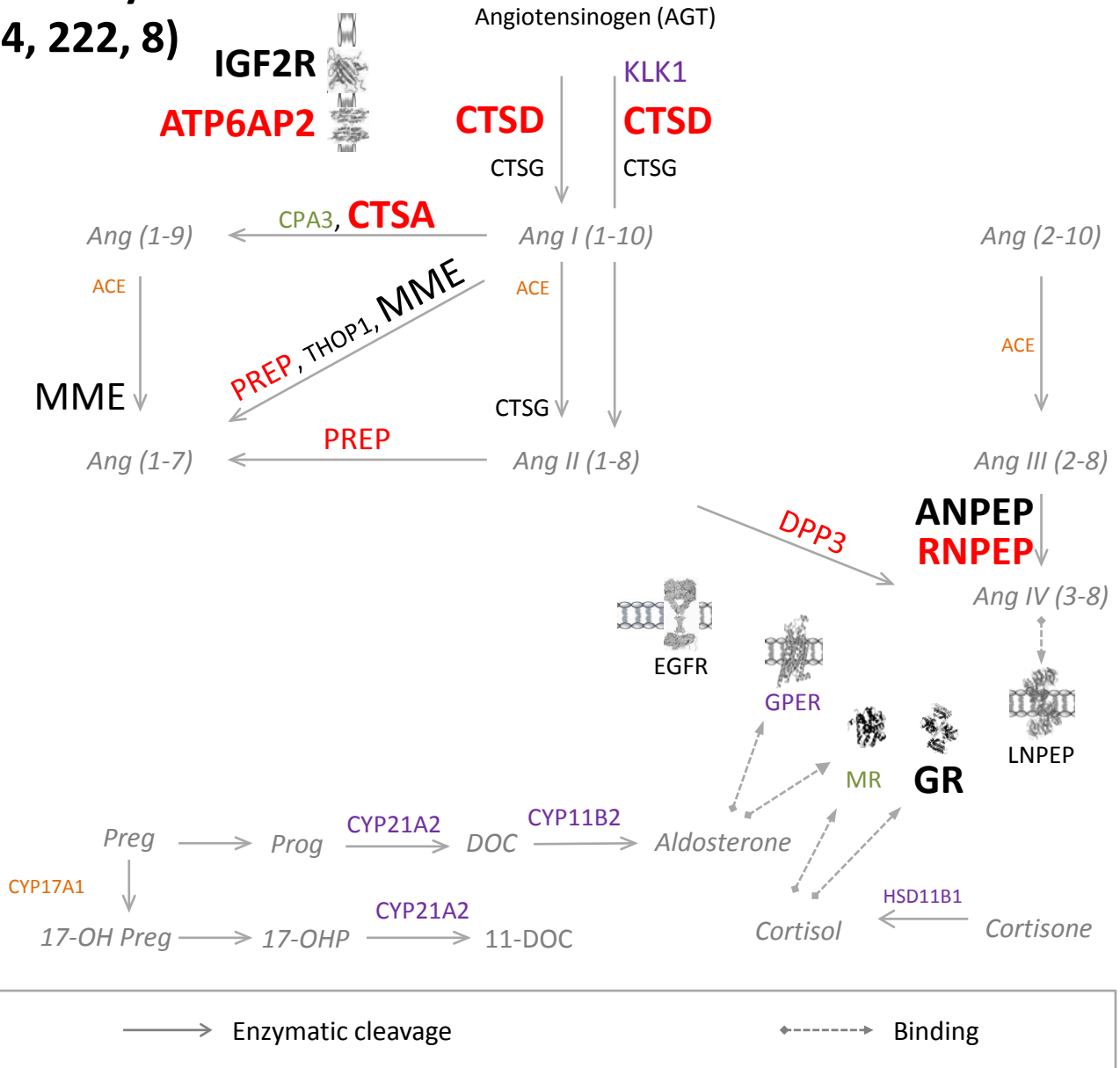
# Bone Marrow (8, 208, 8)



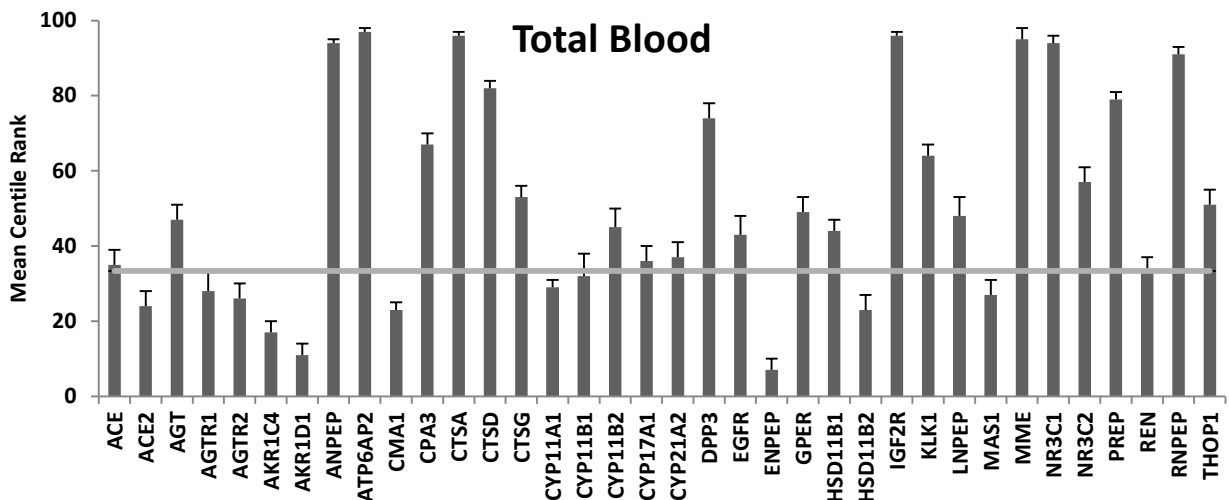
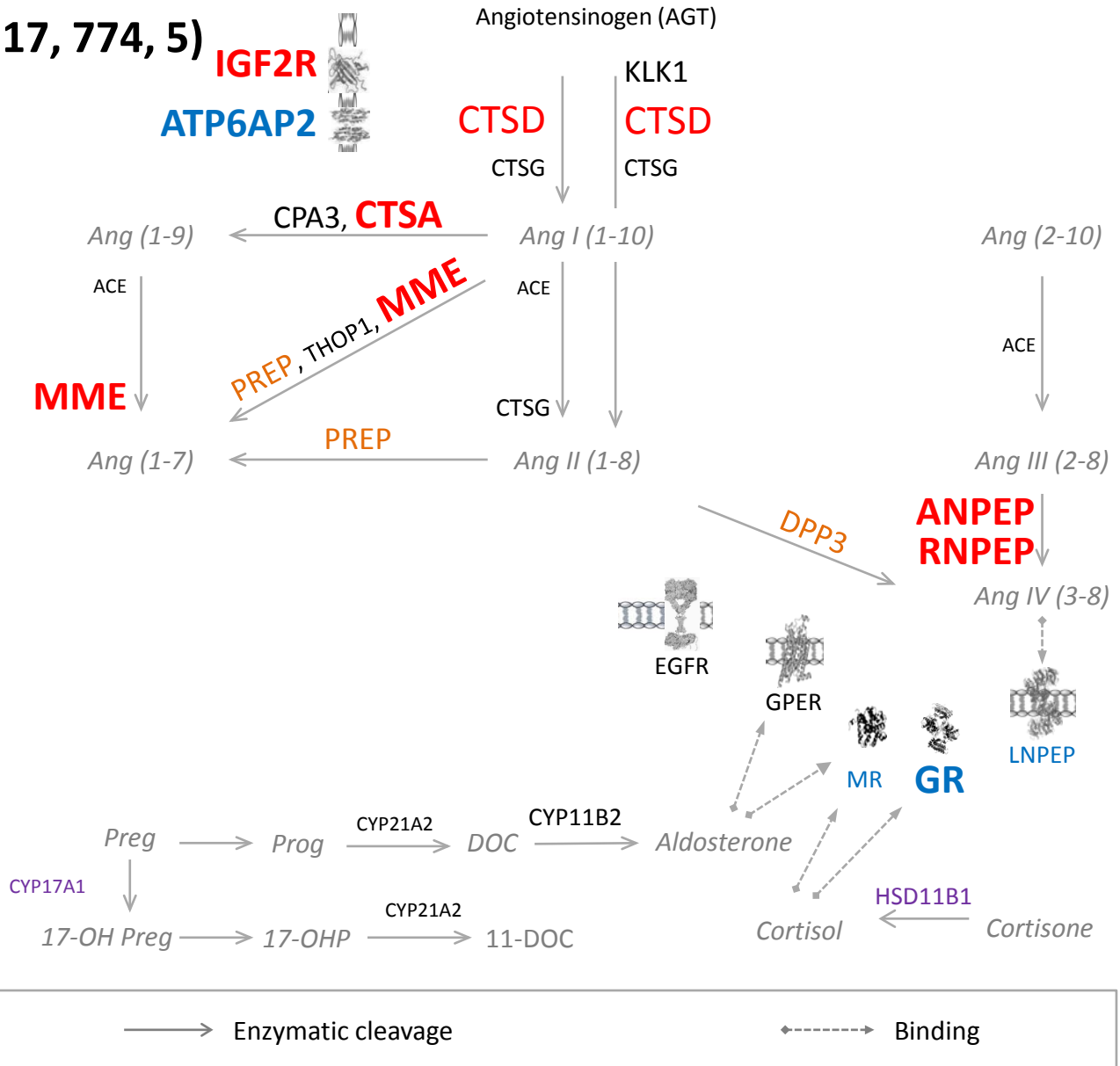
→ Enzymatic cleavage      ◊ Binding



# Leukocytes (4, 222, 8)



# Total Blood (17, 774, 5)



**PBMC**  
**(11, 303, 6)**

