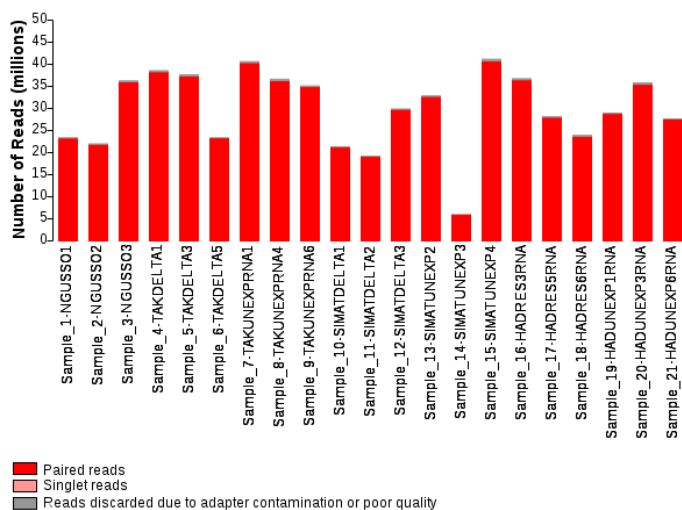


Additional file 1: Supplementary Figures



Fig. S1: Sampling sites in the Sahel region of the four countries.



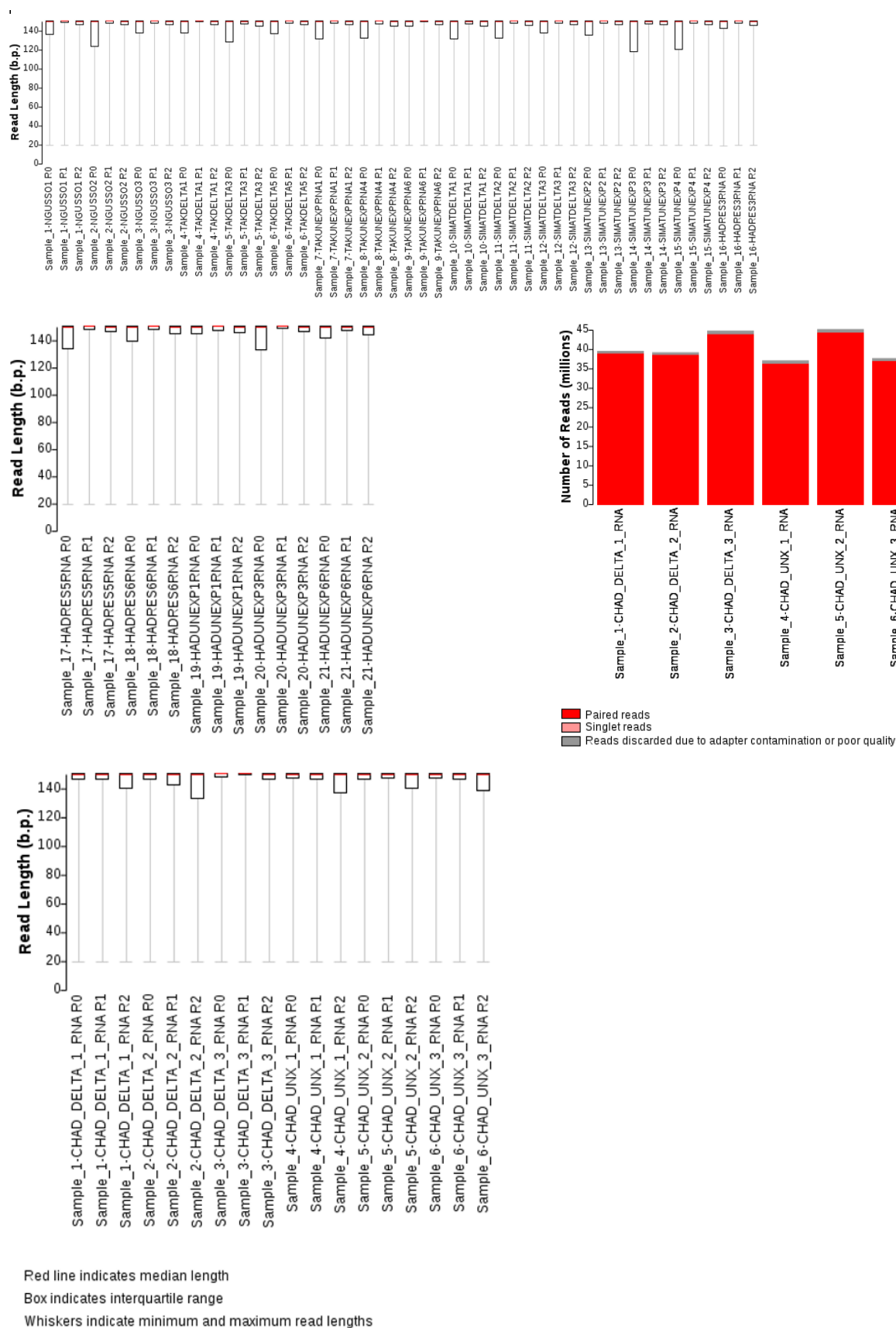


Fig. S2: Summary of total number of reads for each sample and distribution of trimmed read length for forward (R1) and reverse (R2) reads and reads unpaired after trimming (R0).

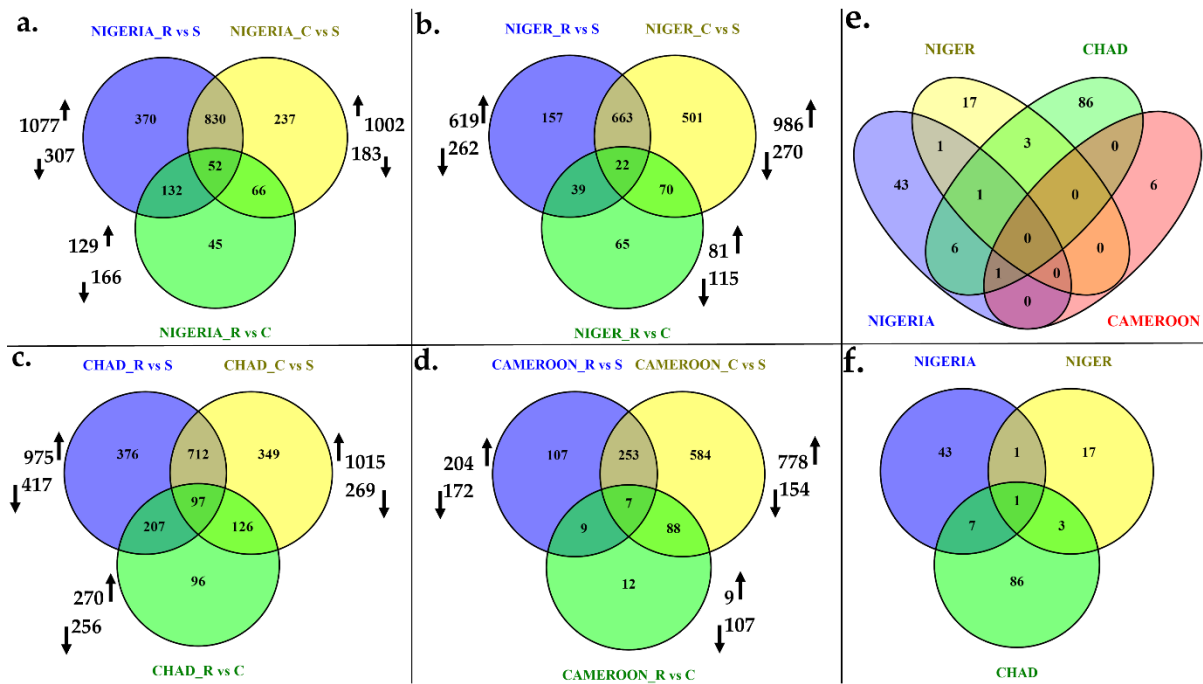


Fig. S3: Venn diagrams comparing the summary the differentially expressed (DE) genes between resistant (R), unexposed (C) and susceptible (S) samples with a transcription ratio $\log_2FC \geq 1$ in either direction, and a corrected p value < 0.05 .

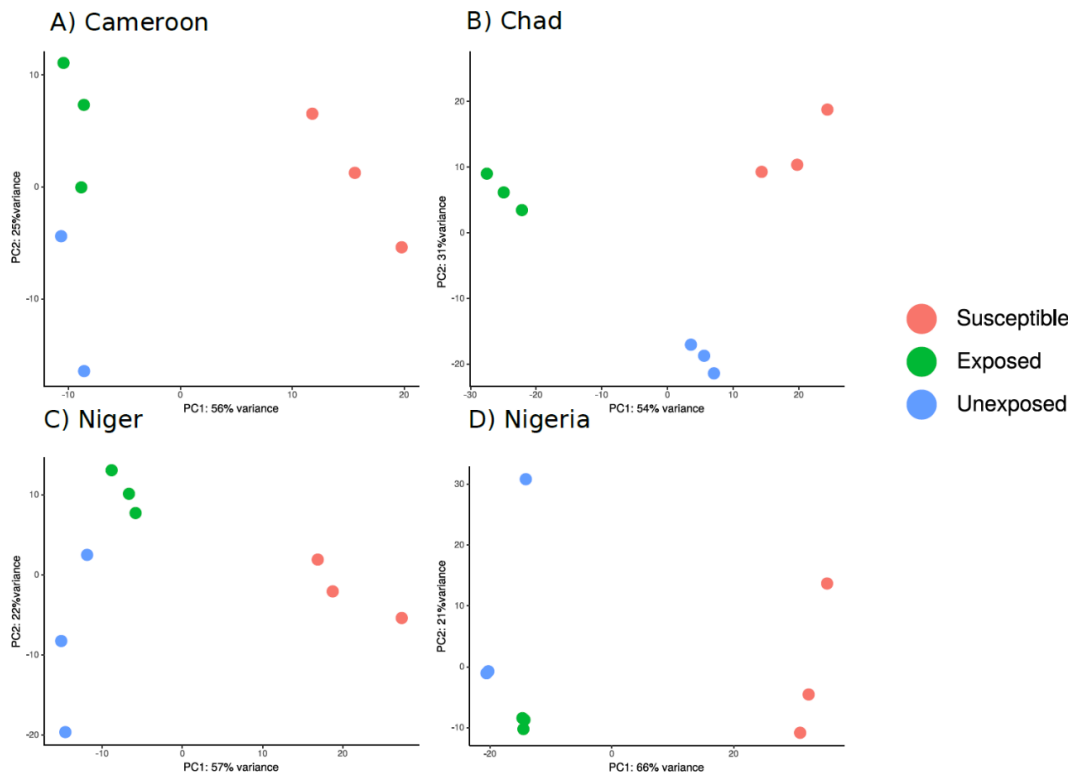


Fig. S4: Principal component analysis of the 500 most variable genes from all RNAseq experimental arms in the data from the four countries.

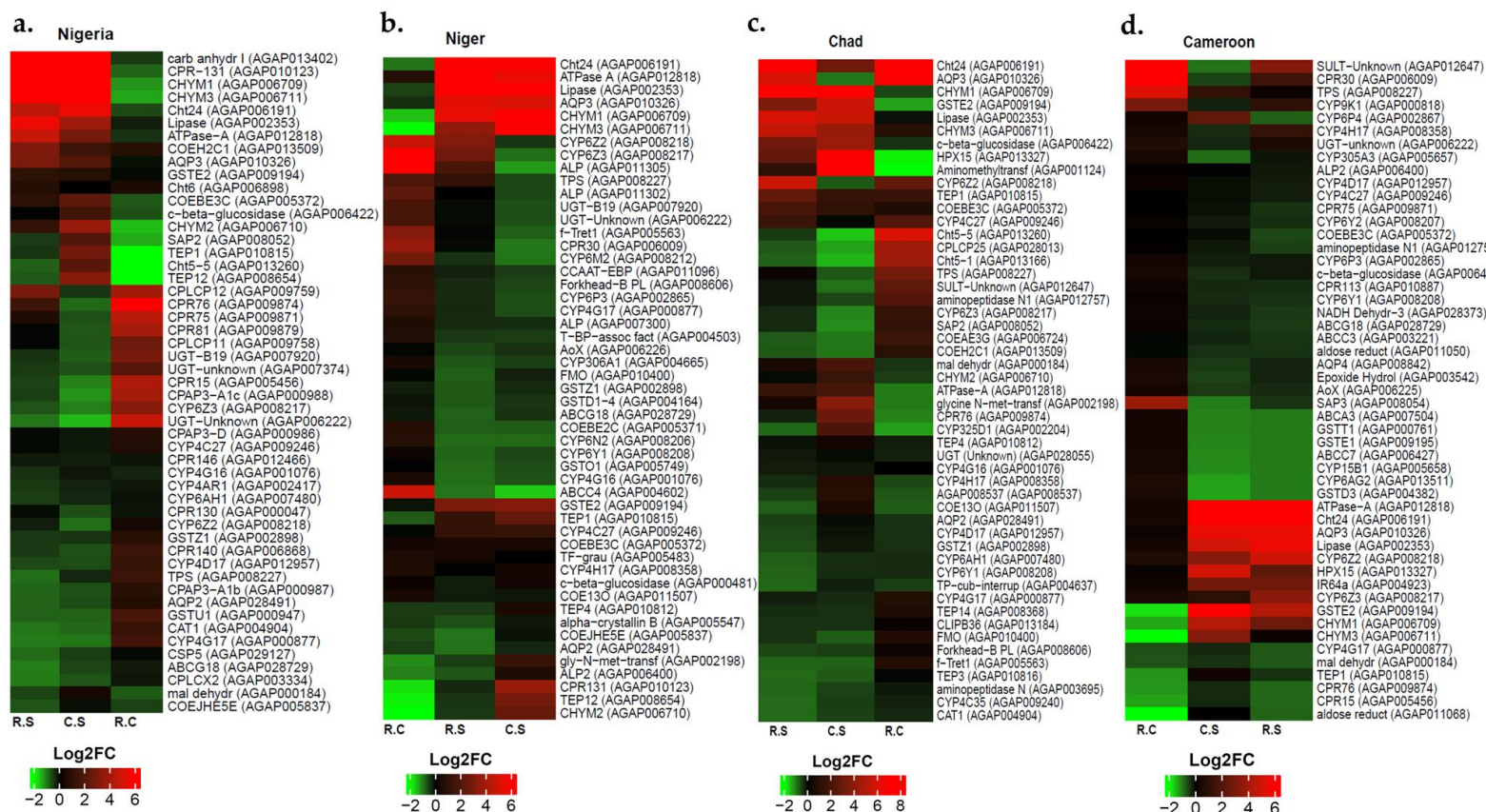
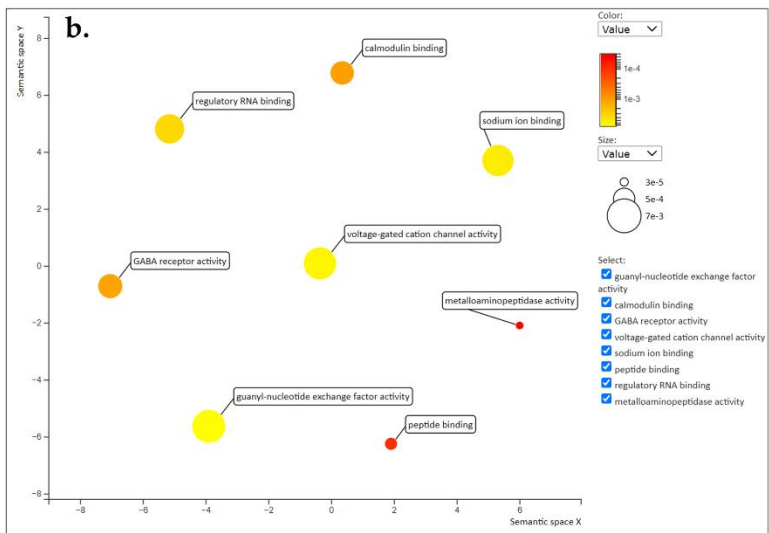
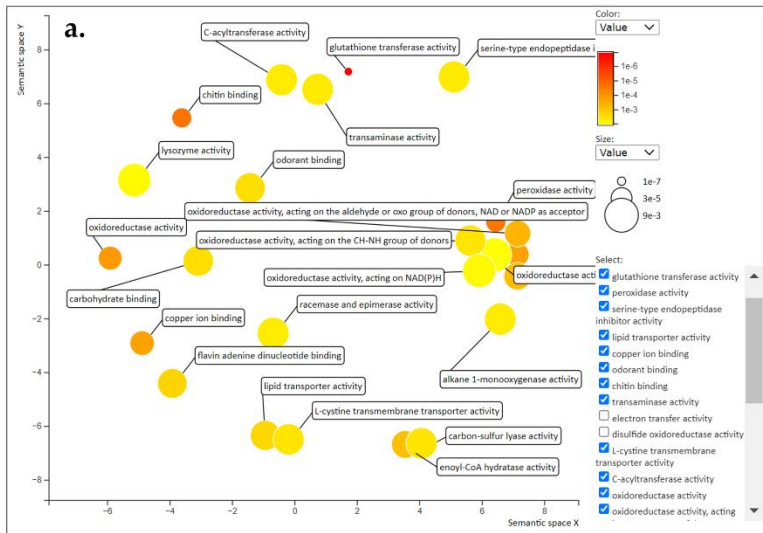
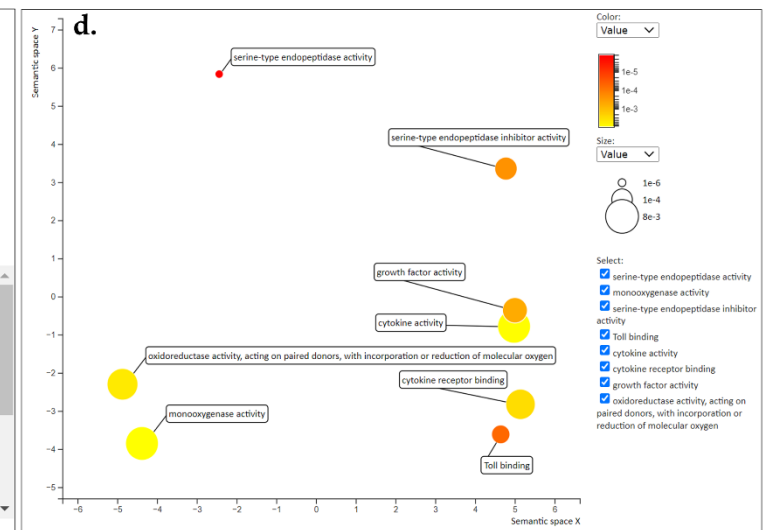
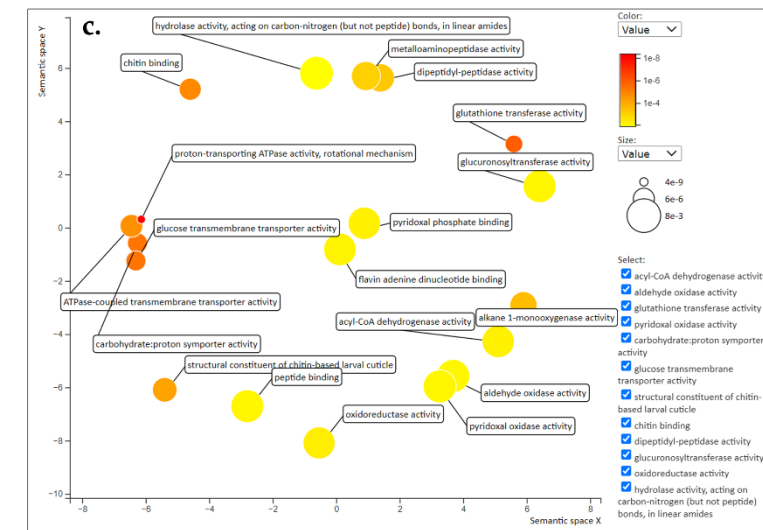


Fig. S5: A heatmap showing the top 50 overexpressed genes in *An. coluzzii* populations from the Sahel region of each country. a. for Nigeria b., c. and d. for Niger, Chad and Cameroon. Several genes including chymotrypsins, CYP45Os, aquaporins, glutathione S-transferases and carboxylesterases are commonly upregulated across the Sahel of the four countries.



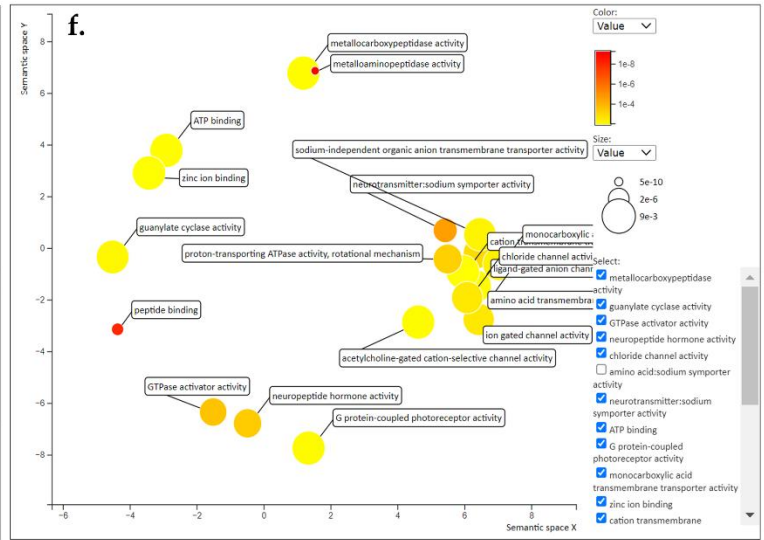
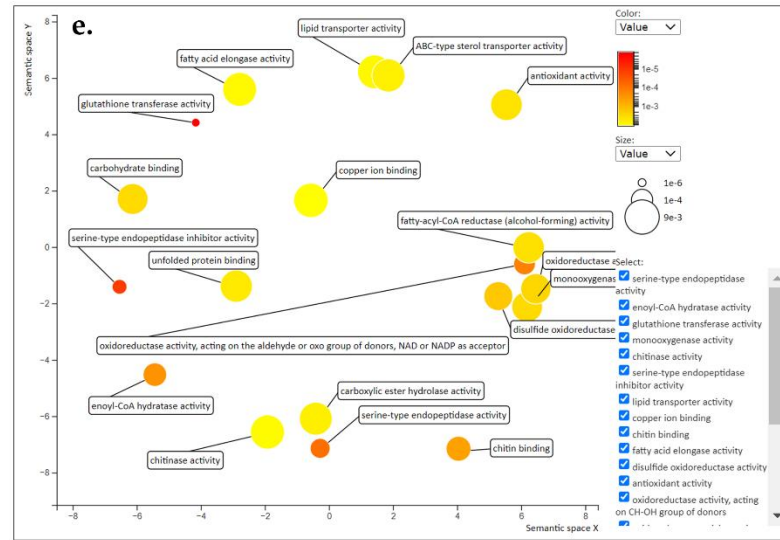
Term ID	Name	Frequency	Pin?	Value	Uniqueness	Dispensability
GO:0004867	serine-type endopeptidase inhibitor activity	0.121%		0.0039	0.91	0.00
GO:0015184	L-cysteine transmembrane transporter activity	0.001%		0.0030	0.98	0.00
GO:0016616	oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	1.855%		0.0095	0.80	0.00
GO:0030246	carbohydrate binding	0.797%		0.0023	0.98	0.00
GO:0003796	lyszyme activity	0.043%		0.0078	0.93	0.03
GO:0016408	C-acyltransferase activity	0.080%		0.0040	0.95	0.03
GO:0016846	carbon-sulfur lyase activity	0.134%		0.0030	0.94	0.03
GO:0016854	racemase and epimerase activity	0.375%		0.0042	0.93	0.03
GO:005549	odorant binding	0.051%		0.0023	0.99	0.04
GO:0003061	chitin binding	0.116%		0.0000	0.98	0.05
GO:0016491	oxidoreductase activity	12.887%		0.0001	0.95	0.05
GO:0050660	flavin adenine dinucleotide binding	1.631%		0.0014	0.97	0.06
GO:0005507	copper ion binding	0.292%		0.0002	0.98	0.14
GO:0003843	transaminase activity	0.728%		0.0039	0.94	0.20
GO:0004364	glutathione transferase activity	0.086%		0.0000	0.95	0.20
GO:0016855	alkane 1-monoxygenase activity	0.001%		0.0040	0.98	0.23
GO:0055319	lipid transporter activity	0.146%		0.0017	0.98	0.30
GO:0015036	disulfide oxidoreductase activity	0.326%		0.0005	0.83	0.37
GO:0016645	oxidoreductase activity, acting on the CH-NH group of donors	0.350%		0.0030	0.83	0.37
GO:0004601	peroxidase activity	0.427%		0.0000	0.77	0.38

Term ID	Name	Frequency	Pin?	Value	Uniqueness	Dispensability
GO:0005085	guanylyl-nucleotide exchange factor activity	0.309%		0.0070	0.90	0.00
GO:0016917	GABA receptor activity	0.027%		0.0011	0.95	0.00
GO:0022843	voltage-gated cation channel activity	0.155%		0.0060	0.43	0.00
GO:0031402	sodium ion binding	0.009%		0.0048	0.91	0.00
GO:0070006	metalloaminopeptidase activity	0.153%		0.0000	1.00	0.00
GO:0061980	regulatory RNA binding	0.013%		0.0031	0.99	0.03
GO:0005516	calmodulin binding	0.135%		0.0009	0.99	0.03
GO:0042277	peptide binding	0.100%		0.0001	0.99	0.04
GO:0008273	calcium, potassium:sodium antiporter activity	0.006%		0.0048	0.49	0.47
GO:0046961	proton-transporting ATPase activity, rotational mechanism	0.115%		0.0023	0.53	0.57
GO:0099095	ligand-gated anion channel activity	0.006%		0.0008	0.49	0.64
GO:0022848	acetylcholine-gated cation-selective channel activity	0.024%		0.0000	0.43	0.70
GO:0005323	amino acid:sodium symporter activity	0.045%		0.0001	0.45	0.72
GO:0005328	neurotransmitter:sodium symporter activity	0.001%		0.0000	0.58	0.73
GO:0008028	monocarboxylic acid transmembrane transporter activity	0.052%		0.0013	0.54	0.74
GO:0022839	ion gated channel activity	0.054%		0.0000	0.53	0.74
GO:0005254	chloride channel activity	0.123%		0.0000	0.45	0.80
GO:0005245	voltage-gated calcium channel activity	0.031%		0.0011	0.44	0.81
GO:0015121	amino acid transmembrane transporter activity	0.268%		0.0000	0.59	0.83
GO:0030955	sodium ion binding	0.068%		0.0048	0.91	0.86
GO:0005096	GTPase activator activity	0.247%		0.0003	0.90	0.87
GO:0005249	voltage-gated potassium channel activity	0.119%		0.0022	0.41	0.90



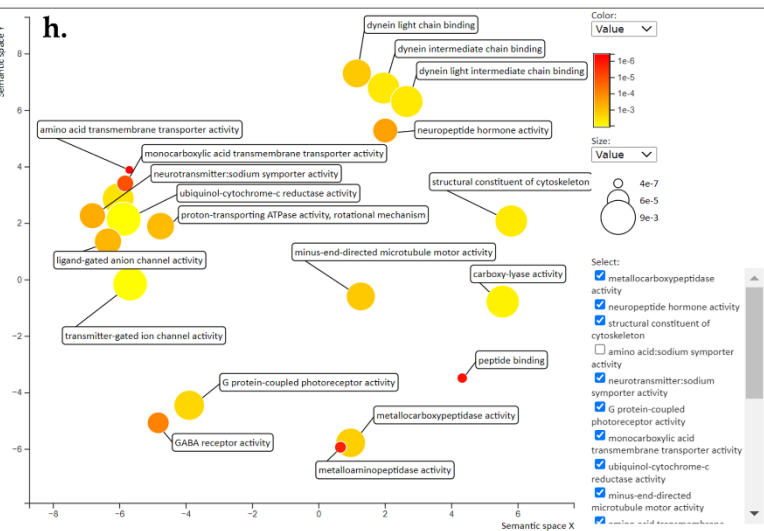
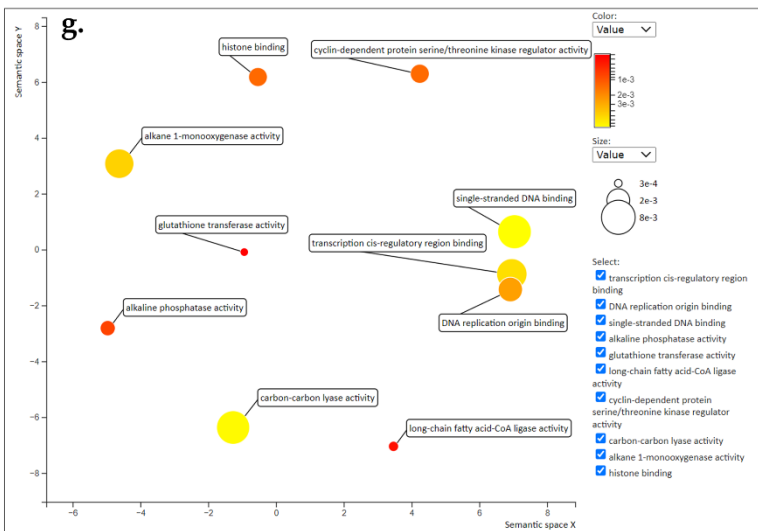
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GO:0008010	structural constituent of chitin-based larval cuticle	0.002%		0.0000	1.00	0.00
GO:0016811	hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds, in linear amides	0.737%		0.0084	0.93	0.00
GO:0042227	peptide binding	0.100%		0.0051	0.98	0.00
GO:0042626	ATPase-coupled transmembrane transporter activity	1.389%		0.0000	0.83	0.00
GO:0004732	pyridoxal oxidase activity	0.000%		0.0055	0.87	0.02
GO:0015020	glucuronosyltransferase activity	0.043%		0.0051	0.96	0.03
GO:0016491	oxidoreductase activity	12.887%		0.0032	0.97	0.05
GO:0050660	flavin adenine dinucleotide binding	1.631%		0.0044	0.96	0.05
GO:0008061	chitin binding	0.116%		0.0000	0.98	0.05
GO:0004364	glutathione transferase activity	0.086%		0.0000	0.96	0.16
GO:0003995	acyl-CoA dehydrogenase activity	0.152%		0.0039	0.92	0.16
GO:0016855	alkane 1-monoxygenase activity	0.001%		0.0002	0.93	0.20
GO:0070006	metalloaminopeptidase activity	0.153%		0.0006	0.89	0.23
GO:0030178	pyridoxal phosphate binding	1.138%		0.0038	0.96	0.31
GO:0005355	glucose transmembrane transporter activity	0.012%		0.0000	0.86	0.33
GO:0008239	dipeptidyl-peptidase activity	0.046%		0.0004	0.89	0.65
GO:0005351	carbohydrate:proton symporter activity	0.026%		0.0000	0.80	0.71
GO:0046961	proton-transporting ATPase activity, rotational mechanism	0.115%		0.0000	0.83	0.71
GO:0004031	aldehyde oxidase activity	0.002%		0.0055	0.86	0.80

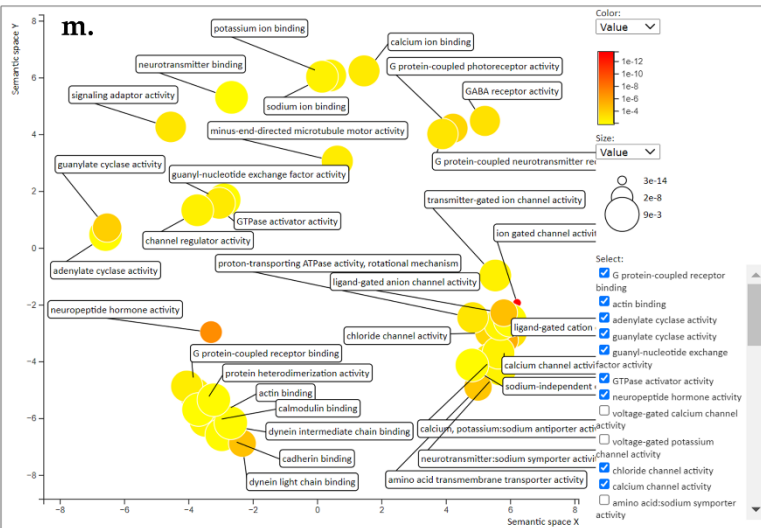
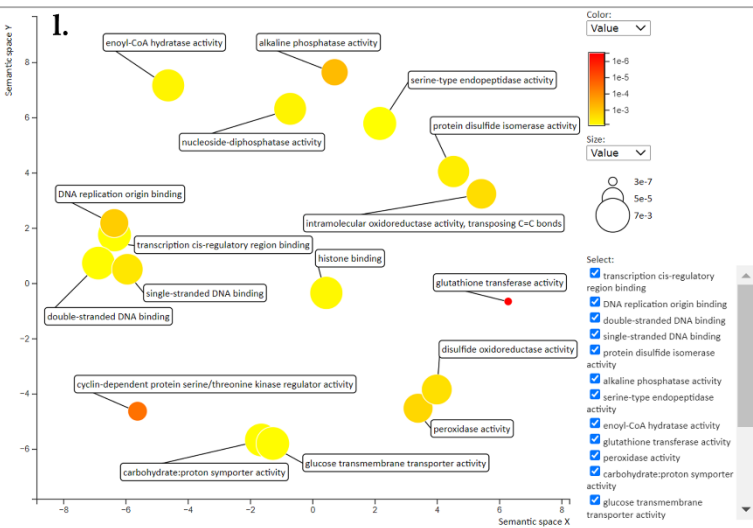
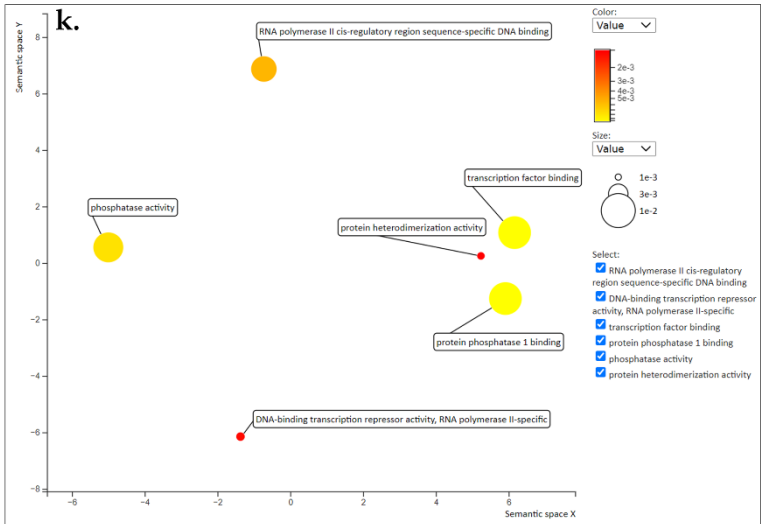
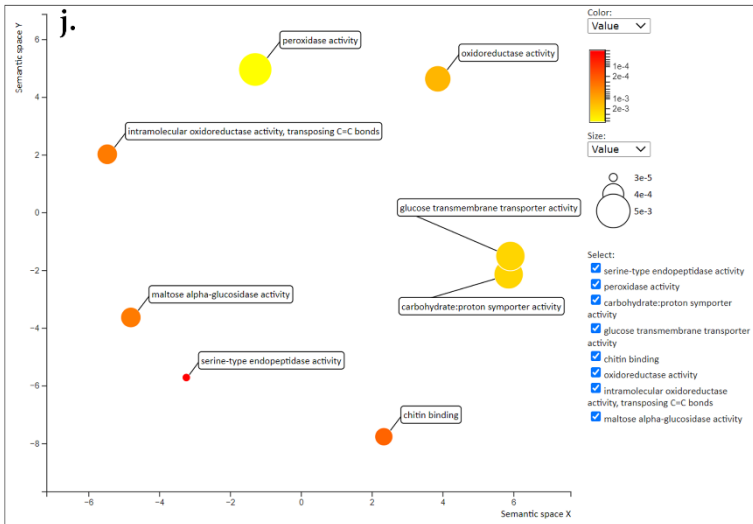
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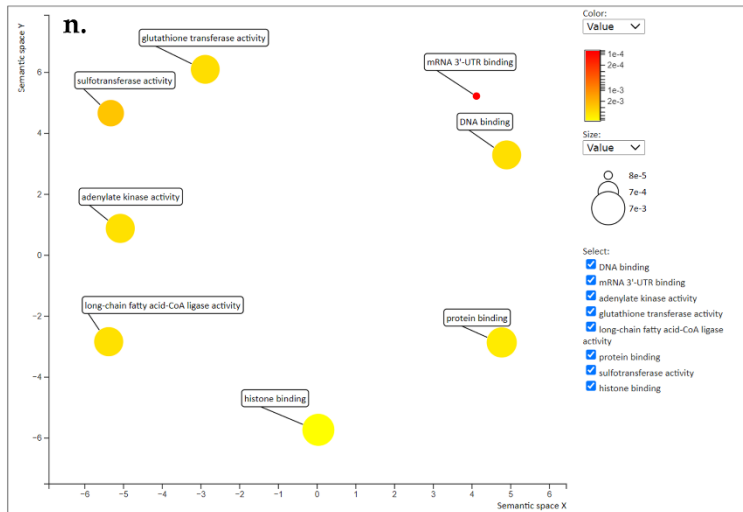


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GO:0005319	lipid transporter activity	0.146%		0.0076	0.94	0.00
GO:0005507	copper ion binding	0.292%		0.0093	0.99	0.00
GO:0016209	antioxidant activity	0.725%		0.0036	0.91	0.00
GO:0004602	peroxidase activity	0.427%		0.0008	0.73	0.91
GO:0000019	fatty-acyl-CoA reductase (alcohol-forming) activity	0.018%		0.0033	0.81	0.02
GO:0009922	fatty acid elongase activity	0.028%		0.0078	0.96	0.02
GO:0004300	enoyl-CoA hydratase activity	0.051%		0.0002	0.97	0.02
GO:0003081	chitin binding	0.116%		0.0004	0.99	0.04
GO:001092	unfolded protein binding	0.424%		0.0045	0.90	0.05
GO:0030246	carbohydrate binding	0.797%		0.0027	0.98	0.05
GO:0004364	glutathione transferase activity	0.086%		0.0000	0.96	0.16
GO:0052689	carboxylic ester hydrolase activity	0.694%		0.0055	0.92	0.21
GO:0004252	serine-type endopeptidase activity	0.893%		0.0001	0.92	0.27
GO:0004497	monooxygenase activity	1.211%		0.0026	0.80	0.27
GO:0015026	disulfide oxidoreductase activity	0.326%		0.0014	0.82	0.35
GO:0016614	oxidoreductase activity, acting on CH-OH group of donors	2.116%		0.0023	0.79	0.43
GO:0034041	ABC-type sterol transporter activity	0.000%		0.0058	0.94	0.57
GO:0016620	oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor	0.593%		0.0001	0.77	0.70

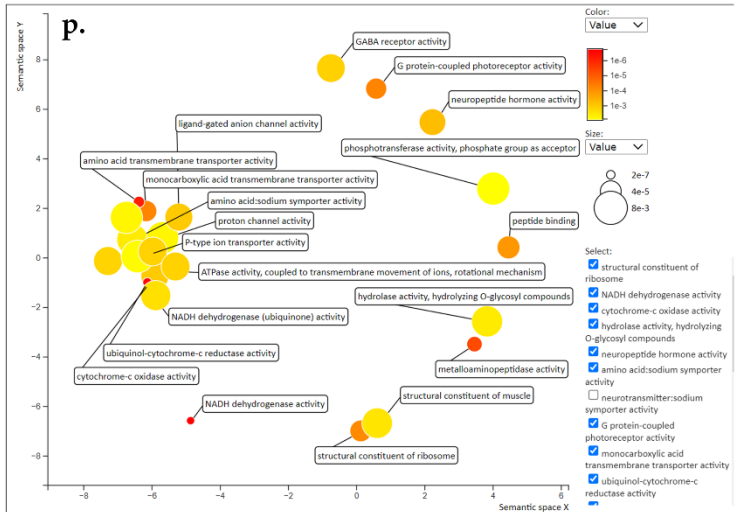
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GO:0004181	metalcarboxypeptidase activity	0.086%		0.0081	0.90	0.00
GO:0008270	zinc ion binding	3.639%		0.0092	0.96	0.00
GO:0008324	cation transmembrane transporter activity	2.405%		0.0090	0.93	0.00
GO:0008020	G protein-coupled photoreceptor activity	0.003%		0.0078	0.91	0.01
GO:0042277	peptide binding	0.100%		0.0000	0.98	0.05
GO:0043393	guanylate cyclase activity	0.024%		0.0059	0.97	0.10
GO:005184	neuropeptide hormone activity	0.013%		0.0003	0.87	0.25
GO:0055524	ATP binding	13.644%		0.0081	0.96	0.27
GO:0055328	neurotransmitter:sodium symporter activity	0.001%		0.0000	0.63	0.43
GO:0015347	sodium-independent organic anion transmembrane transporter activity	0.001%		0.0048	0.60	0.44
GO:0050596	GTPase activator activity	0.247%		0.0002	0.91	0.54
GO:0022848	acetylcholine-gated cation-selective channel activity	0.024%		0.0078	0.49	0.56
GO:0008028	monocarboxylic acid transmembrane transporter activity	0.052%		0.0042	0.54	0.57
GO:0051554	chloride channel activity	0.123%		0.0073	0.51	0.63
GO:0046961	proton-transporting ATPase activity, rotational mechanism	0.115%		0.0005	0.56	0.65
GO:0022839	ion gated channel activity	0.054%		0.0022	0.63	0.65
GO:0055283	amino acid:sodium symporter activity	0.045%		0.0009	0.50	0.74
GO:0099095	ligand-gated anion channel activity	0.006%		0.0022	0.55	0.80
GO:0070006	metalcarboxypeptidase activity	0.153%		0.0000	0.90	0.83
GO:0015171	amino acid transmembrane transporter activity	0.268%		0.0001	0.60	0.83



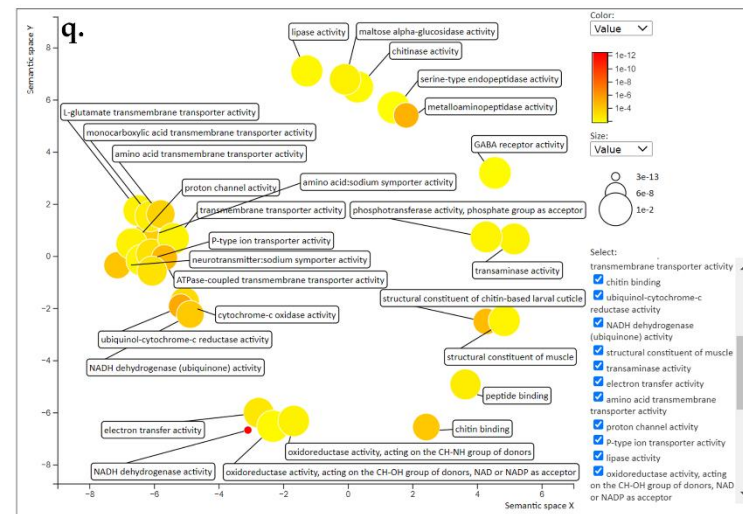




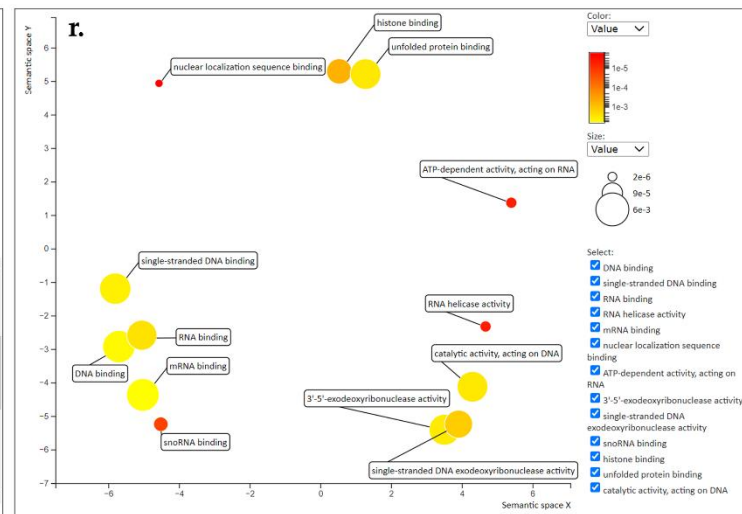
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GO:0004487	long-chain fatty acid-CoA ligase activity	0.034%	0.0039	0.93	0.00	
GO:0043393	histone binding	0.086%	0.0066	0.96	0.00	
GO:004364	glutathione transferase activity	0.086%	0.0037	0.90	0.02	
GO:003730	mRNA 3'-UTR binding	0.026%	0.0001	0.91	0.04	
GO:0005515	protein binding	4.557%	0.0047	0.94	0.05	
GO:0005146	sulfotransferase activity	0.121%	0.0024	0.90	0.17	
GO:0004017	adenylate kinase activity	0.059%	0.0039	0.85	0.20	
GO:0003677	DNA binding	11.354%	0.0038	0.88	0.26	



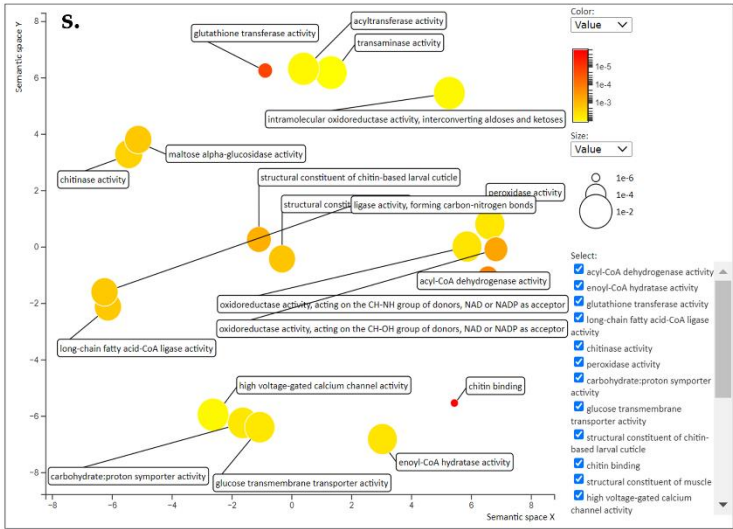
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GO:0003027	structural constituent of muscle	0.004%	0.0025	0.96	0.00	
GO:0015662	P-type ion transporter activity	0.107%	0.0065	0.46	0.00	
GO:0016776	phosphotransferase activity, phosphate group as acceptor	0.361%	0.0076	0.99	0.00	
GO:0016917	GABA receptor activity	0.027%	0.0011	0.96	0.00	
GO:0005184	neuropeptide hormone activity	0.013%	0.0005	0.97	0.01	
GO:0004553	hydrolyase activity, hydrolyzing O-glycosyl compounds	1.613%	0.0033	0.97	0.03	
GO:0043227	peptide binding	0.100%	0.0001	1.00	0.03	
GO:0070006	metallopeptidase activity	0.153%	0.0000	0.97	0.24	
GO:0015217	ADP transmembrane transporter activity	0.020%	0.0051	0.57	0.43	
GO:0008020	G protein-coupled photoreceptor activity	0.003%	0.0000	0.93	0.46	
GO:0003735	structural constituent of ribosome	2.348%	0.0001	0.96	0.50	
GO:0015252	proton channel activity	0.315%	0.0051	0.49	0.52	
GO:0009095	ligand-gated anion channel activity	0.006%	0.0008	0.60	0.58	
GO:0005283	amino acid:sodium symporter activity	0.045%	0.0034	0.44	0.61	
GO:0008137	NADH dehydrogenase (ubiquinone) activity	0.260%	0.0021	0.45	0.61	
GO:0044769	ATPase activity, coupled to transmembrane movement of ions, rotational mechanism	0.115%	0.0012	0.52	0.62	
GO:0046961	proton-transporting ATPase activity, rotational mechanism	0.115%	0.0003	0.44	1.00	



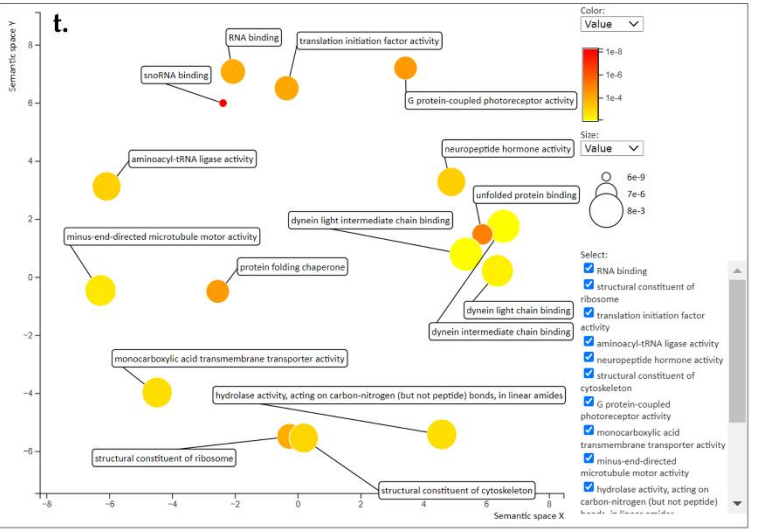
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GO:0004252	serine-type endopeptidase activity	0.893%	0.0096	0.90	0.00	
GO:0008307	structural constituent of muscle	0.004%	0.0039	0.98	0.00	
GO:0015662	P-type ion transporter activity	0.107%	0.0040	0.55	0.00	
GO:0016917	GABA receptor activity	0.027%	0.0073	1.00	0.00	
GO:0043227	peptide binding	0.100%	0.0016	1.00	0.00	
GO:0016776	phosphotransferase activity, phosphate group as acceptor	0.361%	0.0037	0.96	0.03	
GO:0016616	oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	1.855%	0.0061	0.85	0.04	
GO:0008061	chitin binding	0.116%	0.0001	1.00	0.04	
GO:0004568	chitinase activity	0.057%	0.0058	0.92	0.21	
GO:0008483	transaminase activity	0.728%	0.0036	0.96	0.23	
GO:0016298	lipase activity	0.261%	0.0049	0.93	0.24	
GO:0008010	structural constituent of chitin-based larval cuticle	0.002%	0.0000	0.98	0.33	
GO:0016643	oxidoreductase activity, acting on the CH-NH group of donors	0.350%	0.0028	0.86	0.37	
GO:0005311	L-glutamate transmembrane transporter activity	0.004%	0.0028	0.65	0.39	
GO:0009035	electron transfer activity	1.194%	0.0011	0.77	0.42	
GO:0032450	maltose alpha-glucosidase activity	0.006%	0.0028	0.91	0.47	
GO:0005328	neurotransmitter:sodium symporter activity	0.001%	0.0000	0.65	0.47	
GO:0015252	proton channel activity	0.315%	0.0028	0.57	0.52	
GO:0022852	transmembrane transporter activity	9.001%	0.0033	0.61	0.53	
GO:0070006	metallopeptidase activity	0.153%	0.0000	0.91	0.54	



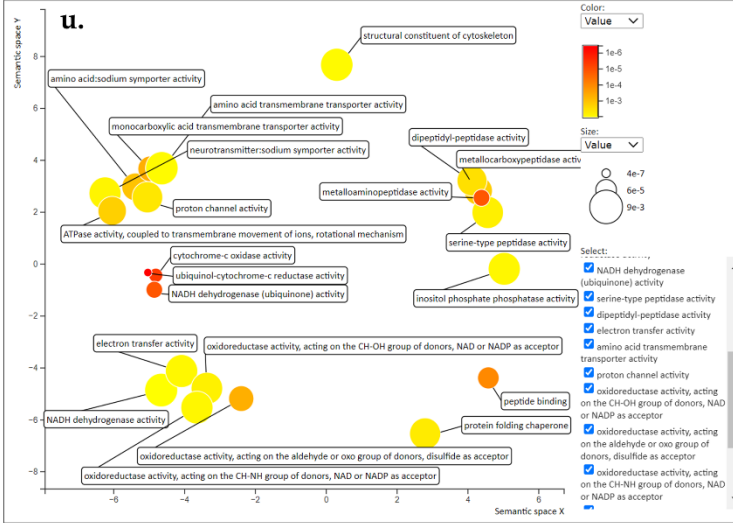
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GO:0009186	ATP-dependent activity, acting on RNA	0.334%	0.0000	0.92	0.00	
GO:0140097	catalytic activity, acting on DNA	2.626%	0.0028	0.79	0.00	
GO:0003139	nuclear localization sequence binding	0.010%	0.0000	0.96	0.04	
GO:0015082	unfolded protein binding	0.424%	0.0028	0.87	0.05	
GO:003697	single-stranded DNA binding	0.255%	0.0035	0.81	0.22	
GO:003677	DNA binding	11.354%	0.0048	0.75	0.33	
GO:0008296	3'-5'-exonuclease activity	0.010%	0.0031	0.78	0.39	
GO:0003015	snRNA binding	0.048%	0.0000	0.80	0.40	
GO:0043393	histone binding	0.086%	0.0005	0.88	0.47	
GO:0003723	RNA binding	5.630%	0.0023	0.76	0.53	
GO:0003724	RNA helicase activity	0.307%	0.0000	0.73	0.54	
GO:0008297	single-stranded DNA exonuclease activity	0.006%	0.0011	0.78	0.70	



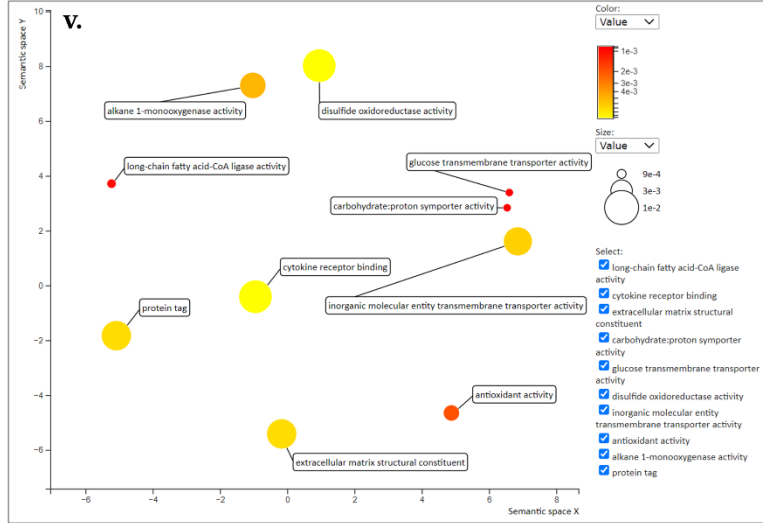
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GO:0000561	chitin binding	0.116%		0.0000	1.00	0.00
GO:0003302	structural constituent of muscle	0.004%		0.0013	0.96	0.00
GO:0008331	high voltage-gated calcium channel activity	0.001%		0.0001	0.93	0.00
GO:0008483	transaminase activity	0.728%		0.0100	0.92	0.00
GO:0004300	enoyl-CoA hydratase activity	0.051%		0.0039	0.97	0.03
GO:0004568	chitinase activity	0.057%		0.0020	0.92	0.03
GO:0016561	intramolecular oxidoreductase activity, interconverting aldoses and ketoses	0.309%		0.0001	0.96	0.03
GO:0004601	peroxidase activity	0.427%		0.0042	0.86	0.03
GO:0016872	ligase activity, forming carbon-nitrogen bonds	1.271%		0.0015	0.90	0.04
GO:0004364	glutathione transferase activity	0.086%		0.0000	0.93	0.20
GO:0005323	glucose transmembrane transporter activity	0.012%		0.0044	0.90	0.22
GO:0016746	acyltransferase activity	3.062%		0.0079	0.91	0.29
GO:0003955	acyl-CoA dehydrogenase activity	0.152%		0.0001	0.87	0.30
GO:0016646	oxidoreductase activity, acting on the CH-NH group of donors, NAD or NADP as acceptor	0.269%		0.0039	0.87	0.31
GO:0008010	structural constituent of chitin-based larval cuticle	0.002%		0.0006	0.96	0.33
GO:0016616	oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	1.855%		0.0004	0.85	0.38



Term ID	Name	Frequency	Pin?	Value	Uniqueness	Dispensability
GO:0008028	monooxygenase activity	0.052%		0.0014	1.00	0.00
GO:0005669	minus-end-directed microtubule motor activity	0.049%		0.0023	1.00	0.00
GO:0016811	hydrolyase activity, acting on carbon-nitrogen (but not peptide) bonds, in linear amides	0.737%		0.0014	1.00	0.00
GO:0051939	dynein light intermediate chain binding	0.026%		0.0080	0.80	0.00
GO:0044183	protein folding chaperone	0.019%		0.0000	1.00	0.01
GO:0005200	structural constituent of cytoskeleton	0.076%		0.0008	0.91	0.01
GO:0004612	aminoacyl-tRNA ligase activity	0.895%		0.0006	1.00	0.03
GO:0003743	translation initiation factor activity	0.394%		0.0001	0.84	0.04
GO:0008020	G protein-coupled photoreceptor activity	0.003%		0.0000	0.94	0.16
GO:0045503	dynein light chain binding	0.003%		0.0037	0.82	0.31
GO:0001233	RNA binding	5.630%		0.0001	0.89	0.32
GO:0005184	neurotrophin receptor activity	0.013%		0.0006	0.76	0.34
GO:0045505	dynein intermediate chain binding	0.030%		0.0080	0.80	0.36
GO:0030515	snoRNA binding	0.048%		0.0000	0.89	0.41
GO:0051082	unfolded protein binding	0.424%		0.0000	0.77	0.43
GO:0003735	structural constituent of ribosome	2.348%		0.0001	0.92	0.63



Term ID	Name	Frequency	Pin?	Value	Uniqueness	Dispensability
GO:0003954	NADH dehydrogenase activity	0.374%		0.0094	0.76	0.00
GO:0015171	amino acid transmembrane transporter activity	0.268%		0.0079	0.68	0.00
GO:0004272	peptide binding	0.100%		0.0001	1.00	0.00
GO:0044183	protein folding chaperone	0.019%		0.0043	0.99	0.01
GO:0005200	structural constituent of cytoskeleton	0.076%		0.0076	0.99	0.01
GO:0052745	inositol phosphate phosphatase activity	0.046%		0.0067	0.89	0.02
GO:0008236	serine-type peptidase activity	1.328%		0.0051	0.75	0.21
GO:0004332	serine-type aminopeptidase activity	0.893%		0.0001	0.76	0.94
GO:0005328	neurotransmitter:sodium symporter activity	0.001%		0.0064	0.69	0.25
GO:0016624	oxidoreductase activity, acting on the aldehyde or oxo group of donors, disulfide as acceptor	0.123%		0.0004	0.82	0.29
GO:0016646	oxidoreductase activity, acting on the CH-NH group of donors, NAD or NADP as acceptor	0.269%		0.0067	0.81	0.31
GO:0005055	electron transfer activity	1.194%		0.0071	0.69	0.36
GO:0044769	ATPase activity, coupled to transmembrane movement of ions, rotational mechanism	0.115%		0.0015	0.64	0.37
GO:0005245	proton-transporting ATPase activity, rotational mechanism	0.115%		0.0001	0.57	1.00
GO:0016616	oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	1.855%		0.0053	0.70	0.42



Term ID	Name	Frequency	Pin?	Value	Uniqueness	Dispensability
GO:0005126	cytokine receptor binding	0.094%		0.0096	1.00	0.00
GO:0005201	extracellular matrix structural constituent	0.037%		0.0070	1.00	0.00
GO:0015316	disulfide oxidoreductase activity	0.326%		0.0096	0.95	0.00
GO:0015318	inorganic molecular entity transmembrane transporter activity	2.924%		0.0062	0.84	0.00
GO:0031386	protein tag	0.011%		0.0070	1.00	0.00
GO:0016209	antioxidant activity	0.725%		0.0019	0.99	0.01
GO:0004467	long-chain fatty acid-CoA ligase activity	0.034%		0.0010	0.98	0.02
GO:0018685	alkane 1-monooxygenase activity	0.001%		0.0048	0.95	0.21
GO:0005355	glucose transmembrane transporter activity	0.012%		0.0009	0.70	0.35
GO:0005351	carbohydrate:proton symporter activity	0.026%		0.0009	0.77	0.71

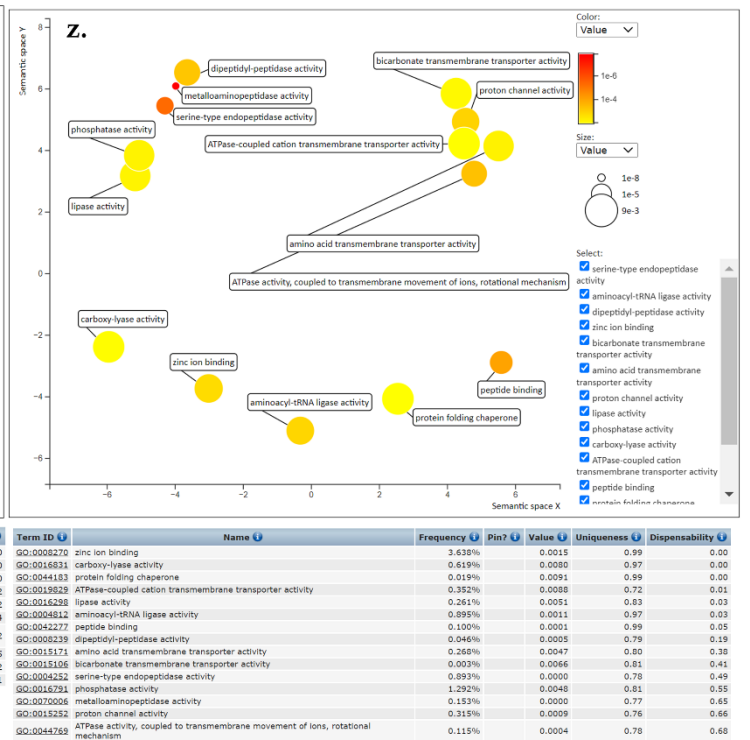
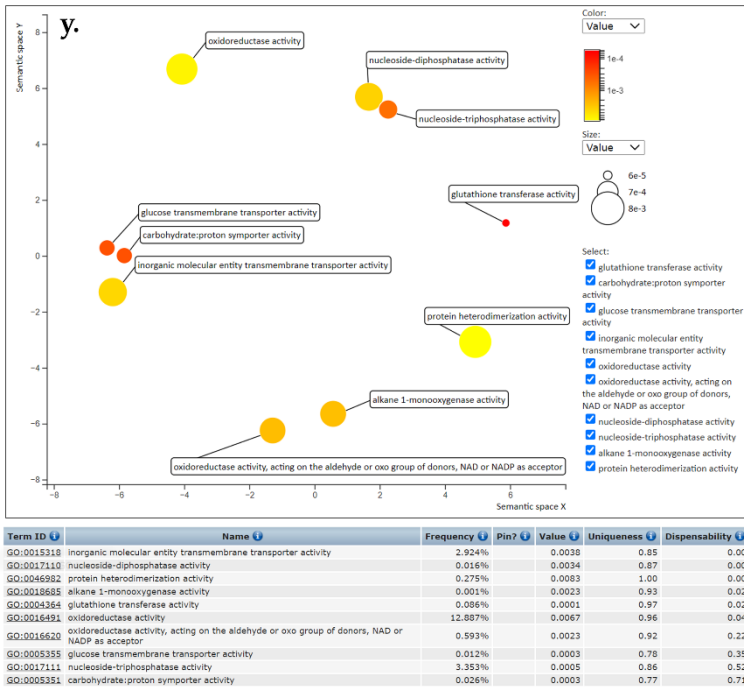
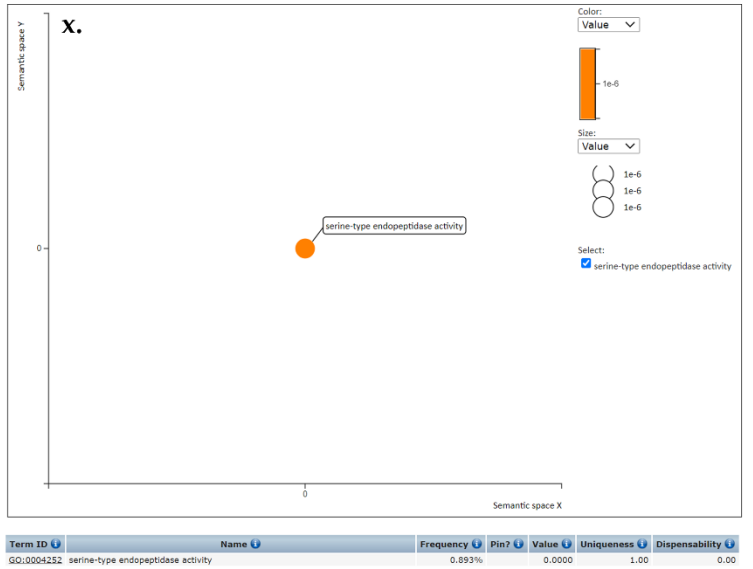
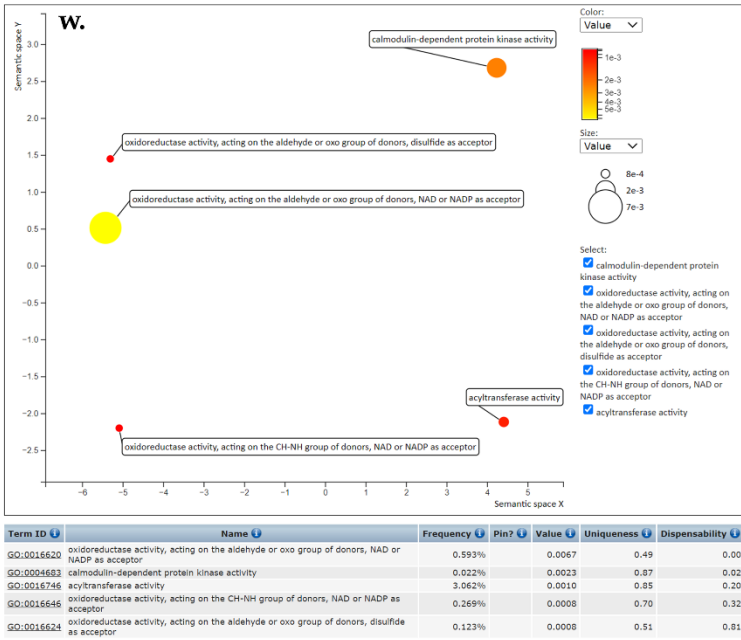


Fig. S6: Revigo Scatter and Table Views of the GO terms over-represented in all comparisons (R vs S, R vs C and C vs S) for data from Nigeria, Niger, Chad and Cameroon.

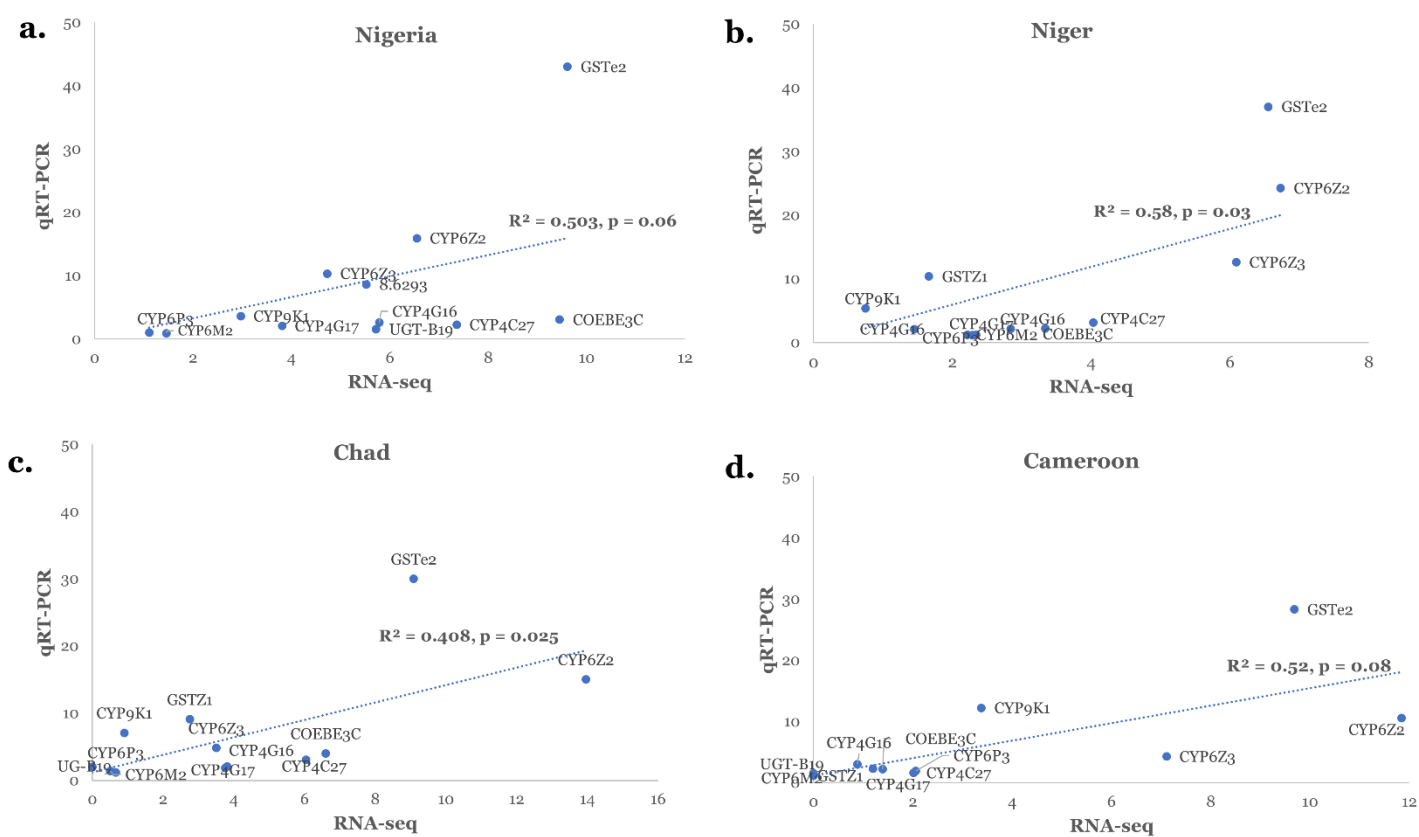


Fig. S7: Validation of RNA-seq results using qRT-PCR: correlation between RNA-seq fold changes and those obtained from qRT-PCR for 12 metabolic resistance genes.

a.

Population	n	S	Syn	Nonsyn	h	H _d	π (k)	D (Tajima)	D* (Fu and Li)
Nigeria	4	2	2	0	2	0.667	0.00090	1.893 ^{ns}	1.893 ^{ns}
Niger	4	42	36	6	3	0.833	0.01848	2.006 ^{ns}	2.006 ^{ns}
Chad	4	0	0	0	1	0.00	0.0000	0.000	0.000
Cameroon	4	23	20	3	2	0.500	0.0078	-0.857 ^{ns}	0.857 ^{ns}
Ngoussou	4	1	1	0	2	0.500	0.00034	-0.612 ^{ns}	-0.612 ^{ns}
All	20	75	65	12	10	0.921	0.01648	0.501 ^{ns}	1.298 ^{ns}

b.

Hap #	Freq.	Sequences
Hap_1:	2	>Nigeria2 >Nigeria3
Hap_2:	2	>Nigeria1 >Nigeria7
Hap_3:	1	>Niger1
Hap_4:	1	>Niger2
Hap_5:	2	>Niger3 >Niger4
Hap_6:	4	>Chad1 >Chad2 >Chad3 >Chad6
Hap_7:	3	>Cameroon1 >Cameroon2 >Cameroon3
Hap_8:	1	>Cameroon4
Hap_9:	3	>Ngoussou2 >Ngoussou4 >Ngoussou6
Hap_10:	1	>Ngoussou3

c.

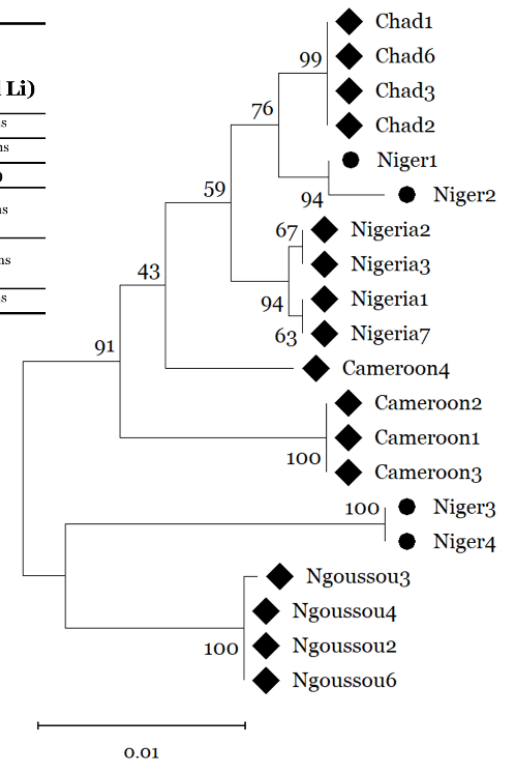


Fig. S8: Polymorphism analysis of full length cDNA of CYP6Z2. **a.** Summary statistics for polymorphisms of *CYP6Z2* cDNA across the Sahel countries. n = number of sequences (n); S, number of polymorphic sites; h, haplotype; H_d, haplotype diversity Syn, Synonymous mutations; Nonsyn, Non-synonymous mutations; π, nucleotide diversity (k= mean number of nucleotide differences); Tajima's D and Fu and Li's D statistics, ns, not significant. **b.** *CYP6Z2* cDNA haplotypes and its frequencies, **c.** a maximum likelihood phylogenetic tree of *CYP6Z2* cDNA sequences.

				20	c-myb		40		60	δEF1	
>NigeriaAL1	CAGGTTCA	AG	CTATTCG	CGG	TAGTTAACTA	GTCAAATAAA	GTGTAG	AATT	TAAAG	CACCC	60
>NigerAL1	CAGGTTCA	AG	CTATTCG	CGG	TAGTTAACTA	GTCAAATAAA	GTGTAG	AATT	TAAAG	CACCT	60
>NigeriaDE1	CAGGTTCA	TG	CTATTCG	CGG	TGTTTAACTA	GTCAAATAAA	GTGTAG	GATT	TAAAG	CACCT	60
>Ngoussou1	CAGGTTCA	TG	CTATTCG	CGG	TGTTTAACTA	GTCAAATAAA	GTGTAG	GATT	TAAAG	CACCT	60

	NMP4			80	FOX L1		100		120		
>NigeriaAL1	AGT	AACGT	AT	TTCT	TGTGCA	TAAAAAAACAG	GAATTCGCTT	CTGCTTTTAT	GT	ACG	AAGTA 120
>NigerAL1	AGT	AACGT	TTT	TTCT	TGTGCA	TAAAAAAACAG	GAATTCGCTT	CTGCTTTTAT	GT	-TGCAGTA	119
>NigeriaDE1	AGT	AACGT	TTT	TTCT	TGTGCA	TAAAAAAACAG	GAATTCGCTT	CTGCTTTTAT	GT	-TGCAGTA	119
>Ngoussou1	AGT	AACGT	TTT	TTCT	TGTGCA	TAAAAAAACAG	GAATTCGCTT	CTGCTTTTAT	GT	-TGCAGTA	119

	C-EST/GrH-TF			140			160	AhR1	NMP4		180
>NigeriaAL1	CGA	AGAACCG	GAATGAGTAT	GAAATAAAATT	CGCCGACACG	CACACAA	CAA	CACC	AAACCCC	180	
>NigerAL1	CGA	AGAACCG	GAATGAGTAT	GAAATAAAATT	CGCCGACACG	CACACAAAAA	CACC	AAACCCC	179		
>NigeriaDE1	CGA	AGAACCG	GAATGAGTAT	GAAATAAAATT	CGCCGACACG	CACACAAAAA	CACC	AAACCCC	179		
>Ngoussou1	CGA	AGAACCG	GAATGAGTAT	GAAATAAAATT	CGCCGACACG	CACACAAAAA	CACC	AAACCCC	179		

	GATA			200	NF-κB		220		240	GC Box1	
>NigeriaAL1	AAGTAATGCT	TTATCTCGGG	CCCTTCCAAC	GAA	CACA	GTC	ACACATCC	AA	AGCAT	GGGGC	240
>NigerAL1	AAGTAATGCT	TTATCTCGGG	CCCTTCCAAC	GAATACAATC	ACACATCCGA	AGCAT	GGGGC	239			
>NigeriaDE1	AAGTAATGCT	TTATCTCGGG	CCCTTCCAAC	GAATACAATC	ACACATCCGA	AGCAT	GGGGC	239			
>Ngoussou1	AAGTAATGCT	TTATCTCGGG	CCCTTCCAAC	GAATACAATC	ACACATCCGA	AGCAT	GGGGC	239			

	AREB			260		280	CAAT Box	Initiator, Inr		300	
>NigeriaAL1	GTTTGCTATG	CTTGGGGTCG	ATGCTACAAA	CATCCACAGC	CAATCA	TCAG	TT	GGGTGTG	300		
>NigerAL1	GTTTGCTATG	CTTGGGGTCG	ATGCTACAAA	CATCCACAGC	CAATCA	TCAG	TT	CGGGTGTG	299		
>NigeriaDE1	GTTTGCTATG	CTTGGGGTCG	ATGCTACAAA	CATCCACAGC	CAATCA	TCAG	TT	CGGGTGTG	299		
>Ngoussou1	GTTTGCTATG	CTTGGGGTCG	ATGCTACAAA	CATCCACAGC	CAATCA	TCAG	TT	CGGGTGTG	299		

	TSS			320		340					
>NigeriaAL1	TCTCTTGAAC	GTGTACGGTG	TGTGTCCATC	CA	TTTTTTAG	TTCGCTGCGA	AA	352			
>NigerAL1	TCTCTTGAAC	GTGTACGGTG	TGTGTCCATC	CAGTTTTT	TTAG	TTCGCTGCGA	AA	351			
>NigeriaDE1	TCTCTTGAAC	GTGTACGGTG	TGTGTCCATC	CAGTTTTT	TTAG	TTCGCTGCGA	AA	351			
>Ngoussou1	TCTCTTGAAC	GTGTACGGTG	TGTGTCCATC	CAGTTTTT	TTAG	TTCGCTGCGA	AA	351			

Fig. S9: Comparative alignment of the *GSTe2* 5'-UTR fragments from the various haplotypes, showing putative transcription factors binding sites (blue boxes), and polymorphic positions (in red and highlighted in pink). The arthropod Inr consensus sequence is in green box, the transcription start site indicated with red arrow, and the 3'-UTR of *GSTe1* and 5'-UTR of *GSTe2* indicated with dashed lines.

a.

Hap# Freq. Sequences

Hap_1: 75 NigeriaDE1 NigeriaDE2 NigeriaDE3 NigeriaDE4 NigeriaDE11
NigeriaDE15 NigeriaDE16 NigeriaDE20 NigeriaDE26 Ngoussou1
Ngoussou2 Ngoussou4 Ngoussou5 Ngoussou7 Ngoussou9 Ngoussou11 Ngoussou13
NigerDE1 NigerDE2 NigerDE3 NigerDE4 NigerDE5 NigerDE6 NigerDE7 NigerDE8
NigerDE11 NigerDE12 ChadAL1 ChadAL3 ChadAL4 ChadAL5 ChadAL6 ChadAL7
ChadAL9 ChadAL10 ChadDE1 ChadDE2 ChadDE3 ChadDE4 ChadDE6 ChadDE7 ChadDE9
ChadDE11 ChadDE13 ChadDE24 CameroonAL1 CameroonAL2 CameroonAL3 CameroonAL4
CameroonAL8 CameroonAL9 CameroonAL11 CameroonDE1 CameroonDE2 CameroonDE3
CameroonDE4 CameroonDE14 CameroonDE12 CameroonDE11 CameroonDE8
CameroonDE10 CameroonDE6 NigeriaAL7 NigeriaAL4 NigeriaAL8 NigeriaAL17 NigeriaAL2

Hap_2: 1 NigeriaDE29

Hap_3: 1 NigeriaAL3

Hap_4: 1 NigeriaAL5

Hap_5: 4 NigerAL1 NigerAL9 NigerAL10 NigerAL11

Hap_6: 8 NigeriaAL1 NigeriaAL6 NigeriaAL9 ChadAL2 ChadAL3
CameroonAL5 CameroonAL25 CameroonAL7

b. 0000001111 222223
0246680116 11 23993
927095246848941 33
Hap_1 TTGTTATTCATAGATCG
Hap_2G.....
Hap_3C.....
Hap_4 ..ACAG. CACCGA .AG.
Hap_5 AAA.....
Hap_6 AAACA. .CACCGA...GC

c.

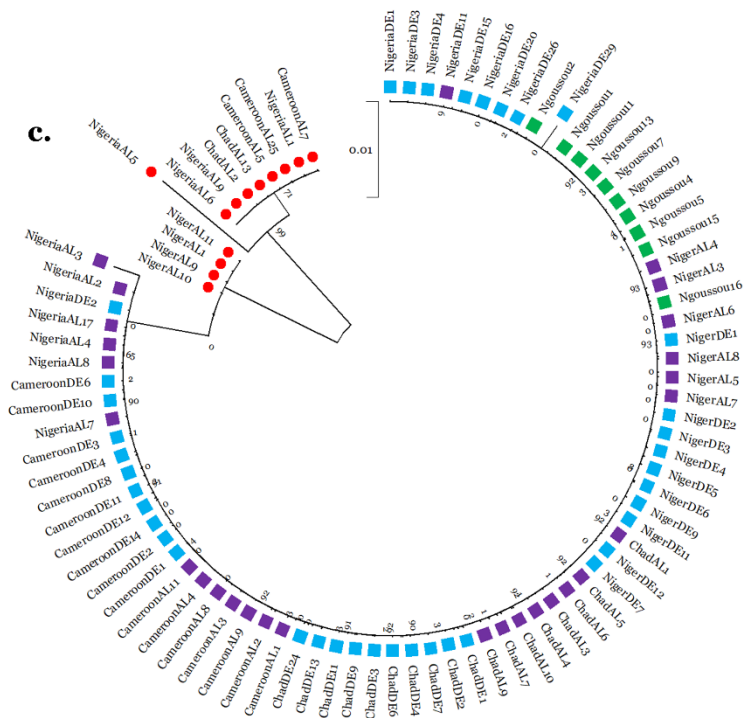


Fig. S10: Genetic variability of the *GSTe2* 5'-UTR fragments from Nigeria, Niger, Chad, Cameroon and Ngoussou populations. a. the six haplotypes of the 5'-UTR with respective frequencies, **b.** polymorphic positions with numbers on top indicating the nucleotide position in the 351 bp fragment, **c.** maximum likelihood phylogenetic tree of the 90 sequences, showing the DDT-alive sequences with mutations forming a clade specific to its phenotype.

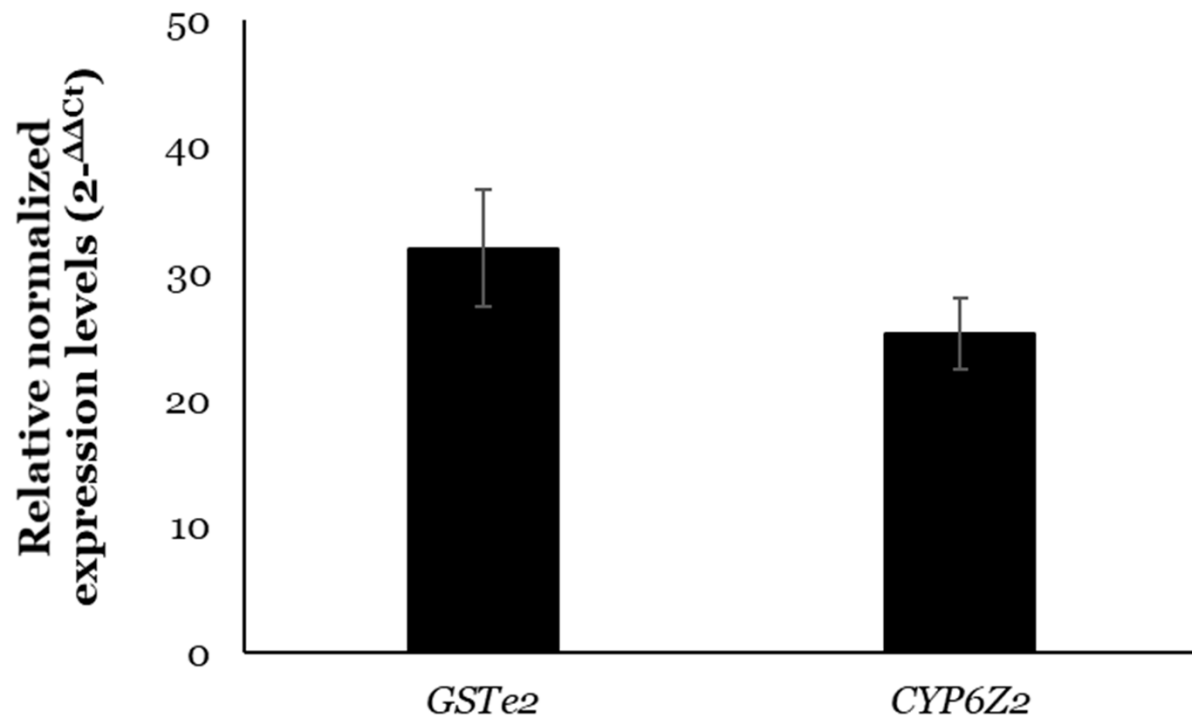


Fig. S11: qRT-PCR validation of the overexpression of *GSTe2* and *CYP6Z2*. The relative expression of the *GSTe2* and *CYP6Z2* in the experimental transgenic *D. melanogaster* in relation to control flies. Data shown are the mean \pm standard deviation ($n = 6$).