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Supplementary Information for

Polar Bear Evolution is marked by Rapid Changes in Gene Copy Number in Response to Dietary Shift

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Datasets S1 to S2

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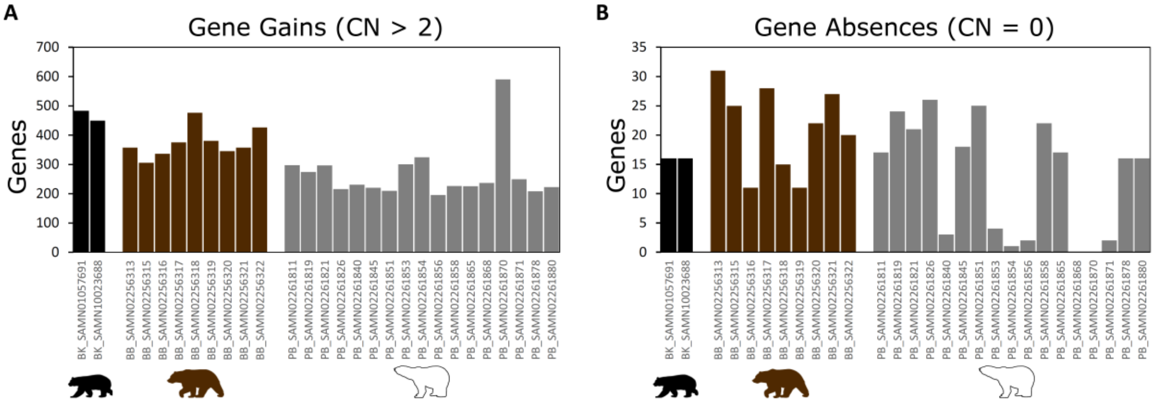

Fig S1. Gene gain (A) and absence (B) frequencies across bear individuals. Gains are defined as estimates of gene copy number > 2 by both Control-FreeC and BDN. Absences are defined as estimates of gene copy number = 0 by both Control-FreeC and BDN. BKB_ = black bear, BB_ = brown bear, and PB_ = polar bear.

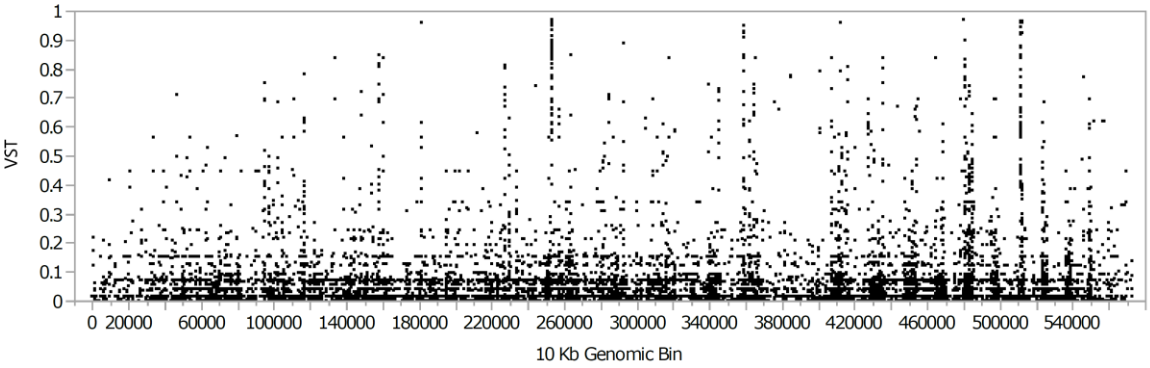

Fig. S2. Genome-wide copy number divergence between brown bear and polar bear. Manhattan plot of V_{ST} values (Y-axis) for each 10 Kb bin with a 2 Kb sliding window (X-axis) in the polar bear reference genome. Genome-wide mean V_{ST} = 0.006.

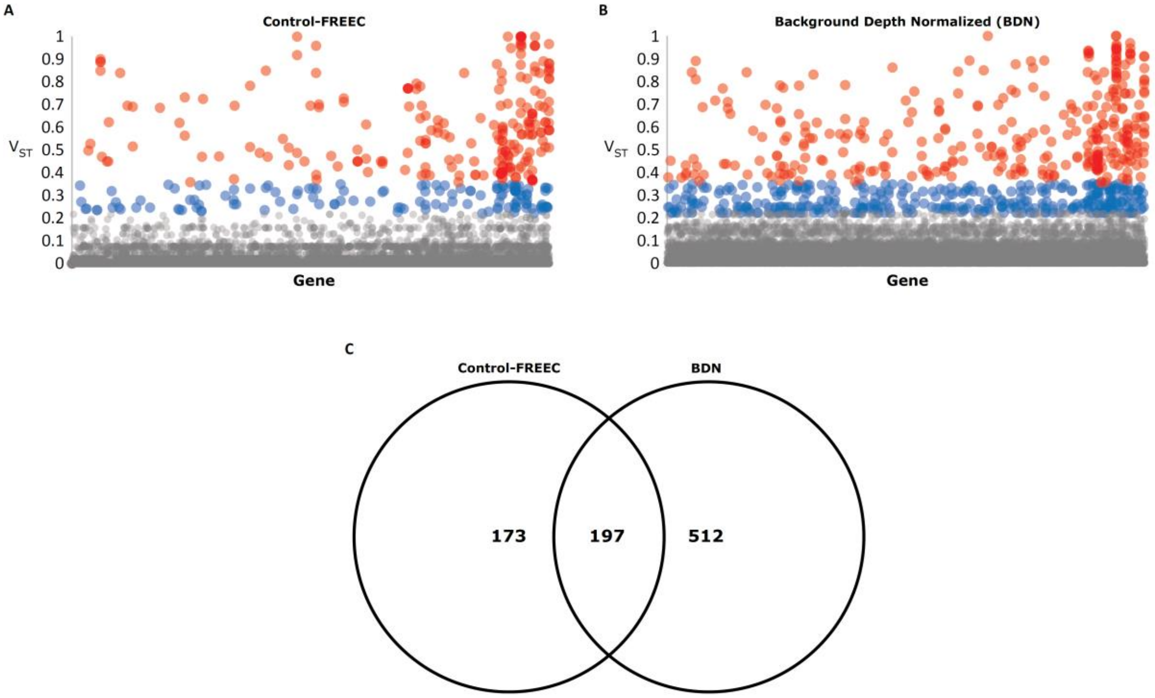

Fig. S3. Overlap between V_{ST} values from Control-FREEC and BDN gene copy number estimates. Manhattan plot of gene V_{ST} values using Control-FREEC (A) and BDN (B) gene copy number estimates. Red points = $V_{ST} > 0.35$ (extremely CN differentiated), blue points = $V_{ST} > 0.22$ and $VST \leq 0.35$ (CN differentiated), and gray points = $V_{ST} \leq 0.22$. (C) Venn diagram of copy number differentiated genes ($V_{ST} > 0.22$) between the Control-FREEC and BDN methods.

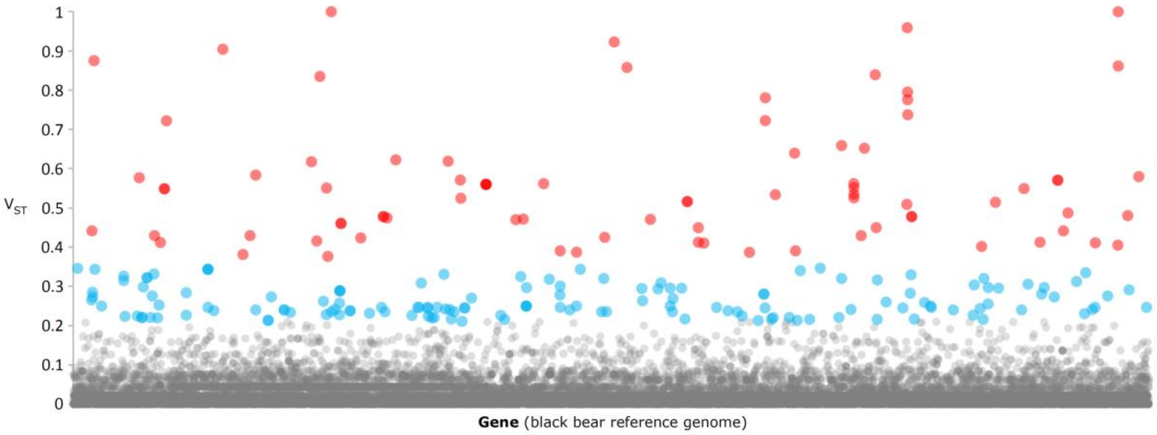

Fig. S4. Manhattan plot of gene V_{ST} values from Control-FREEC gene copy number estimates relative to the black bear reference genome. Red points = $V_{ST} > 0.35$ (extremely CN differentiated), blue points = $V_{ST} > 0.22$ and $V_{ST} \leq 0.35$ (CN differentiated), and gray points = $V_{ST} \leq 0.22$.

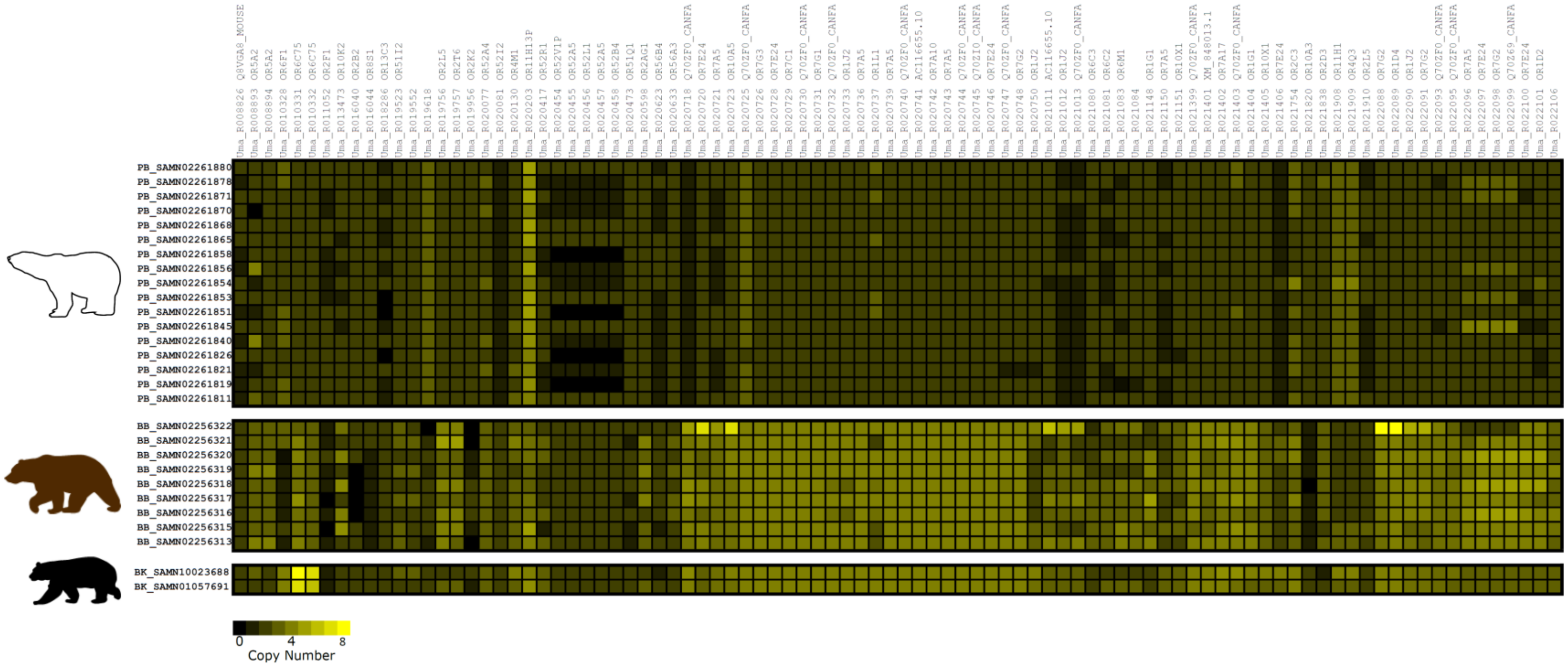

Fig. S5. Heatmap of predicted gene copy number for the subset of differentiated genes (V_{ST} > 0.22) predicted to encode olfactory receptors. Black and yellow represent copy numbers of zero and 8, respectively. Polar bear gene identifiers, along with either human or dog annotations when available, are labeled above each gene. Gene copy number estimates are from Control-FREEC.

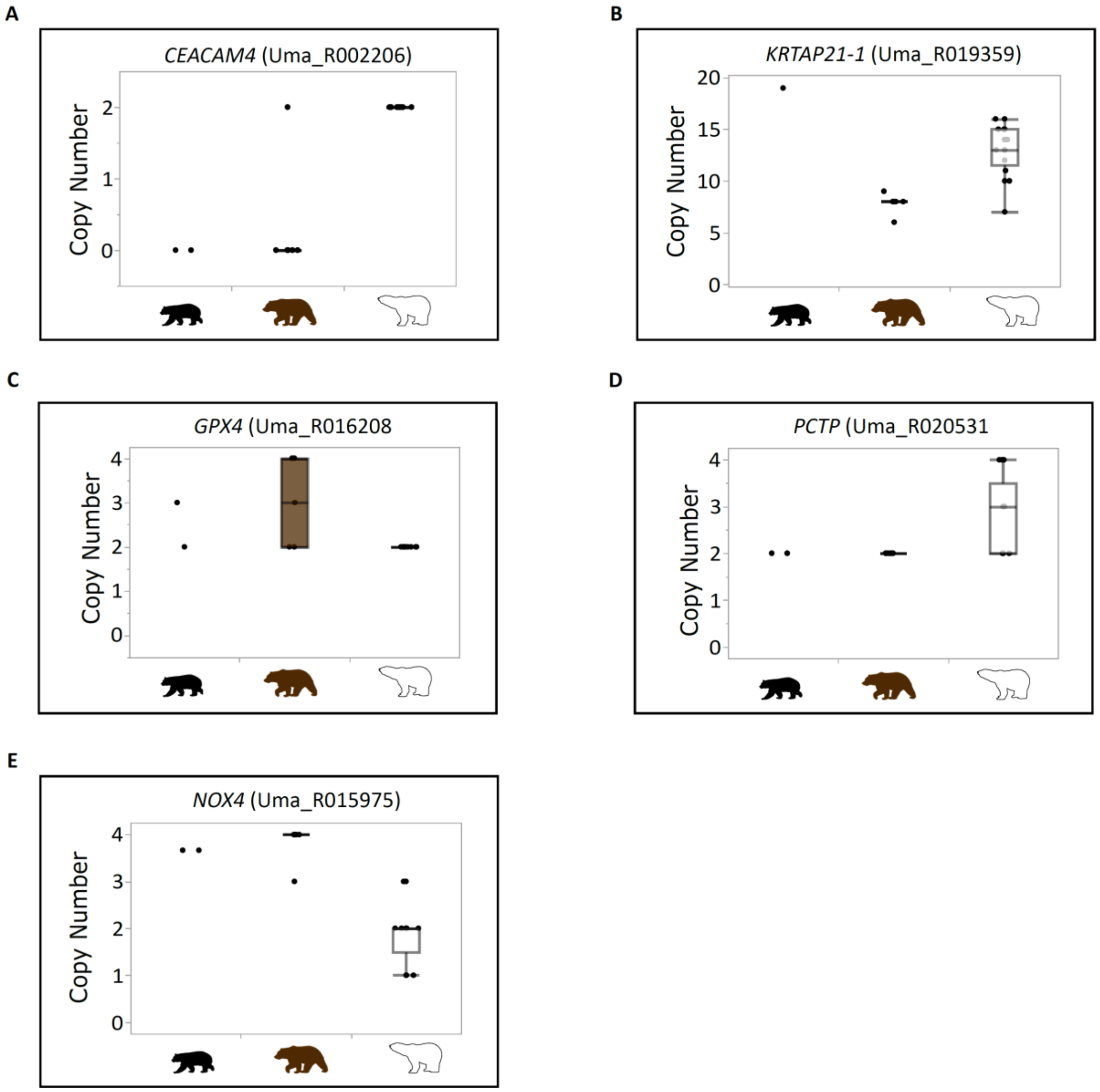

Fig. S6. Copy number distribution of differentiated ecologically relevant genes. Box and whisker plots of gene copy number for genes involved in immunity (A), morphology (B), and metabolism (C-E). CNs are from Control-FREEC estimates. Each dot represents the diploid copy number (Y-axis) for a given bear individual (X-axis). The box plot displays the median value, 1st quartile, and 3rd quartile. Whiskers are drawn to the furthest point with 1.5x the inter quartile range (3rd quartile minus the 1st quartile) from the box. The black bear does not include a box and whisker plot because the analysis included only two individuals.

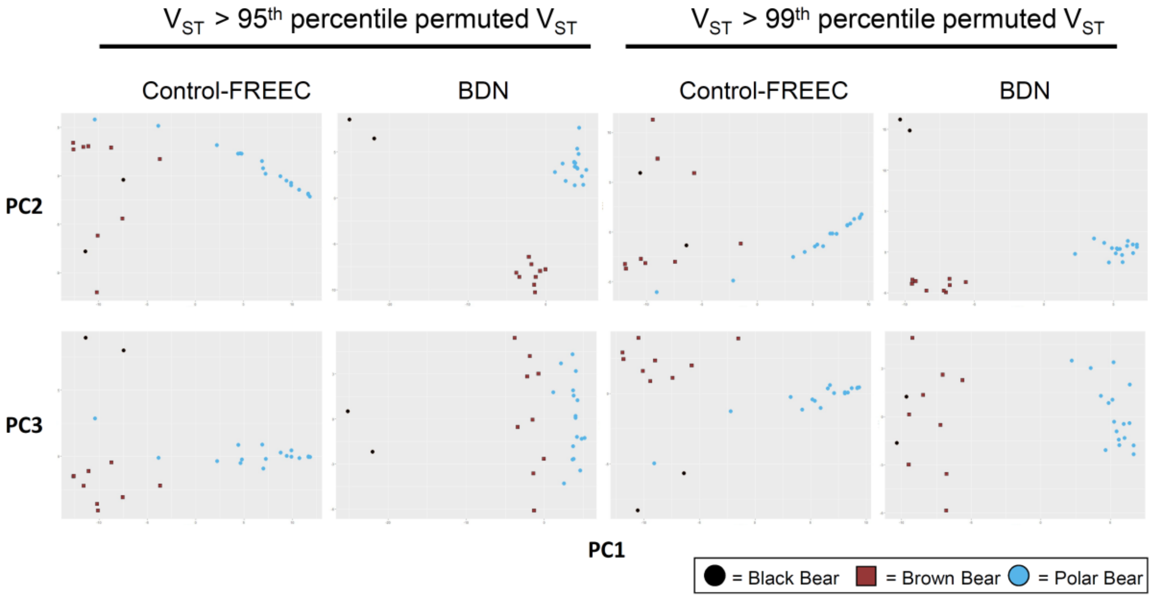

Fig. S7. Principal component analysis of copy number differentiated genes. Principal component analysis performed on gene copy number counts in all bear individuals as called by either Control-FREEC or BDN. In every case, the first three principal components (PC1, PC2, and PC3) explained over 80% of the measured CN variance. The 95th and 99th percentile V_{ST} cutoffs for each gene were determined by permutation tests.

Table S1. Percentage of mapped reads against the reference polar bear and black bear genomes. BB = brown bear, BK = black bear, and PB_ = polar bear.

Sample	Polar Bear	Black Bear
BB_SAMN02256313	98.01	97.57
BB_SAMN02256315	97.3	97.14
BB_SAMN02256316	98.33	98
BB_SAMN02256317	97.5	97.14
BB_SAMN02256318	98.55	98.15
BB_SAMN02256319	98.19	97.91
BB_SAMN02256320	97.36	97.19
BB_SAMN02256321	96.7	96.44
BB_SAMN02256322	90.46	90.12
BK_SAMN01057691	97.82	98.06
BK_SAMN10023688	97.86	98.75
PB_SAMN02261811	98.47	97.71
PB_SAMN02261819	98.65	97.82
PB_SAMN02261821	99.07	98.12
PB_SAMN02261826	99	98.28
PB_SAMN02261840	98.08	97.63
PB_SAMN02261845	98.19	97.59
PB_SAMN02261851	98.33	97.91
PB_SAMN02261853	98.54	98.03
PB_SAMN02261854	97.63	97.37
PB_SAMN02261856	96.87	95.2
PB_SAMN02261858	98.27	97.65
PB_SAMN02261865	98.54	97.94
PB_SAMN02261868	98.38	97.9
PB_SAMN02261870	98.01	97.39
PB_SAMN02261871	98.14	97.73
PB_SAMN02261878	98.62	98.16
PB_SAMN02261880	98.28	97.78

Table S2. GO Biological Process enrichment for polar bear genes displaying gain (copy number > 2) with both CNV estimation methods in at least one individual. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	**Genes in list**	**Total genes**	**Functional Category**
3.40E-06	147	2727	Catabolic process
3.40E-06	135	2414	Cellular catabolic process
3.60E-06	66	911	MRNA metabolic process
1.50E-05	31	293	Regulation of mRNA metabolic process
2.10E-05	21	150	Antibiotic metabolic process
4.80E-05	78	1252	Cellular macromolecule catabolic process
5.10E-05	89	1506	Macromolecule catabolic process
1.00E-04	44	568	MRNA processing
1.10E-04	39	479	RNA splicing
1.10E-04	120	2282	Organic substance catabolic process
1.90E-04	64	1005	RNA processing
3.10E-04	199	4374	Regulation of nucleobase-containing compound metabolic process
3.30E-04	25	251	Gene silencing
3.30E-04	55	833	Drug metabolic process
3.40E-04	32	377	RNA splicing, via transesterification reactions with bulged adenosine as nucleophile
3.40E-04	32	377	MRNA splicing, via spliceosome
3.50E-04	44	611	Nucleobase-containing compound catabolic process
3.60E-04	32	380	RNA splicing, via transesterification reactions
3.60E-04	47	676	Aromatic compound catabolic process
3.70E-04	39	516	Detection of chemical stimulus involved in sensory perception of smell
3.80E-04	213	4798	Regulation of gene expression
3.80E-04	60	958	Regulation of catabolic process
3.90E-04	46	662	Heterocycle catabolic process
4.10E-04	46	664	Cellular nitrogen compound catabolic process
4.50E-04	48	709	Organic cyclic compound catabolic process
9.50E-04	52	816	Detection of stimulus
1.10E-03	41	588	Detection of chemical stimulus involved in sensory perception
1.10E-03	39	548	Sensory perception of smell
1.10E-03	12	77	Positive regulation of mRNA metabolic process
1.50E-03	31	398	RNA catabolic process
1.50E-03	202	4628	Heterocycle biosynthetic process
1.50E-03	43	644	Detection of stimulus involved in sensory perception
1.50E-03	182	4089	Regulation of RNA metabolic process
1.50E-03	208	4791	Organic cyclic compound biosynthetic process
1.60E-03	29	364	MRNA catabolic process

1.60E-03	202	4635	Aromatic compound biosynthetic process
1.60E-03	42	627	Detection of chemical stimulus
2.20E-03	106	2142	Small molecule metabolic process
2.20E-03	185	4205	Regulation of cellular macromolecule biosynthetic process
2.20E-03	198	4559	Nucleobase-containing compound biosynthetic process
2.30E-03	70	1270	Chromosome organization
2.50E-03	51	838	Regulation of cellular catabolic process
2.80E-03	16	147	Regulation of mRNA processing
2.90E-03	42	648	Sensory perception of chemical stimulus
2.90E-03	189	4345	Regulation of macromolecule biosynthetic process
2.90E-03	38	564	Posttranscriptional regulation of gene expression
3.10E-03	197	4570	Regulation of biosynthetic process
3.20E-03	17	166	Gene silencing by RNA
3.70E-03	142	3112	Negative regulation of metabolic process
3.70E-03	16	152	Intracellular steroid hormone receptor signaling pathway
4.40E-03	25	315	Regulation of gene expression, epigenetic
4.40E-03	193	4495	Regulation of cellular biosynthetic process
4.70E-03	23	279	Cellular response to steroid hormone stimulus
5.10E-03	21	244	Nuclear-transcribed mRNA catabolic process
5.30E-03	16	158	Regulation of mRNA catabolic process
6.50E-03	44	723	Translation
6.80E-03	8	45	Positive regulation of mRNA catabolic process
7.40E-03	9	58	Antibiotic catabolic process
7.40E-03	173	3999	Nucleic acid-templated transcription
8.20E-03	4	9	Ovulation from ovarian follicle
9.20E-03	7	36	Termination of RNA polymerase II transcription
9.20E-03	130	2872	Negative regulation of macromolecule metabolic process
9.20E-03	173	4021	RNA biosynthetic process
9.20E-03	17	185	Negative regulation of mitotic cell cycle phase transition
1.00E-02	29	418	Response to steroid hormone
1.10E-02	170	3956	Transcription, DNA-templated
1.10E-02	10	76	Androgen receptor signaling pathway
1.10E-02	44	748	Peptide biosynthetic process
1.10E-02	95	1984	Organonitrogen compound biosynthetic process
1.20E-02	172	4022	Organelle organization
1.50E-02	22	289	Negative regulation of mitotic cell cycle
1.50E-02	131	2943	Transcription by RNA polymerase II
1.60E-02	71	1404	Regulation of hydrolase activity
1.60E-02	61	1163	Organic acid metabolic process
1.60E-02	50	902	Peptide metabolic process

1.60E-02	6	29	Retrograde protein transport, ER to cytosol
1.60E-02	6	29	Endoplasmic reticulum to cytosol transport
1.60E-02	14	144	Drug catabolic process
1.80E-02	32	502	Covalent chromatin modification
1.90E-02	47	842	Chromatin organization
2.00E-02	52	962	Response to organic cyclic compound
2.00E-02	17	202	Negative regulation of cell cycle phase transition
2.10E-02	121	2709	Negative regulation of cellular metabolic process
2.10E-02	4	12	Positive regulation of nuclear-transcribed mRNA poly(A) tail shortening
2.20E-02	7	43	Nuclear-transcribed mRNA poly(A) tail shortening
2.20E-02	5	21	Ovulation
2.30E-02	25	363	Regulation of translation
2.30E-02	61	1188	Cellular amide metabolic process
2.30E-02	35	579	Cellular response to organic cyclic compound
2.40E-02	11	102	Regulation of mRNA splicing, via spliceosome
2.50E-02	64	1267	Carbohydrate derivative metabolic process
2.60E-02	17	209	Steroid hormone mediated signaling pathway
2.60E-02	7	45	Response to dexamethasone
2.60E-02	14	154	Regulation of G1/S transition of mitotic cell cycle
2.70E-02	20	268	Hormone-mediated signaling pathway
2.80E-02	53	1007	Protein catabolic process
2.90E-02	11	105	Negative regulation of G1/S transition of mitotic cell cycle
3.50E-02	48	898	Amide biosynthetic process
3.50E-02	4	14	Regulation of nuclear-transcribed mRNA poly(A) tail shortening
3.50E-02	13	142	Negative regulation of translation
3.60E-02	2	2	Glucosamine catabolic process
3.60E-02	90	1952	Negative regulation of gene expression
3.60E-02	21	298	Macroautophagy
3.60E-02	30	488	Histone modification
3.60E-02	27	422	Regulation of cellular amide metabolic process
3.60E-02	10	93	Mitochondrial ATP synthesis coupled electron transport
3.60E-02	13	144	Regulation of RNA splicing
3.60E-02	36	624	Negative regulation of cell cycle
3.60E-02	8	62	Protein K48-linked ubiquitination
3.60E-02	11	109	Negative regulation of cell cycle G1/S phase transition
3.60E-02	2	2	Positive regulation of telomerase RNA reverse transcriptase activity
3.60E-02	2	2	Positive regulation of ubiquitin-specific protease activity
3.60E-02	2	2	Regulation of nucleotide-excision repair

3.70E-02	3	7	CDP-choline pathway
3.70E-02	62	1248	Organophosphate metabolic process
3.70E-02	10	94	ATP synthesis coupled electron transport
3.70E-02	60	1202	Intracellular protein transport
3.70E-02	5	25	Histone mRNA metabolic process
3.70E-02	22	321	Negative regulation of cell cycle process
3.70E-02	45	837	Positive regulation of hydrolase activity
3.70E-02	27	427	Regulation of cell cycle phase transition
3.90E-02	6	37	Protein deglycosylation
4.20E-02	88	1920	Intracellular transport
4.20E-02	20	284	Rhythmic process
4.20E-02	112	2551	Negative regulation of nitrogen compound metabolic process
4.20E-02	159	3823	Regulation of nucleic acid-templated transcription
4.20E-02	21	305	Intrinsic apoptotic signaling pathway
4.20E-02	28	455	Positive regulation of catabolic process
4.30E-02	30	500	Autophagy
4.30E-02	30	500	Process utilizing autophagic mechanism
4.30E-02	23	348	Regulation of chromosome organization
4.50E-02	11	115	Protein deacylation
4.50E-02	57	1143	Oxoacid metabolic process
4.50E-02	25	393	Regulation of mitotic cell cycle phase transition
4.50E-02	159	3836	Regulation of RNA biosynthetic process
4.50E-02	31	526	Purine ribonucleotide metabolic process
4.50E-02	44	828	Cellular protein catabolic process
4.70E-02	30	505	Glycerolipid metabolic process
4.70E-02	34	596	Purine-containing compound metabolic process
4.70E-02	34	596	Establishment of protein localization to organelle
4.70E-02	38	689	Modification-dependent macromolecule catabolic process
4.70E-02	14	171	Regulation of cell cycle G1/S phase transition
4.70E-02	8	68	Histone H4 acetylation
4.80E-02	156	3765	Regulation of transcription, DNA-templated
4.80E-02	18	250	Cell cycle checkpoint
4.90E-02	11	118	Nucleotide-excision repair
5.00E-02	20	292	Response to xenobiotic stimulus

Table S3. GO Biological Process enrichment for brown bear genes displaying gain (copy number > 2) with both CNV estimation methods in at least one individual. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	**Genes in list**	**Total genes**	**Functional Category**
5.10E-32	61	516	Detection of chemical stimulus involved in sensory perception of smell
6.70E-32	64	588	Detection of chemical stimulus involved in sensory perception
2.40E-31	65	627	Detection of chemical stimulus
4.10E-31	61	548	Sensory perception of smell
7.20E-31	65	644	Detection of stimulus involved in sensory perception
7.10E-30	64	648	Sensory perception of chemical stimulus
1.80E-27	68	816	Detection of stimulus
3.50E-21	70	1110	Sensory perception
1.20E-15	74	1546	G protein-coupled receptor signaling pathway
5.00E-15	74	1589	Nervous system process
7.30E-13	88	2321	System process

Table S4. GO Biological Process enrichment for polar bear genes displaying absence (copy number = 0) with both CNV estimation methods in at least one individual. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	**Genes in list**	**Total genes**	**Functional Category**
1.00E-04	7	548	Sensory perception of smell
1.00E-04	7	516	Detection of chemical stimulus involved in sensory perception of smell
1.00E-04	7	648	Sensory perception of chemical stimulus
1.00E-04	7	627	Detection of chemical stimulus
1.00E-04	7	644	Detection of stimulus involved in sensory perception
1.00E-04	7	588	Detection of chemical stimulus involved in sensory perception
4.00E-04	7	816	Detection of stimulus
2.50E-03	7	1110	Sensory perception
3.10E-03	8	1589	Nervous system process
5.40E-03	2	27	Histone lysine demethylation
6.30E-03	2	33	Protein demethylation
6.30E-03	2	33	Protein dealkylation
6.30E-03	2	31	Histone demethylation
1.00E-02	7	1546	G protein-coupled receptor signaling pathway
2.30E-02	8	2321	System process
2.40E-02	2	72	Demethylation

Table S5. GO Biological Process enrichment for brown bear genes displaying absence (copy number = 0) with both CNV estimation methods in at least one individual. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	Genes in list	Total genes	Functional Category
4.50E-11	14	648	Sensory perception of chemical stimulus
4.50E-11	14	627	Detection of chemical stimulus
4.50E-11	14	644	Detection of stimulus involved in sensory perception
4.50E-11	14	588	Detection of chemical stimulus involved in sensory perception
4.50E-11	13	516	Detection of chemical stimulus involved in sensory perception of smell
8.00E-11	13	548	Sensory perception of smell
6.30E-10	14	816	Detection of stimulus
3.10E-08	14	1110	Sensory perception
1.90E-06	14	1546	G protein-coupled receptor signaling pathway
2.30E-06	14	1589	Nervous system process
2.00E-04	14	2321	System process
2.50E-04	2	4	L-arginine import across plasma membrane
3.90E-04	2	5	L-arginine transmembrane transport
4.20E-04	2	6	Ornithine transport
4.20E-04	2	6	L-lysine transport
4.20E-04	2	6	L-ornithine transmembrane transport
4.20E-04	2	6	L-lysine transmembrane transport
4.20E-04	2	6	Arginine transmembrane transport
5.60E-04	2	7	L-arginine transport
8.60E-04	2	9	Arginine transport
8.60E-04	2	9	Basic amino acid transmembrane transport
2.10E-03	2	14	Basic amino acid transport
5.00E-03	2	22	Amino acid import across plasma membrane
6.20E-03	2	25	Amino acid import
6.90E-03	2	27	Histone lysine demethylation
8.80E-03	2	31	Histone demethylation
9.00E-03	2	33	Protein demethylation
9.00E-03	3	131	Amino acid transport
9.00E-03	2	33	Protein dealkylation
2.00E-02	2	50	L-alpha-amino acid transmembrane transport
3.10E-02	3	212	Translational initiation
3.10E-02	2	65	L-amino acid transport
3.70E-02	2	72	Demethylation
4.60E-02	2	83	Amino acid transmembrane transport

4.60E-02	2	84	Positive regulation of ossification
4.80E-02	2	87	Drug transmembrane transport

Table S7. Enrichment of genes differentiated by copy number ($V_{ST} > 0.22$) between brown bear and polar bear. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	**Genes in list**	**Total genes**	**Functional Category**
7.80E-42	37	429	Olfactory transduction
2.80E-39	37	516	Detection of chemical stimulus involved in sensory perception of smell
2.80E-39	37	516	Olfactory receptor activity
6.60E-39	35	429	Reactome:R-HSA-381753 Olfactory Signaling Pathway
1.60E-38	37	548	Sensory perception of smell
1.90E-37	37	588	Detection of chemical stimulus involved in sensory perception
1.70E-36	37	627	Detection of chemical stimulus
2.00E-36	36	571	Reactome:R-HSA-418555 G alpha (s) signalling events
3.70E-36	37	644	Detection of stimulus involved in sensory perception
4.10E-36	37	648	Sensory perception of chemical stimulus
1.80E-32	37	816	Detection of stimulus
1.40E-30	38	1006	G protein-coupled receptor activity
1.10E-27	37	1110	Sensory perception
8.60E-26	36	1155	Reactome:R-HSA-388396 GPCR downstream signalling
4.70E-25	36	1215	Reactome:R-HSA-372790 Signaling by GPCR
1.00E-24	39	1582	Transmembrane signaling receptor activity
6.80E-24	38	1546	G protein-coupled receptor signaling pathway
1.70E-23	38	1589	Nervous system process
2.80E-22	39	1850	Signaling receptor activity
8.50E-22	39	1910	Molecular transducer activity
9.30E-19	39	2321	System process
1.50E-15	38	2690	Reactome:R-HSA-162582 Signal Transduction
9.80E-07	7	89	Reactome:R-HSA-2168880 Scavenging of heme from plasma
1.10E-06	7	91	GeneSetDB:EHMN Arachidonic acid metabolism
2.20E-06	7	101	GeneSetDB:EHMN Leukotriene metabolism
6.20E-06	7	118	Reactome:R-HSA-2173782 Binding and Uptake of Ligands by Scavenger Receptors
8.00E-06	3	4	Recon X:ALOX12
9.90E-06	10	354	MSigDB:chr11p15
1.70E-05	6	85	Reactome:R-HSA-173623 Classical antibody-mediated complement activation
2.20E-05	6	89	Reactome:R-HSA-2730905 Role of LAT2/NTAL/LAB on calcium mobilization
2.40E-05	6	91	Reactome:R-HSA-2029481 FCGR activation
2.70E-05	6	93	Reactome:R-HSA-166786 Creation of C4 and C2 activators

4.00E-05	6	100	Reactome:R-HSA-166663 Initial triggering of complement
4.80E-05	6	104	Reactome:R-HSA-2871809 FCERI mediated Ca+2 mobilization
4.80E-05	6	104	Reactome:R-HSA-2029485 Role of phospholipids in phagocytosis
4.90E-05	6	105	Reactome:R-HSA-2871796 FCERI mediated MAPK activation
1.30E-04	6	124	Reactome:R-HSA-977606 Regulation of Complement cascade
2.00E-04	6	135	Reactome:R-HSA-166658 Complement cascade
2.40E-04	6	140	Reactome:R-HSA-2029482 Regulation of actin dynamics for phagocytic cup formation
3.80E-04	4	41	GeneSetDB:EHMN Prostaglandin formation from arachidonate
4.00E-04	6	154	Reactome:R-HSA-2871837 FCERI mediated NF-kB activation
4.30E-04	2	2	Recon X:LTA4H
5.60E-04	6	165	Reactome:R-HSA-2029480 Fcgamma receptor (FCGR) dependent phagocytosis
6.20E-04	7	254	Wiki:GPCRs, Class A Rhodopsin-like
7.00E-04	7	260	MSigDB:chr22q11
8.60E-04	6	180	Reactome:R-HSA-8978868 Fatty acid metabolism
1.10E-03	2	3	Recon X:CHEBI
1.10E-03	2	3	CTD:CHEBI
1.10E-03	2	3	CTD:CHEBI
1.60E-03	3	22	GeneSetDB:MATADOR acarbose
1.70E-03	6	206	Reactome:R-HSA-198933 Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell
1.70E-03	6	207	Reactome:R-HSA-2454202 Fc epsilon receptor (FCERI) signaling
1.80E-03	6	211	Recon X:SLC7A9
1.90E-03	6	213	Reactome:R-HSA-202733 Cell surface interactions at the vascular wall
1.90E-03	2	4	L-arginine import across plasma membrane
2.70E-03	4	73	Metabolism of xenobiotics by cytochrome P450
2.90E-03	2	5	L-arginine transmembrane transport
2.90E-03	2	5	L-ornithine transmembrane transporter activity
2.90E-03	2	5	L-lysine transmembrane transporter activity
2.90E-03	3	28	GeneSetDB:MATADOR melphalan
2.90E-03	2	5	DrugBank:CHEBI:18019
3.90E-03	2	6	Ornithine transport
3.90E-03	2	6	L-lysine transport
3.90E-03	2	6	L-ornithine transmembrane transport
3.90E-03	2	6	L-lysine transmembrane transport
3.90E-03	2	6	Arginine transmembrane transport

3.90E-03	2	6	Carbonyl reductase (NADPH) activity
3.90E-03	2	6	Arginine transmembrane transporter activity
4.90E-03	4	90	Wiki:GPCRs, Other
5.00E-03	2	7	Recon X:CHEBI
5.00E-03	2	7	Recon X:CHEBI
5.00E-03	2	7	Recon X:CHEBI
5.00E-03	2	7	Recon X:CHEBI
5.00E-03	2	7	L-arginine transport
5.00E-03	2	7	CTD:CHEBI
5.60E-03	3	38	DrugBank:CHEBI:16856
5.90E-03	8	530	MSigDB:chr19p13
6.30E-03	2	8	Recon X:CHEBI
6.30E-03	2	8	Recon X:CHEBI
7.70E-03	2	9	Recon X:CHEBI
7.70E-03	2	9	Arginine transport
7.70E-03	2	9	Basic amino acid transmembrane transport
9.10E-03	4	111	Long-chain fatty acid metabolic process
9.20E-03	2	10	Recon X:CHEBI
9.20E-03	2	10	Recon X:CHEBI
9.20E-03	2	10	Recon X:CHEBI
1.10E-02	2	11	Recon X:CHEBI
1.10E-02	2	11	GeneSetDB:MATADOR acipimox
1.10E-02	2	11	GeneSetDB:MATADOR pantethine
1.30E-02	3	53	Glutathione metabolic process
1.30E-02	2	12	Basic amino acid transmembrane transporter activity
1.30E-02	2	12	CTD:CHEBI
1.30E-02	3	54	Glutathione metabolism
1.30E-02	5	222	Reactome:R-HSA-211859 Biological oxidations
1.30E-02	3	55	MiRTarBase:hsa-miR-5011-3p
1.40E-02	2	13	CTD:CHEBI
1.50E-02	2	15	IntAct:MPDZ
1.50E-02	2	15	Recon X:BTD
1.50E-02	2	17	Recon X:CHEBI
1.50E-02	2	15	Recon X:CHEBI
1.50E-02	2	14	Recon X:CHEBI
1.50E-02	2	16	Recon X:CHEBI
1.50E-02	2	17	Recon X:TPSAB1
1.50E-02	2	17	Recon X:TPSB2
1.50E-02	2	17	Recon X:TPSD1
1.50E-02	3	59	Reactome:R-HSA-2142753 Arachidonic acid metabolism
1.50E-02	2	15	Reactome:R-HSA-211935 Fatty acids
1.50E-02	4	143	Wiki:NRF2 pathway
1.50E-02	6	382	Sulfur compound metabolic process

1.50E-02	2	14	Basic amino acid transport
1.50E-02	2	18	Acyl-CoA hydrolase activity
1.50E-02	3	62	Arachidonic acid metabolism
1.50E-02	4	138	GeneSetDB:EHMN Tyrosine metabolism
1.50E-02	2	18	GeneSetDB:EHMN Vitamin E metabolism
1.50E-02	2	17	GeneSetDB:MATADOR 19-nortestosterone
1.50E-02	4	140	GeneSetDB:MATADOR clofibrate
1.50E-02	2	18	GeneSetDB:MATADOR doxazosin
1.50E-02	2	15	GeneSetDB:MATADOR Ronicol
1.50E-02	2	16	GeneSetDB:MATADOR Triton WR-1339
1.50E-02	2	18	GeneSetDB:STITCH C14865(CID011954073)
1.50E-02	2	18	GeneSetDB:STITCH C14865(CID111954073)
1.50E-02	2	18	GeneSetDB:T3DB Antimony
1.50E-02	2	18	GeneSetDB:T3DB Antimony(III) ethoxide
1.50E-02	2	18	GeneSetDB:T3DB Antimony(III) isopropoxide
1.50E-02	2	18	GeneSetDB:T3DB Antimony acetate
1.50E-02	2	18	GeneSetDB:T3DB Antimony monosulfide
1.50E-02	2	18	GeneSetDB:T3DB Antimony pentachloride
1.50E-02	2	18	GeneSetDB:T3DB Antimony pentasulfide
1.50E-02	2	18	GeneSetDB:T3DB Antimony pentoxide
1.50E-02	2	18	GeneSetDB:T3DB Antimony tetramer
1.50E-02	2	18	GeneSetDB:T3DB Antimony tribromide
1.50E-02	2	18	GeneSetDB:T3DB Antimony trichloride
1.50E-02	2	18	GeneSetDB:T3DB Antimony trioxide
1.50E-02	2	18	GeneSetDB:T3DB Antimony triselenide
1.50E-02	2	18	GeneSetDB:T3DB Antimony trisulfide
1.50E-02	2	18	GeneSetDB:T3DB Chlorofluorotrimethylantimony
1.50E-02	2	18	GeneSetDB:T3DB Chlorohydroxytriphenylantimony
1.50E-02	2	18	GeneSetDB:T3DB Diantimony diselenide
1.50E-02	2	18	GeneSetDB:T3DB Diantimony tetrasulfide
1.50E-02	2	18	GeneSetDB:T3DB Dibromotributylantimony
1.50E-02	2	18	GeneSetDB:T3DB Dichlorotribenzylantimony
1.50E-02	2	18	GeneSetDB:T3DB Dioxygenyl hexafluoroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Diphenyl(o-tolyl)antimony
1.50E-02	2	18	GeneSetDB:T3DB Hexafluoroantimonic acid
1.50E-02	2	18	GeneSetDB:T3DB Lithium hexafluoroantimonate(V)
1.50E-02	2	18	GeneSetDB:T3DB Magic acid (fluorosulfuric acid-antimony pentafluoride)
1.50E-02	2	18	GeneSetDB:T3DB Nitronium hexafluoroantimonate(V)
1.50E-02	2	18	GeneSetDB:T3DB Nitrosonium (nitrosyl) hexafluoroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Potassium antimonyl tartrate trihydrate
1.50E-02	2	18	GeneSetDB:T3DB Potassium hexafluoroantimonate(V)
1.50E-02	2	18	GeneSetDB:T3DB Potassium hexahydroxoantimonate(V)

1.50E-02	2	18	GeneSetDB:T3DB Potassium pyroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Sodium hexafluoroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Sodium thioantimonate(V)
1.50E-02	2	18	GeneSetDB:T3DB Stibine
1.50E-02	2	18	GeneSetDB:T3DB Tetrabutylantimony(V) bromide
1.50E-02	2	18	GeneSetDB:T3DB Tetraphenylantimony bromide
1.50E-02	2	18	GeneSetDB:T3DB Triantimony disulfide
1.50E-02	2	18	GeneSetDB:T3DB Triethyloxonium hexachloroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Trimethylantimony bromide
1.50E-02	2	18	GeneSetDB:T3DB Trimethylantimony dichloride
1.50E-02	2	18	GeneSetDB:T3DB Trimethylantimony diiodide
1.50E-02	2	18	GeneSetDB:T3DB Trimethyloxonium hexachlorantimonate
1.50E-02	2	18	GeneSetDB:T3DB Triphenylantimony
1.50E-02	2	18	GeneSetDB:T3DB Triphenylantimony diacetate
1.50E-02	2	18	GeneSetDB:T3DB Triphenylantimony dibenzoate
1.50E-02	2	18	GeneSetDB:T3DB Triphenylantimony dichloride
1.50E-02	2	18	GeneSetDB:T3DB Triphenylcarbenium hexachloroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Triphenylthioantimonate
1.50E-02	2	18	GeneSetDB:T3DB Tris(1-naphthyl)antimony
1.50E-02	2	18	GeneSetDB:T3DB Tris(3-(trifluoromethyl)phenyl)antimony
1.50E-02	2	18	GeneSetDB:T3DB Tris(4-bromophenyl)aminium hexachloroantimonate
1.50E-02	2	18	GeneSetDB:T3DB Tris(4-bromophenyl)antimony
1.50E-02	2	18	GeneSetDB:T3DB Tris(dimethylamino)antimony
1.50E-02	2	18	GeneSetDB:T3DB Tris(o-tolyl)antimony
1.50E-02	2	18	GeneSetDB:T3DB Tris(p-tolyl)antimony
1.50E-02	2	17	ITFP:CLIC2
1.50E-02	3	63	MSigDB:LEE LIVER CANCER ACOX1 UP
1.50E-02	4	134	MSigDB:SERVITJA LIVER HNF1A TARGETS UP
1.50E-02	2	15	MSigDB:MODULE 431
1.50E-02	2	17	SMPDB:Doxorubicin Metabolism Pathway
1.50E-02	2	14	DrugBank:CHEBI:15729
1.50E-02	4	157	MSigDB:HALLMARK FATTY ACID METABOLISM
1.50E-02	2	19	Recon X:CPA1
1.50E-02	2	19	Recon X:CPA2
1.50E-02	2	19	Recon X:CPA6
1.50E-02	2	19	GeneSetDB:STITCH bromoacetaldehyde(CID000105131)
1.50E-02	2	19	GeneSetDB:STITCH bromoacetaldehyde(CID100105131)
1.50E-02	2	19	GeneSetDB:STITCH DNP-SG(CID000097535)
1.50E-02	2	19	GeneSetDB:STITCH DNP-SG(CID100097535)
1.50E-02	2	19	GeneSetDB:T3DB Zinc antimonide

1.60E-02	2	20	Recon X:CHEBI
1.60E-02	2	20	CoA hydrolase activity
1.60E-02	2	20	GeneSetDB:MATADOR ciprofibrate
1.60E-02	2	20	GeneSetDB:MATADOR glibenclamide
1.60E-02	2	20	GeneSetDB:MATADOR rosuvastatin
1.60E-02	2	20	GeneSetDB:MATADOR tibolone
1.60E-02	2	20	GeneSetDB:STITCH 1,1-dichloroethylene epoxide(CID000119521)
1.60E-02	2	20	GeneSetDB:STITCH 1,1-dichloroethylene epoxide(CID100119521)
1.60E-02	2	20	GeneSetDB:STITCH chloroacetyl chloride(CID000006577)
1.60E-02	2	20	GeneSetDB:STITCH chloroacetyl chloride(CID100006577)
1.60E-02	2	20	GeneSetDB:T3DB Aluminium antimonide
1.60E-02	2	20	GeneSetDB:T3DB Dichlorotris(4-bromophenyl)antimony
1.70E-02	3	77	MSigDB:SANA RESPONSE TO IFNG UP
1.70E-02	2	21	Recon X:ACE2
1.70E-02	2	21	GeneSetDB:STITCH 2,2-dichloroacetaldehyde(CID000006576)
1.70E-02	2	21	GeneSetDB:STITCH 2,2-dichloroacetaldehyde(CID100006576)
1.70E-02	2	21	GeneSetDB:STITCH bromobenzene-3,4-oxide(CID000108121)
1.70E-02	2	21	GeneSetDB:STITCH bromobenzene-3,4-oxide(CID100108121)
1.70E-02	2	21	GeneSetDB:STITCH bromobenzene 2,3-epoxide(CID003036760)
1.70E-02	2	21	GeneSetDB:STITCH bromobenzene 2,3-epoxide(CID103036760)
1.70E-02	2	21	GeneSetDB:T3DB Antimony potassium tartate
1.70E-02	2	21	MSigDB:YANG MUC2 TARGETS DUODENUM 6MO DN
1.80E-02	2	22	Wiki:Glutathione metabolism
1.80E-02	2	22	Amino acid import across plasma membrane
1.80E-02	3	81	Chemical carcinogenesis
1.80E-02	3	81	GeneSetDB:EHMN Tryptophan metabolism
1.80E-02	2	22	GeneSetDB:STITCH ethylene dibromide(CID000007839)
1.80E-02	2	22	GeneSetDB:STITCH ethylene dibromide(CID100007839)
1.80E-02	3	81	MSigDB:SANA TNF SIGNALING UP
1.80E-02	2	22	MSigDB:MODULE 310
1.80E-02	2	22	Inoh:Cystinosis, ocular nonnephropathic
1.80E-02	3	82	MSigDB:chr1q44
1.80E-02	4	175	Wiki:Metapathway biotransformation Phase I and II
1.90E-02	3	83	GeneSetDB:EHMN Xenobiotics metabolism
1.90E-02	2	23	Glutathione derivative metabolic process

1.90E-02	2	23	Glutathione derivative biosynthetic process
1.90E-02	2	23	GeneSetDB:STITCH C14802(CID011954053)
1.90E-02	2	23	GeneSetDB:STITCH C14802(CID111954053)
1.90E-02	2	23	MSigDB:YANG MUC2 TARGETS DUODENUM 3MO DN
2.00E-02	2	24	Recon X:SLC16A10
2.00E-02	2	24	GeneSetDB:MATADOR gemfibrozil
2.00E-02	2	24	GeneSetDB:STITCH C14800(CID011954051)
2.00E-02	2	24	GeneSetDB:STITCH C14800(CID111954051)
2.10E-02	2	25	Recon X:CHEBI
2.10E-02	2	25	Amino acid import
2.10E-02	2	25	GeneSetDB:EHMN De novo fatty acid biosynthesis
2.10E-02	2	25	GeneSetDB:STITCH (1S,2R)-naphthalene 1,2-oxide(CID011094749)
2.10E-02	2	25	GeneSetDB:STITCH (1S,2R)-naphthalene 1,2-oxide(CID100108063)
2.10E-02	2	25	GeneSetDB:STITCH C14786(CID000155957)
2.10E-02	4	186	MSigDB:GSE1566 WT VS EZH2 KO LN TCELL DN
2.10E-02	4	185	MSigDB:GSE42021 CD24INT VS CD24LOW TCONV THYMUS UP
2.10E-02	2	25	Humancyc:Guanidinoacetate Methyltransferase Deficiency (GAMT Deficiency)
2.10E-02	4	187	MSigDB:KONDO PROSTATE CANCER WITH H3K27ME3
2.20E-02	2	26	GeneSetDB:EHMN Putative anti-Inflammatory metabolites formation from EPA
2.20E-02	4	190	MSigDB:GSE37533 PPARG2 FOXP3 VS FOXP3 TRANSDUCED CD4 TCELL DN
2.20E-02	4	190	MSigDB:GSE42021 CD24HI VS CD24LOW TCONV THYMUS DN
2.30E-02	4	191	MSigDB:GSE42021 CD24HI VS CD24INT TCONV THYMUS DN
2.30E-02	4	192	MSigDB:GSE42021 TREG VS TCONV PLN UP
2.30E-02	4	193	MSigDB:GSE37533 PPARG1 FOXP3 VS FOXP3 TRANSDUCED CD4 TCELL DN
2.30E-02	4	193	MSigDB:GSE37533 PPARG1 FOXP3 VS PPARG2 FOXP3 TRANSDUCED CD4 TCELL PIOGLITAZONE TREATED DN
2.30E-02	3	94	GeneSetDB:STITCH reduced glutathione(CID000124886)
2.30E-02	2	27	GeneSetDB:STITCH trichloroethene(CID000006575)
2.30E-02	2	27	GeneSetDB:STITCH trichloroethene(CID100006575)
2.30E-02	4	194	MSigDB:GSE42021 CD24HI VS CD24INT TREG THYMUS DN
2.50E-02	2	28	GeneSetDB:STITCH aldophosphamide(CID000107744)
2.50E-02	2	28	GeneSetDB:STITCH aldophosphamide(CID100107744)
2.50E-02	3	96	GeneSetDB:STITCH reduced glutathione(CID100000745)
2.50E-02	2	28	GeneSetDB:T3DB Silver(I) hexafluoroantimonate

2.50E-02	2	28	GeneSetDB:MPO abnormal social/conspecific interaction
2.50E-02	2	28	CTD:CHEBI
2.60E-02	3	98	GeneSetDB:EHMN Androgen and estrogen biosynthesis and metabolism
2.60E-02	2	29	Glutathione transferase activity
2.80E-02	2	30	GeneSetDB:STITCH benzo[a]pyrene 4,5-oxide(CID000037786)
2.80E-02	2	30	GeneSetDB:STITCH benzo[a]pyrene 4,5-oxide(CID100037786)
2.90E-02	2	31	Recon X:SLC43A1
3.10E-02	3	106	Reactome:R-HSA-211945 Phase I - Functionalization of compounds
3.10E-02	2	32	GeneSetDB:MATADOR estrogen
3.10E-02	3	106	CTD:KEAP1
3.30E-02	2	33	Reactome:R-HSA-352230 Amino acid transport across the plasma membrane
3.40E-02	7	671	Reactome:R-HSA-109582 Hemostasis
3.50E-02	2	34	GeneSetDB:STITCH NSC647529(CID000000745)
3.60E-02	3	112	GeneSetDB:EHMN Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine
3.60E-02	2	35	GeneSetDB:MATADOR fluvastatin
3.60E-02	2	35	GeneSetDB:MATADOR probucol
3.80E-02	2	36	GeneSetDB:STITCH 1-chloro-2,4-dinitrobenzene(CID000000006)
3.80E-02	2	36	GeneSetDB:STITCH 1-chloro-2,4-dinitrobenzene(CID100000006)
3.80E-02	2	36	MSigDB:CERIBELLI GENES INACTIVE AND BOUND BY NFY
3.80E-02	3	116	Recon X:SLC5A10
3.80E-02	3	116	Recon X:SLC5A12
3.80E-02	3	116	Recon X:SLC5A2
3.80E-02	3	116	Icosanoid metabolic process
3.90E-02	2	37	Reactome:R-HSA-156590 Glutathione conjugation
3.90E-02	2	37	Reactome:R-HSA-77289 Mitochondrial Fatty Acid Beta-Oxidation
3.90E-02	2	37	GeneSetDB:STITCH benzo[a]pyrene-7,8-dihydrodiol(CID000025892)
3.90E-02	2	37	GeneSetDB:STITCH benzo[a]pyrene-7,8-dihydrodiol(CID100025892)
3.90E-02	2	37	MSigDB:MODULE 286
4.10E-02	2	38	Oxygen binding
4.10E-02	3	120	Xenobiotic metabolic process
4.20E-02	3	122	Recon X:SLC3A1
4.20E-02	3	122	Recon X:SLC5A3
4.20E-02	3	122	MiRTarBase:hsa-miR-5694
4.50E-02	5	384	Fatty acid metabolic process

4.60E-02	3	126	Recon X:SLC27A5
4.60E-02	3	126	Recon X:SLC5A9
4.60E-02	7	722	Reactome:R-HSA-5653656 Vesicle-mediated transport
4.80E-02	2	42	Recon X:MLYCD
4.90E-02	4	251	MSigDB:chr12q13
5.00E-02	3	131	Recon X:ALDH3A1
5.00E-02	3	131	Amino acid transport

Table S7. Enrichment of genes extremely differentiated by copy number ($V_{ST} > 0.35$) between brown bear and polar bear. Enrichment analysis was conducted via ShinyGoV0.51 (http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	**Genes in list**	**Total genes**	**Functional Category**
9.30E-23	21	429	Olfactory transduction
1.30E-21	20	429	Reactome:R-HSA-381753 Olfactory Signaling Pathway
1.30E-21	21	516	Detection of chemical stimulus involved in sensory perception of smell
1.30E-21	21	516	Olfactory receptor activity
3.20E-21	21	548	Sensory perception of smell
1.20E-20	21	588	Detection of chemical stimulus involved in sensory perception
3.80E-20	21	627	Detection of chemical stimulus
5.80E-20	21	644	Detection of stimulus involved in sensory perception
5.80E-20	21	648	Sensory perception of chemical stimulus
1.50E-19	20	571	Reactome:R-HSA-418555 G alpha (s) signalling events
5.60E-18	21	816	Detection of stimulus
3.70E-16	21	1006	G protein-coupled receptor activity
2.50E-15	21	1110	Sensory perception
9.90E-14	20	1155	Reactome:R-HSA-388396 GPCR downstream signalling
1.70E-13	22	1582	Transmembrane signaling receptor activity
1.80E-13	22	1589	Nervous system process
2.10E-13	20	1215	Reactome:R-HSA-372790 Signaling by GPCR
1.40E-12	21	1546	G protein-coupled receptor signaling pathway
3.50E-12	22	1850	Signaling receptor activity
6.30E-12	22	1910	Molecular transducer activity
2.90E-11	23	2321	System process
5.60E-09	22	2690	Reactome:R-HSA-162582 Signal Transduction
3.00E-08	7	101	GeneSetDB:EHMN Leukotriene metabolism
7.20E-07	6	91	GeneSetDB:EHMN Arachidonic acid metabolism
4.30E-05	4	41	GeneSetDB:EHMN Prostaglandin formation from arachidonate
1.50E-04	2	2	Recon X:LTA4H
2.70E-04	6	254	Wiki:GPCRs, Class A Rhodopsin-like
3.60E-04	3	22	GeneSetDB:MATADOR acarbose
3.90E-04	4	73	Metabolism of xenobiotics by cytochrome P450
3.90E-04	2	3	Recon X:CHEBI
7.60E-04	2	4	Recon X:ALOX12
7.70E-04	4	89	Reactome:R-HSA-2168880 Scavenging of heme from plasma
1.50E-03	7	530	MSigDB:chr19p13
1.70E-03	5	222	Reactome:R-HSA-211859 Biological oxidations
1.70E-03	2	6	Carbonyl reductase (NADPH) activity

2.00E-03	2	7	Recon X:CHEBI
2.00E-03	2	7	Recon X:CHEBI
2.00E-03	2	7	Recon X:CHEBI
2.00E-03	2	7	Recon X:CHEBI
2.00E-03	4	118	Reactome:R-HSA-2173782 Binding and Uptake of Ligands by Scavenger Receptors
2.60E-03	2	8	Recon X:CHEBI
2.60E-03	2	8	Recon X:CHEBI
3.20E-03	2	9	Recon X:CHEBI
3.20E-03	4	138	GeneSetDB:EHMN Tyrosine metabolism
3.20E-03	4	140	GeneSetDB:MATADOR clofibrate
3.40E-03	4	143	Wiki:NRF2 pathway
3.60E-03	2	10	Recon X:CHEBI
3.60E-03	2	10	Recon X:CHEBI
3.60E-03	2	10	Recon X:CHEBI
4.10E-03	2	11	Recon X:CHEBI
4.10E-03	2	11	GeneSetDB:MATADOR acipimox
4.10E-03	2	11	GeneSetDB:MATADOR pantethine
4.20E-03	2	15	IntAct:MPDZ
4.20E-03	2	17	Recon X:CHEBI
4.20E-03	2	15	Recon X:CHEBI
4.20E-03	2	14	Recon X:CHEBI
4.20E-03	2	16	Recon X:CHEBI
4.20E-03	4	180	Reactome:R-HSA-8978868 Fatty acid metabolism
4.20E-03	2	15	Reactome:R-HSA-211935 Fatty acids
4.20E-03	2	18	Acyl-CoA hydrolase activity
4.20E-03	3	62	Arachidonic acid metabolism
4.20E-03	3	81	Chemical carcinogenesis
4.20E-03	3	81	GeneSetDB:EHMN Tryptophan metabolism
4.20E-03	2	18	GeneSetDB:EHMN Vitamin E metabolism
4.20E-03	3	83	GeneSetDB:EHMN Xenobiotics metabolism
4.20E-03	2	17	GeneSetDB:MATADOR 19-nortestosterone
4.20E-03	2	18	GeneSetDB:MATADOR doxazosin
4.20E-03	2	15	GeneSetDB:MATADOR Ronicol
4.20E-03	2	16	GeneSetDB:MATADOR Triton WR-1339
4.20E-03	2	18	GeneSetDB:STITCH C14865(CID011954073)
4.20E-03	2	18	GeneSetDB:STITCH C14865(CID111954073)
4.20E-03	2	18	GeneSetDB:T3DB Antimony
4.20E-03	2	18	GeneSetDB:T3DB Antimony(III) ethoxide
4.20E-03	2	18	GeneSetDB:T3DB Antimony(III) isopropoxide
4.20E-03	2	18	GeneSetDB:T3DB Antimony acetate
4.20E-03	2	18	GeneSetDB:T3DB Antimony monosulfide
4.20E-03	2	18	GeneSetDB:T3DB Antimony pentachloride
4.20E-03	2	18	GeneSetDB:T3DB Antimony pentasulfide

4.20E-03	2	18	GeneSetDB:T3DB Antimony pentoxide
4.20E-03	2	18	GeneSetDB:T3DB Antimony tetramer
4.20E-03	2	18	GeneSetDB:T3DB Antimony tribromide
4.20E-03	2	18	GeneSetDB:T3DB Antimony trichloride
4.20E-03	2	18	GeneSetDB:T3DB Antimony trioxide
4.20E-03	2	18	GeneSetDB:T3DB Antimony triselenide
4.20E-03	2	18	GeneSetDB:T3DB Antimony trisulfide
4.20E-03	2	18	GeneSetDB:T3DB Chlorofluorotrimethylantimony
4.20E-03	2	18	GeneSetDB:T3DB Chlorohydroxytriphenylantimony
4.20E-03	2	18	GeneSetDB:T3DB Diantimony diselenide
4.20E-03	2	18	GeneSetDB:T3DB Diantimony tetrasulfide
4.20E-03	2	18	GeneSetDB:T3DB Dibromotributylantimony
4.20E-03	2	18	GeneSetDB:T3DB Dichlorotribenzylantimony
4.20E-03	2	18	GeneSetDB:T3DB Dioxygenyl hexafluoroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Diphenyl(o-tolyl)antimony
4.20E-03	2	18	GeneSetDB:T3DB Hexafluoroantimonic acid
4.20E-03	2	18	GeneSetDB:T3DB Lithium hexafluoroantimonate(V)
4.20E-03	2	18	GeneSetDB:T3DB Magic acid (fluorosulfuric acid-antimony pentafluoride)
4.20E-03	2	18	GeneSetDB:T3DB Nitronium hexafluoroantimonate(V)
4.20E-03	2	18	GeneSetDB:T3DB Nitrosonium (nitrosyl) hexafluoroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Potassium antimonyl tartrate trihydrate
4.20E-03	2	18	GeneSetDB:T3DB Potassium hexafluoroantimonate(V)
4.20E-03	2	18	GeneSetDB:T3DB Potassium hexahydroxoantimonate(V)
4.20E-03	2	18	GeneSetDB:T3DB Potassium pyroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Sodium hexafluoroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Sodium thioantimonate(V)
4.20E-03	2	18	GeneSetDB:T3DB Stibine
4.20E-03	2	18	GeneSetDB:T3DB Tetrabutylantimony(V) bromide
4.20E-03	2	18	GeneSetDB:T3DB Tetraphenylantimony bromide
4.20E-03	2	18	GeneSetDB:T3DB Triantimony disulfide
4.20E-03	2	18	GeneSetDB:T3DB Triethyloxonium hexachloroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Trimethylantimony bromide
4.20E-03	2	18	GeneSetDB:T3DB Trimethylantimony dichloride
4.20E-03	2	18	GeneSetDB:T3DB Trimethylantimony diiodide
4.20E-03	2	18	GeneSetDB:T3DB Trimethyloxonium hexachlorantimonate
4.20E-03	2	18	GeneSetDB:T3DB Triphenylantimony
4.20E-03	2	18	GeneSetDB:T3DB Triphenylantimony diacetate
4.20E-03	2	18	GeneSetDB:T3DB Triphenylantimony dibenzoate
4.20E-03	2	18	GeneSetDB:T3DB Triphenylantimony dichloride
4.20E-03	2	18	GeneSetDB:T3DB Triphenylcarbenium hexachloroantimonate

4.20E-03	2	18	GeneSetDB:T3DB Triphenylthioantimonate
4.20E-03	2	18	GeneSetDB:T3DB Tris(1-naphthyl)antimony
4.20E-03	2	18	GeneSetDB:T3DB Tris(3-(trifluoromethyl)phenyl)antimony
4.20E-03	2	18	GeneSetDB:T3DB Tris(4-bromophenyl)aminium hexachloroantimonate
4.20E-03	2	18	GeneSetDB:T3DB Tris(4-bromophenyl)antimony
4.20E-03	2	18	GeneSetDB:T3DB Tris(dimethylamino)antimony
4.20E-03	2	18	GeneSetDB:T3DB Tris(o-tolyl)antimony
4.20E-03	2	18	GeneSetDB:T3DB Tris(p-tolyl)antimony
4.20E-03	3	77	MSigDB:SANA RESPONSE TO IFNG UP
4.20E-03	3	81	MSigDB:SANA TNF SIGNALING UP
4.20E-03	2	15	MSigDB:MODULE 431
4.20E-03	4	193	MSigDB:GSE37533 PPARG1 FOXP3 VS FOXP3 TRANSDUCED CD4 TCELL DN
4.20E-03	4	190	MSigDB:GSE37533 PPARG2 FOXP3 VS FOXP3 TRANSDUCED CD4 TCELL DN
4.20E-03	4	193	MSigDB:GSE37533 PPARG1 FOXP3 VS PPARG2 FOXP3 TRANSDUCED CD4 TCELL PIOGLITAZONE TREATED DN
4.20E-03	4	192	MSigDB:GSE42021 TREG VS TCONV PLN UP
4.20E-03	4	194	MSigDB:GSE42021 CD24HI VS CD24INT TREG THYMUS DN
4.20E-03	4	191	MSigDB:GSE42021 CD24HI VS CD24INT TCONV THYMUS DN
4.20E-03	4	190	MSigDB:GSE42021 CD24HI VS CD24LOW TCONV THYMUS DN
4.20E-03	4	157	MSigDB:HALLMARK FATTY ACID METABOLISM
4.20E-03	2	17	SMPDB:Doxorubicin Metabolism Pathway
4.20E-03	2	13	CTD:CHEBI
4.20E-03	2	12	CTD:CHEBI
4.20E-03	3	85	Reactome:R-HSA-173623 Classical antibody-mediated complement activation
4.50E-03	2	19	GeneSetDB:STITCH bromoacetaldehyde(CID000105131)
4.50E-03	2	19	GeneSetDB:STITCH bromoacetaldehyde(CID100105131)
4.50E-03	2	19	GeneSetDB:STITCH DNP-SG(CID000097535)
4.50E-03	2	19	GeneSetDB:STITCH DNP-SG(CID100097535)
4.50E-03	2	19	GeneSetDB:T3DB Zinc antimonide
4.50E-03	2	20	Recon X:CHEBI
4.50E-03	4	211	Recon X:SLC7A9
4.50E-03	3	91	Reactome:R-HSA-2029481 FCGR activation
4.50E-03	3	89	Reactome:R-HSA-2730905 Role of LAT2/NTAL/LAB on calcium mobilization
4.50E-03	3	90	Wiki:GPCRs, Other
4.50E-03	2	20	CoA hydrolase activity
4.50E-03	2	20	GeneSetDB:MATADOR ciprofibrate

4.50E-03	2	20	GeneSetDB:MATADOR glibenclamide
4.50E-03	2	20	GeneSetDB:MATADOR rosuvastatin
4.50E-03	2	20	GeneSetDB:MATADOR tibolone
4.50E-03	2	20	GeneSetDB:STITCH 1,1-dichloroethylene epoxide(CID000119521)
4.50E-03	2	20	GeneSetDB:STITCH 1,1-dichloroethylene epoxide(CID100119521)
4.50E-03	2	20	GeneSetDB:STITCH chloroacetyl chloride(CID000006577)
4.50E-03	2	20	GeneSetDB:STITCH chloroacetyl chloride(CID100006577)
4.50E-03	2	20	GeneSetDB:T3DB Aluminium antimonide
4.50E-03	2	20	GeneSetDB:T3DB Dichlorotris(4-bromophenyl)antimony
4.50E-03	5	382	Sulfur compound metabolic process
4.60E-03	3	93	Reactome:R-HSA-166786 Creation of C4 and C2 activators
4.60E-03	2	21	GeneSetDB:STITCH 2,2-dichloroacetaldehyde(CID000006576)
4.60E-03	2	21	GeneSetDB:STITCH 2,2-dichloroacetaldehyde(CID100006576)
4.60E-03	2	21	GeneSetDB:STITCH bromobenzene-3,4-oxide(CID000108121)
4.60E-03	2	21	GeneSetDB:STITCH bromobenzene-3,4-oxide(CID100108121)
4.60E-03	2	21	GeneSetDB:STITCH bromobenzene 2,3-epoxide(CID003036760)
4.60E-03	2	21	GeneSetDB:STITCH bromobenzene 2,3-epoxide(CID103036760)
4.60E-03	3	94	GeneSetDB:STITCH reduced glutathione(CID000124886)
4.60E-03	2	21	GeneSetDB:T3DB Antimony potassium tartate
4.60E-03	2	21	MSigDB:YANG MUC2 TARGETS DUODENUM 6MO DN
4.90E-03	3	96	GeneSetDB:STITCH reduced glutathione(CID100000745)
5.00E-03	2	22	GeneSetDB:STITCH ethylene dibromide(CID000007839)
5.00E-03	2	22	GeneSetDB:STITCH ethylene dibromide(CID100007839)
5.00E-03	2	22	MSigDB:MODULE 310
5.00E-03	2	22	Inoh:Cystinosis, ocular nonnephropathic
5.10E-03	3	98	GeneSetDB:EHMN Androgen and estrogen biosynthesis and metabolism
5.20E-03	3	100	Reactome:R-HSA-166663 Initial triggering of complement
5.20E-03	2	23	Glutathione derivative metabolic process
5.20E-03	2	23	Glutathione derivative biosynthetic process
5.20E-03	2	23	GeneSetDB:STITCH C14802(CID011954053)
5.20E-03	2	23	GeneSetDB:STITCH C14802(CID111954053)
5.20E-03	2	23	MSigDB:YANG MUC2 TARGETS DUODENUM 3MO DN
5.60E-03	2	24	GeneSetDB:MATADOR gemfibrozil

5.60E-03	2	24	GeneSetDB:STITCH C14800(CID011954051)
5.60E-03	2	24	GeneSetDB:STITCH C14800(CID111954051)
5.70E-03	3	104	Reactome:R-HSA-2871809 FCERI mediated Ca+2 mobilization
5.70E-03	3	104	Reactome:R-HSA-2029485 Role of phospholipids in phagocytosis
5.70E-03	2	25	Recon X:CHEBI
5.70E-03	3	105	Reactome:R-HSA-2871796 FCERI mediated MAPK activation
5.70E-03	3	106	Reactome:R-HSA-211945 Phase I - Functionalization of compounds
5.70E-03	2	25	GeneSetDB:EHMN De novo fatty acid biosynthesis
5.70E-03	2	25	GeneSetDB:STITCH (1S,2R)-naphthalene 1,2-oxide(CID011094749)
5.70E-03	2	25	GeneSetDB:STITCH (1S,2R)-naphthalene 1,2-oxide(CID100108063)
5.70E-03	2	25	GeneSetDB:STITCH C14786(CID000155957)
5.70E-03	2	25	Humancyc:Guanidinoacetate Methyltransferase Deficiency (GAMT Deficiency)
5.70E-03	3	106	CTD:KEAP1
6.20E-03	2	26	GeneSetDB:EHMN Putative anti-Inflammatory metabolites formation from EPA
6.50E-03	3	111	Long-chain fatty acid metabolic process
6.60E-03	2	27	GeneSetDB:STITCH trichloroethene(CID000006575)
6.60E-03	2	27	GeneSetDB:STITCH trichloroethene(CID100006575)
6.90E-03	2	28	GeneSetDB:STITCH aldophosphamide(CID000107744)
6.90E-03	2	28	GeneSetDB:STITCH aldophosphamide(CID100107744)
6.90E-03	2	28	GeneSetDB:T3DB Silver(I) hexafluoroantimonate
6.90E-03	2	28	CTD:CHEBI
7.40E-03	2	29	Glutathione transferase activity
7.80E-03	3	120	Xenobiotic metabolic process
7.80E-03	2	30	GeneSetDB:STITCH benzo[a]pyrene 4,5-oxide(CID000037786)
7.80E-03	2	30	GeneSetDB:STITCH benzo[a]pyrene 4,5-oxide(CID100037786)
8.50E-03	3	124	Reactome:R-HSA-977606 Regulation of Complement cascade
8.80E-03	2	32	GeneSetDB:MATADOR estrogen
9.30E-03	4	281	MiRDB:hsa-miR-3668
9.80E-03	3	131	Recon X:ALDH3A1
9.80E-03	2	34	GeneSetDB:STITCH NSC647529(CID000000745)
9.80E-03	3	132	Lipoprotein metabolic process
9.80E-03	3	132	CTD:NFE2L2
1.00E-02	2	35	GeneSetDB:MATADOR fluvastatin
1.00E-02	2	35	GeneSetDB:MATADOR probucol
1.00E-02	3	134	MSigDB:SERVITJA LIVER HNF1A TARGETS UP

1.00E-02	3	135	Reactome:R-HSA-166658 Complement cascade
1.10E-02	2	36	GeneSetDB:STITCH 1-chloro-2,4-dinitrobenzene(CID000000006)
1.10E-02	2	36	GeneSetDB:STITCH 1-chloro-2,4-dinitrobenzene(CID100000006)
1.10E-02	2	36	MSigDB:CERIBELLI GENES INACTIVE AND BOUND BY NFY
1.10E-02	2	37	Reactome:R-HSA-156590 Glutathione conjugation
1.10E-02	2	37	GeneSetDB:STITCH benzo[a]pyrene-7,8-dihydrodiol(CID000025892)
1.10E-02	2	37	GeneSetDB:STITCH benzo[a]pyrene-7,8-dihydrodiol(CID100025892)
1.10E-02	2	37	MSigDB:MODULE 286
1.10E-02	3	140	Reactome:R-HSA-2029482 Regulation of actin dynamics for phagocytic cup formation
1.10E-02	3	140	Oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor
1.10E-02	2	38	Oxygen binding
1.10E-02	2	38	DrugBank:CHEBI:16856
1.30E-02	4	316	Wiki:Nuclear Receptors Meta-Pathway
1.30E-02	3	151	Oxidoreductase activity, acting on CH-OH group of donors
1.40E-02	2	42	Recon X:MLYCD
1.40E-02	3	154	Reactome:R-HSA-2871837 FCERI mediated NF-kB activation
1.40E-02	3	154	Heme binding
1.50E-02	5	543	Cofactor binding
1.60E-02	2	47	Thiolester hydrolase activity
1.60E-02	3	164	Tetrapyrrole binding
1.60E-02	2	47	GeneSetDB:EHMN Bile acid biosynthesis
1.60E-02	2	47	GeneSetDB:MATADOR desogestrel
1.60E-02	2	47	GeneSetDB:MATADOR pioglitazone
1.60E-02	3	165	Reactome:R-HSA-2029480 Fcgamma receptor (FCGR) dependent phagocytosis
1.70E-02	2	48	GeneSetDB:MATADOR aminoglutethimide
1.70E-02	2	48	GeneSetDB:MATADOR chloral hydrate
1.70E-02	2	48	GeneSetDB:MATADOR diosmetin
1.70E-02	2	48	GeneSetDB:MATADOR ethylmorphine
1.70E-02	2	48	GeneSetDB:MATADOR hexobarbital
1.70E-02	2	48	GeneSetDB:MATADOR streptozotocin
1.70E-02	2	48	GeneSetDB:MATADOR tienilic acid
1.70E-02	2	49	GeneSetDB:MATADOR 8-methoxypsoralen
1.70E-02	2	49	GeneSetDB:MATADOR carteolol
1.70E-02	2	49	GeneSetDB:MATADOR lansoprazole
1.70E-02	2	49	GeneSetDB:MATADOR metyrapone
1.70E-02	2	49	GeneSetDB:MATADOR trimipramine
1.70E-02	2	49	GeneSetDB:STITCH an aldehyde(CID000000712)

1.80E-02	2	50	GeneSetDB:MATADOR diclofenac
1.80E-02	2	51	GeneSetDB:MATADOR tolbutamide
1.80E-02	2	51	GeneSetDB:MATADOR toremifene
1.80E-02	2	51	MSigDB:KRIEG HYPOXIA VIA KDM3A
1.80E-02	3	175	Wiki:Metapathway biotransformation Phase I and II
1.90E-02	5	589	Cofactor metabolic process
1.90E-02	3	178	Cellular response to xenobiotic stimulus
1.90E-02	2	53	Glutathione metabolic process
1.90E-02	2	53	Arachidonic acid metabolic process
2.00E-02	2	54	Glutathione metabolism
2.00E-02	2	54	GeneSetDB:MATADOR propoxyphene
2.00E-02	2	55	Peroxisomal matrix
2.00E-02	2	55	Microbody lumen
2.00E-02	3	185	MSigDB:GSE42021 CD24INT VS CD24LOW TCONV THYMUS UP
2.10E-02	2	56	Recon X:SLCO1A2
2.10E-02	3	186	MSigDB:GSE17721 LPS VS POLYIC 6H BMDC UP
2.10E-02	3	186	MSigDB:GSE21379 WT VS SAP KO TFH CD4 TCELL UP
2.10E-02	3	188	MSigDB:GSE1460 CD4 THYMOCYTE VS NAIVE CD4 TCELL ADULT BLOOD DN
2.10E-02	2	57	Recon X:ABCD1
2.10E-02	2	57	GeneSetDB:MATADOR lovastatin
2.10E-02	3	190	MSigDB:GSE1432 1H VS 24H IFNG MICROGLIA DN
2.10E-02	3	190	MSigDB:GSE23925 LIGHT ZONE VS DARK ZONE BCELL UP
2.10E-02	2	58	GeneSetDB:MATADOR alprazolam
2.10E-02	3	191	MSigDB:GSE10325 BCELL VS LUPUS BCELL DN
2.10E-02	3	191	MSigDB:GSE24634 IL4 VS CTRL TREATED NAIVE CD4 TCELL DAY3 DN
2.10E-02	2	59	Reactome:R-HSA-2142753 Arachidonic acid metabolism
2.10E-02	4	384	Fatty acid metabolic process
2.10E-02	2	59	MSigDB:LEE LIVER CANCER MYC TGFA UP
2.10E-02	3	193	MSigDB:GSE1432 CTRL VS IFNG 6H MICROGLIA DN
2.10E-02	3	193	MSigDB:GSE1432 CTRL VS IFNG 24H MICROGLIA DN
2.10E-02	3	192	MSigDB:GSE1432 1H VS 6H IFNG MICROGLIA DN
2.10E-02	3	193	MSigDB:GSE17721 0.5H VS 24H CPG BMDC DN
2.10E-02	3	192	MSigDB:GSE24634 IL4 VS CTRL TREATED NAIVE CD4 TCELL DAY5 DN
2.10E-02	3	192	MSigDB:GSE42021 TCONV PLN VS CD24HI TCONV THYMUS UP
2.20E-02	3	194	MSigDB:GSE41978 ID2 KO VS BIM KO KLRG1 LOW EFFECTOR CD8 TCELL UP
2.20E-02	3	195	MSigDB:GSE18281 SUBCAPSULAR CORTICAL REGION VS WHOLE CORTEX THYMUS UP

2.20E-02	3	195	MSigDB:GSE42021 TREG PLN VS CD24INT TREG THYMUS DN
2.20E-02	2	60	GeneSetDB:MATADOR aminopyrine
2.20E-02	2	61	Wiki:Oxidation by Cytochrome P450
2.20E-02	2	61	MSigDB:VANHARANTA UTERINE FIBROID DN
2.30E-02	2	62	GeneSetDB:MATADOR bezafibrate
2.40E-02	2	63	Intercellular bridge
2.40E-02	2	63	MSigDB:LEE LIVER CANCER ACOX1 UP
2.50E-02	2	65	Reactome:R-HSA-211897 Cytochrome P450 - arranged by substrate type
2.50E-02	3	207	Reactome:R-HSA-2454202 Fc epsilon receptor (FCERI) signaling
2.50E-02	3	206	Reactome:R-HSA-198933 Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell
2.50E-02	2	65	Transferase activity, transferring alkyl or aryl (other than methyl) groups
2.50E-02	2	65	GeneSetDB:MATADOR rosiglitazone
2.50E-02	3	207	MSigDB:ACEVEDO LIVER CANCER WITH H3K27ME3 DN
2.60E-02	4	413	RegNetwork:FOXA2
2.60E-02	2	67	MiRTarBase:hsa-miR-499a-3p
2.60E-02	3	212	GeneSetDB:STITCH NADP(CID100000929)
2.60E-02	3	213	Reactome:R-HSA-202733 Cell surface interactions at the vascular wall
2.70E-02	2	69	Drug metabolism
2.90E-02	2	73	Platinum drug resistance
2.90E-02	2	73	GeneSetDB:STITCH methanol(CID000000887)
2.90E-02	3	224	GeneSetDB:STITCH NADP(CID000005885)
2.90E-02	2	73	MSigDB:DACOSTA UV RESPONSE VIA ERCC3 COMMON UP
2.90E-02	2	73	CTD:ABCB5
2.90E-02	2	73	CTD:CHEBI
2.90E-02	2	73	CTD:CIAPIN1
2.90E-02	2	73	CTD:RALBP1
2.90E-02	2	73	CTD:RUNX3
2.90E-02	2	73	CTD:ZNRD1
3.00E-02	2	74	CTD:PPP1R1B
3.20E-02	2	76	CTD:SLC22A16
3.30E-02	2	78	Drug metabolism
3.50E-02	2	80	GeneSetDB:MATADOR desferrioxamine
3.50E-02	2	81	GeneSetDB:MATADOR felodipine
3.60E-02	6	1025	CTD:CHEBI
3.90E-02	3	251	MSigDB:chr12q13
3.90E-02	2	86	MSigDB:KIM BIPOLAR DISORDER OLIGODENDROCYTE DENSITY CORR DN
4.10E-02	2	88	Recon X:SLC25A16

4.10E-02	6	1053	Carboxylic acid metabolic process
4.20E-02	2	89	GeneSetDB:MATADOR halothane
4.20E-02	2	89	GeneSetDB:MATADOR paraoxon
4.20E-02	3	260	MSigDB:chr22q11
4.20E-02	2	90	Modified amino acid binding
4.30E-02	4	492	CTD:ABCC1
4.60E-02	9	2142	Small molecule metabolic process
4.80E-02	2	97	GeneSetDB:MATADOR nifedipine

Table S8. Enrichment of genes differentiated by copy number ($V_{ST} > 0.21$) between brown bear and polar bear using the black bear as a reference genome. Enrichment analysis was conducted via ShinyGoV0.51 (Ge and Jung, 2018; http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	Genes in list	Total genes	Functional Category
1.40E-12	34	573	Olfactory receptor activity
1.40E-12	32	500	Olfactory transduction
1.40E-12	34	573	Detection of chemical stimulus involved in sensory perception of smell
2.30E-12	35	625	Detection of chemical stimulus
2.50E-12	34	594	Sensory perception of smell
3.00E-12	34	605	Detection of chemical stimulus involved in sensory perception
3.00E-12	37	717	Detection of stimulus
1.60E-11	34	645	Sensory perception of chemical stimulus
1.60E-11	34	646	Detection of stimulus involved in sensory perception
2.20E-09	37	908	Sensory perception
5.20E-08	35	922	G protein-coupled receptor activity
8.90E-08	41	1245	Nervous system process
1.10E-06	39	1251	Transmembrane signaling receptor activity
4.10E-06	37	1210	G protein-coupled receptor signaling pathway
6.60E-06	40	1402	Signaling receptor activity
1.30E-05	40	1443	Molecular transducer activity
1.20E-04	42	1695	System process
2.40E-03	6	52	Chemical carcinogenesis
3.50E-03	6	56	Arachidonic acid metabolism
4.00E-03	3	7	Astrocyte activation
9.10E-03	2	2	Positive regulation of amyloid fibril formation
9.10E-03	2	2	Astrocyte activation involved in immune response
9.10E-03	2	2	Smooth endoplasmic reticulum calcium ion homeostasis
9.90E-03	60	3344	Response to chemical
1.20E-02	5	47	Retinol metabolism
1.20E-02	6	74	PPAR signaling pathway
1.30E-02	5	48	Metabolism of xenobiotics by cytochrome P450
2.20E-02	3	13	Glial cell activation
2.30E-02	7	118	Heme binding
2.60E-02	6	87	Monooxygenase activity
2.90E-02	7	124	Tetrapyrrole binding
3.00E-02	3	15	Acyl-CoA hydrolase activity
3.60E-02	2	4	Neuron projection maintenance
3.60E-02	2	4	Alpha-beta T cell receptor complex
4.10E-02	3	17	CoA hydrolase activity

4.40E-02	4	39	Fatty acid degradation
4.60E-02	5	68	Cell fate specification
4.60E-02	3	18	Neuroinflammatory response

Table S9. Enrichment of genes extremely differentiated by copy number ($V_{ST} > 0.35$) between brown bear and polar bear using the black bear as a reference genome. Enrichment analysis was conducted via ShinyGoV0.51 (Ge and Jung, 2018; http://bioinformatics.sdstate.edu/go/).

Enrichment FDR	Genes in list	Total genes	Functional Category
2.00E-13	22	573	Olfactory receptor activity
2.00E-13	22	573	Detection of chemical stimulus involved in sensory perception of smell
2.80E-13	22	594	Sensory perception of smell
3.00E-13	22	605	Detection of chemical stimulus involved in sensory perception
4.70E-13	22	625	Detection of chemical stimulus
5.80E-13	20	500	Olfactory transduction
5.80E-13	22	645	Sensory perception of chemical stimulus
5.80E-13	22	646	Detection of stimulus involved in sensory perception
4.30E-12	22	717	Detection of stimulus
4.20E-10	22	908	Sensory perception
5.20E-10	22	922	G protein-coupled receptor activity
6.40E-10	25	1251	Transmembrane signaling receptor activity
1.10E-09	26	1402	Signaling receptor activity
1.90E-09	26	1443	Molecular transducer activity
1.10E-08	23	1210	G protein-coupled receptor signaling pathway
1.80E-08	23	1245	Nervous system process
5.50E-06	23	1695	System process
1.40E-05	7	118	Heme binding
1.80E-05	7	124	Tetrapyrrole binding
3.50E-05	6	87	Monooxygenase activity
5.00E-05	7	146	Oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen
6.80E-05	7	155	Iron ion binding
6.80E-05	5	56	Arachidonic acid metabolism
3.60E-04	4	39	Fatty acid degradation
5.20E-04	3	15	Acyl-CoA hydrolase activity
7.00E-04	4	47	Retinol metabolism
7.10E-04	3	17	CoA hydrolase activity
9.80E-04	4	52	Chemical carcinogenesis
1.50E-03	2	4	Alpha-beta T cell receptor complex
1.50E-03	28	3344	Response to chemical
2.10E-03	3	25	Biosynthesis of unsaturated fatty acids
3.40E-03	4	74	PPAR signaling pathway
3.70E-03	3	31	Thiolester hydrolase activity
4.10E-03	29	3756	Plasma membrane

4.80E-03	6	231	Fatty acid metabolic process
6.70E-03	29	3876	Cell periphery
7.40E-03	3	41	Xenobiotic metabolic process
7.40E-03	4	95	Inflammatory mediator regulation of TRP channels
9.60E-03	2	11	Arachidonic acid monooxygenase activity
9.60E-03	2	11	Arachidonic acid epoxygenase activity
9.60E-03	2	11	Epoxygenase P450 pathway
1.10E-02	3	48	Metabolism of xenobiotics by cytochrome P450
1.10E-02	2	12	T cell receptor complex
1.10E-02	11	894	Transition metal ion binding
1.20E-02	3	51	Long-chain fatty acid metabolic process
1.20E-02	2	13	Positive thymic T cell selection
1.60E-02	5	209	Sulfur compound metabolic process
1.70E-02	3	59	Acyl-CoA metabolic process
1.70E-02	3	59	Thioester metabolic process
2.10E-02	3	65	Cellular response to xenobiotic stimulus
2.10E-02	7	448	Cofactor binding
2.30E-02	2	19	Exogenous drug catabolic process
2.50E-02	2	20	Proton-transporting two-sector ATPase complex, catalytic domain
2.60E-02	9	735	Oxidoreductase activity
2.80E-02	2	22	Arachidonic acid metabolic process
2.80E-02	3	76	Nucleoside bisphosphate metabolic process
2.80E-02	3	76	Ribonucleoside bisphosphate metabolic process
2.80E-02	3	76	Purine nucleoside bisphosphate metabolic process
2.80E-02	2	22	Thymic T cell selection
2.90E-02	2	23	Proton-transporting ATPase activity, rotational mechanism
3.10E-02	2	24	Oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen
3.50E-02	2	26	Fatty acid elongation
3.50E-02	2	26	Very long-chain fatty acid metabolic process
3.70E-02	2	27	Steroid hydroxylase activity
3.70E-02	2	27	Positive T cell selection
4.10E-02	6	399	Monocarboxylic acid metabolic process
4.10E-02	2	29	Glutathione transferase activity
4.90E-02	2	32	Proton-exporting ATPase activity
4.90E-02	2	32	Primary immunodeficiency

Additional dataset S1 (separate file).
Estimates of gene copy number and differentiation between brown bear and polar bear.

Additional dataset S2 (separate file).
Genes differentiated by copy number ($V_{ST} > 0.22$) between brown bear and polar bear.