ADDITIONAL FILE 3: Supplemental Tables S1-S6

Sex-specific chromatin landscapes in an ultra-compact chordate genome

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Supplemental Table S1. Antibodies for histone PTM ChIP-chip profiles.

Histone PTM	Antibody (Catalog #)	Supplier	Replicates (ovary/testis)
H3K18ac	ab1191	Abcam	2/2
H3K27ac	ab4729	Abcam	2/2
H3K27me1	07-448	Millipore	2/2
H3K27me3	ab6002	Abcam	3/4
H3K36me1	ab9048	Abcam	2/2
H3K36me2	ab9049	Abcam	2/2
H3K36me3	ab9050	Abcam	2/2
H3K4me1	ab8895	Abcam	3/3
H3K4me2	ab32356	Abcam	1/1
H3K4me3	04-745	Millipore	2/2
H3K79me1	ab2886	Abcam	2/2
H3K79me3	ab2621	Abcam	1/2
H3K9me1	ab89906	Abcam	3/2
H3K9me2	ab1220	Abcam	1/1
H3K9me3	ab8898	Abcam	3/2
H3S28P	ab10543	Abcam	2/2
H4ac	06-866	Millipore	2/3
H4K20me1	ab9051	Abcam	2/2
H4K20me3	ab9053	Abcam	2/2
RNAP-S5P	ab5131	Abcam	2/2
RNA polII-S2P	ab5095	Abcam	2/2
RNA polII-CTD	ab5408	Abcam	2/2

Supplemental Table S2. *O. dioica* epigenome 15-state model: tissue-specific proportional genome coverage and ChromHMM emission parameters.

State	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Percent of Genome Coverage															
ovary	7.72	53.87	8.63	11.56	4.18	2.27	0.60	0.27	2.65	1.73	0.02	0.09	1.56	2.97	1.89
testis	0.21	39.20	0.001	0.004	0.02	2.71	9.46	6.02	3.66	7.05	15.48	3.70	4.49	4.40	3.60
ChromHMM emission parameters															
H4ac	0.02874	0.00014	0.99622	0.00000	0.85336	0.20385	0.12141	0.10498	0.08668	0.03729	0.05881	0.13679	0.15455	0.00127	0.98501
H3K27me1	0.00203	0.00000	0.15003	0.06210	0.32737	0.00856	0.00803	0.03409	0.00130	0.00422	0.00052	0.00162	0.27154	0.01366	0.00544
H3K9me1	0.01652	0.00002	0.01506	0.00469	0.08008	0.00317	0.00086	0.00050	0.00569	0.00075	0.00000	0.00041	0.12164	0.01324	0.00424
H4K20me1	0.05953	0.00000	0.13040	0.17588	0.43914	0.09901	0.05421	0.12308	0.01543	0.03319	0.10109	0.14777	0.75603	0.14404	0.05316
H3K79me1	0.03858	0.00015	0.11940	0.11954	0.44294	0.05513	0.04544	0.15427	0.03476	0.08522	0.09003	0.14291	0.77207	0.19383	0.04052
H3K4me1	0.06857	0.00000	0.00824	0.00679	0.13682	0.08830	0.03736	0.24006	0.02849	0.00529	0.00163	0.04197	0.39525	0.05593	0.04816
H3K4me3	0.00112	0.00000	0.00004	0.00040	0.46693	0.00592	0.04842	0.69469	0.09454	0.03784	0.27418	0.22559	0.61287	0.07032	0.01463
H3K27ac	0.00195	0.00007	0.10141	0.00359	0.75396	0.34768	0.76481	0.91800	0.08383	0.02408	0.05126	0.04389	0.32639	0.00793	0.03026
H3K18ac	0.10839	0.00015	0.06958	0.01147	0.23334	0.15921	0.43503	0.84657	0.06474	0.01945	0.00497	0.00382	0.03536	0.00207	0.03774
H3K36me1	0.09032	0.00000	0.10821	0.08830	0.23093	0.20907	0.23136	0.49625	0.02650	0.04601	0.01888	0.02128	0.04237	0.10781	0.10679
H3K4me2	0.06262	0.00000	0.05230	0.07310	0.79428	0.08187	0.00026	0.92972	0.98011	0.00080	0.05081	0.01317	0.22261	0.00010	0.00070
H3S28P	0.00440	0.00000	0.00456	0.00188	0.01976	0.05047	0.01238	0.03706	0.05285	0.01213	0.00593	0.01111	0.08933	0.06477	0.01774
H3K27me3	0.00467	0.00000	0.00000	0.00005	0.00356	0.04557	0.02332	0.05004	0.03181	0.00844	0.03519	0.12120	0.48949	0.10091	0.07685
H4K20me3	0.17678	0.00000	0.00621	0.00288	0.04232	0.01142	0.00526	0.04921	0.01817	0.01639	0.17589	0.25002	0.82354	0.18118	0.04983
H3K9me3	0.00091	0.00011	0.00002	0.00000	0.00037	0.00987	0.01220	0.16998	0.03752	0.00246	0.99858	0.99003	0.77199	0.00196	0.00229
H3K9me2	0.35351	0.00000	0.05519	0.10156	0.29271	0.10333	0.11062	0.30140	0.26702	0.97634	0.99922	0.00070	0.89409	0.00350	0.02645
H3K79me3	0.86131	0.00023	0.22364	0.18398	0.45619	0.01153	0.01137	0.03320	0.05495	0.00549	0.03915	0.06019	0.69212	0.01659	0.08266
H3K36me3	0.41873	0.00041	0.99500	0.98616	0.81073	0.00741	0.00605	0.01500	0.02142	0.00542	0.03557	0.02842	0.43374	0.01104	0.01082
H3K36me2	0.07250	0.00008	0.99901	0.99295	0.95716	0.98975	0.00035	0.07708	0.11065	0.00530	0.00168	0.00205	0.14813	0.00014	0.00037

Supplemental Table S3. Characterization of the 15 chromatin state model in *Oikopleura dioica* by summary of the genomic features enriched in each state.

State	Histone PTMs	Characteristic associated Genomic and Chromatin Features	
		Ovary	Testis
1	**H3K79me3,** H3K36me3 H3K9me2, H4K20me3	silent HD, TF and ZF promoters, low specific gene promoters, silent HD gene bodies **– Silent TFs**	silent HD genes and promoters, ZF and TF promoters, silent TF gene bodies, CTCF
2		unannotated, silent regions	unannotated, silent regions
3	**H4ac, H3K36me3, H3K36me2**	active operons, RNApol II S5P, active gene bodies, low-specific genes, non-TF and some TF and ZF genes, active TARs, UTRs, skipped exons **– Transcriptional elongation, alternatively spliced exons**	RNApol II S5P, active operons, bodies of low specificity genes, non-TF genes p300, X scaffolds **– Transcriptional elongation**
4	**H3K36me3, H3K36me2**	active HD, ZF and TF genes, RNApol II S5P, UTRs, active operons, active non-TF genes **– Transcriptional elongation esp. operons**	silent intergenic TARs, silent operon promoters and bodies, low-specificity gene bodies, CTCF, p300, promoters and gene bodies of active non-TF genes
5	**H4ac, H3K4me2, H3K27ac, H3K36me2, H3K36me3,** H3K4me3, H3K79me1,3, H4K20me1	RNApol II S5P, operon promoters, low-specif and non-TF gene promoters, active ZF and TF promoters, active 3 and 5 UTRs, p300 **- Active promoters esp. operons and low specificity genes**	RNApol II S5P, active low specificity gene bodies, operon gene bodies; silent operon promoters and gene bodies, low specificity gene promoters and bodies; CTCF, p300, X chromosome
6	**H3K36me2,** H3K27ac	active intergenic TARs, active ZF genes – **Intergenic transcription**	skipped exons, active operon and low-specificity gene bodies and non-TFs, silent operons and low-specificity gene bodies, intergenic TARs, 5meC **– Gene bodies, alternatively spliced exons**
7	**H3K27ac,** H3K18ac	silent intergenic TARs, active high specificity ZF and TF promoters; active intergenic TARs, silent TFs, 5meC	active operon and low-specif. gene bodies, active TFs and ZFs, non-TF genes,5UTRs, silent operons and low specificity gene bodies **- Gene bodies**
8	**H3K4me3, H3K27ac, H3K18ac, H3K4me2,** H3K36me1	active high specificity ZF and TF promoters; active low- specificity genes, non-TF gene promoters; active operon promoters, RNApol II S5P, silent non-TF promoters, low and high specificity promoters, silent intergenic TARs	active high specificity ZF and TF promoters; active low- specificity genes, non-TF gene promoters; active operon promoters, RNApol II S5P, active 3 and 5 UTRs, active intergenic TARs **- Active promoters**
9	**H3K4me2,** H3K9me2	active ZFs, TFs and non-TF gene promoters, high-specif promoters. silent operons and ZF promoters **- Active and silent tissue-specific promoters**	active HD genes, CTCF, active high specificity, ZFs and TFs promoter, silent operons and ZFs promoters **- Active and silent promoters**
10	**H3K9me2**	silent intergenic TARs, CTCF, TEs **– Heterochromatin**	no features are enriched over the threshold

11	**H3K9me3, H3K9me2,** H3K4me3	CTCF, silent ZF gene bodies, TEs, p300	Y scaffolds, TEs **- Silent Y-chromosomal regions**
12	**H3K9me3,** H3K4me3, H4K20me3	5meC, CTCF, p300, TEs, silent low specif. genes	**Heterochromatin**
13	**H4K20me1, H3K79me1 H3K4me3, H4K20me3, H3K9me3, H3K9me2, H3K79me3,** H3K4me1**,** H3K27ac**,** H3K36me3	CTCF, TEs **- Silent regions**	active ZF promoters, p300, TE, CTCF, 5meC, Y scaffolds - **Active Y-chromosomal genes and mobile elements, enhancers**
14	H3K27me3, H4K20me1, H4K20me3 H3K79me1, H3K36me1	active HD genes, 5meC, CTCF, TE	active and silent HD genes – **Polycomb domains**
15	**H4ac**	5meC, p300, CTCF, silent intergenic TARs, active high specif. genes	silent intergenic TARs, silent HD and TF promoters and gene bodies **– Silent developmental genes**

The cutoff emission values for inclusion of histone PTMs in the Table was 0.25, except for state 14 (grey font) where emission values were >0.1, but <0.2. Those PTMs with values >0.5 are in bold. TF = transcription factor; ZF = zinc finger protein; high and low specificity genes according to breadth of expression across development (see Methods); TAR = transcriptionally active region; TE = transposable element; unannotated = regions lacking annotation or transcription; 5meC = methylcytosine; esp.- especially. Grey-shaded boxes indicate that the state appeared in a very small (<1%) proportion of the genome in respective tissue. Red/green font indicates transcriptionally silent/active genomic regions. Putative annotation/summaries of composite features associated to states are indicated in bold font where possible. Thresholds on the emission parameters for the state enrichment of each feature were >2.

Supplemental Table S4. Comparison of the 50-chromatin state model to the 15-state model.

50-state model	Features in the ovary	Feature in the testes	15-state model
1	Operons, non-TF promoters, low specif. promoters, RNA polII, skipped exons		5
2	Operons, non-TF promoters, RNA polII		5
3	Operons, RNA polII		3
4	Operons		3
5	Operons, RNA polII		3
6	Operons, UTRs		4
7	Operons		4
8	Operons, UTRs		4
9	HD promoter		1
10	HD promoter, TF and ZF promoter		1
11	High specif. promoters, ZF, TF, operon promoters	Active and silent gene bodies	2
12	Operon bodies, non-TF and low-specif. gene bodies, skipped exons		3
13	Operon bodies, non-TF and low-specif. gene bodies, ZF and TF gene bodies, RNA polII	low specif., non-TFgene bodies, p300	3
14	CTCF, active HD gene bodies	HD promoter and body	13
15		Y-chromosome, TE	11
16		TE	11
17	CTCF	TE upstream TSS	11
18	CTCF, unannotated, TE	TE downstream TSS, Y-scaffolds	11
19		TE, Y-chromosome	11
20		Intergenic TARs, TF promoter, high specif. gene promoters, CTCF, Y-chromosome	11
21	Operons, HD, TF, ZF promoters	HD, TF promoters, intergenic TARs, TF promoters, intergenic TARs	9
22	Intergenic TARs, HD promoter	Broad range of features	10
23	TE, CTCF, HD promoter	CTCF, HD promoter	13

24	CTCF		13
25	TE, operons and non-TF	Intergenic TARs, UTR3s	13
26		5meC, non-TF and non-SL promoter, Y-chromosome	13
27	5meC, CTCF, TFs, ZFs	HD	13
28	CTCF, TE, p300	3`UTRs, high specif., TF, ZF promoters	13
29		RNA polII, high specific, low specif. and non-TF promoters, ZF and TF promoters, operon promoters, CTCF, p300	8
30	RNA polII, high and low specif. promoters and gene bodies	RNA polII, active specific, low specif. and non-TF promoters, operon promoters, 5 and 3`UTRs, intergenic TARs	
31	RNA polII, UTRs, ZF and TFs promoters, CTCF	RNA polII, active non-TF promoters, operon promoters, 5 and 3`UTRs, gene bodies, intergenic TARs	
32	High specif. promoters and gene bodies, HD, TF and ZFs promoters	High specific. promoters, low specific promoters, operon promoters, operon, non-TF promoters	
33	High specif. gene body	HD gene body	9
34	High specif., TFs, ZFs promoters, 5`UTRs,	CTCF, p300, intergenic TARs,	5
35	intergenic TARs	active and silent low specif. gene, non-TF, operons, intergenic TARs,	6
36	specif. TFs, ZF, operon promoters	low specif. gene, non-TF, operons, CTCF	6
37	active and silent specif. TFs, intergenic TARs	low specif. gene, non-TF, operons,	8
38		ZF, TF, HD, low specif, operon gene bodies	8
39	intergenic TARs, TE	operon, ZF, HD gene bodies, active and silent intergenic TARs	8
40	CTCF, intergenic TARs	5 `UTRs, RNA polII	8
41	ZF, TF gene bodies, HD gene bodies, intergenic TARs	RNA polII, intergenic TARs, high specif. promoters and gene bodies,	7
42	HD promoter, low specif. gene bodies	intergenic TARs, 5 `UTRs, RNA polII, high specif. promoters	7
43	TF, ZF, HD promoters and gene bodies	TF, ZF, HD promoters and gene bodies	1
44	5meC, high specif genes, TFs,	TF, ZF promoters, ZF, TF gene bodies	15
45	RNA polII, TFs	intergenic TARs, HD, ZF gene bodies	15
46	Silent ZF, TF, HD promoters and gene bodies - Polycomb domains	ZF, HD promoters and gene bodies, intergenic TARs, X-chromosome, CTCF - Polycomb domains	13
47	unannotated, broad range	unannotated, broad range	2

48	5meC, CTCF, p300	5meC, CTCF, p300	12
49	Active and silent high specific. promoters and bodies, HD, TFs, intergenic TARs	RNA polII, high specific. promoters	8
50	CTCF, active 5`UTRs	CTCF, p300	12 / 13

Expansion of certain states (15-state model) into several sub-states (50-state model) is indicated by the color code assigned to each of the 15 states. Grey shading in the middle rows indicate states covering <0,01% (< 7 kb total) of the genome. Red type, features associated with transcriptionally silent regions; Green type, features associated with transcriptionally active regions; Black type, no particular association with active or silent regions. TF, transcription factor; ZF, zinc finger genes; HD, homeodomain genes; specific., specificity; TAR, transcriptionally active region

Supplemental Table S5. GO terms associated with chromatin state enrichment clusters based on the *O. dioica* 15-chromatin state epigenome model.

State	Ovary			Testis		
	Clusters	Genomic Features	GO terms	Clusters	Genomic Features	GO terms
1	1	silent promoters	Chordate embryonic development, cell fate commitment, calcium ion binding, positive and negative regulation of transcription, organ morphogenesis, positive regulation of metabolic process and gene expression – **Embryonic development**	16	silent genes	M-phase, growth, Wnt signaling, gastrulation, growth, embryonic development, organ development, apoptosis, cell proliferation, microtubule-based process, tissue development, positive and negative regulation of cell proliferation, transcription, ribosome biogenesis, translation, signal transduction, microtubule based process, membrane organization – **Embryonic development**
	31	silent genes	Transcription, cell adhesion, developmental process, muscle differentiation, nervous system development, sex differentiation, tissue development, positive regulation of cell proliferation, cell growth, embryonic morphogenesis, Wnt signaling, tube development, organ morphogenesis – **Embryonic development**			
3	16	active gene bodies, TSS and TES	ATP binding, DNA binding, DNA replication, Golgi apparatus, chromatin organization, cell morphogenesis, biosynthesis, glucose, alcohol, amono acid metabolism, embryo development, reproduction, M phase, translation, cell adhesion, ectoderm development, cell proliferation, meiosis, mitochondria – **Maternal transcripts, Oogenesis, Housekeeping genes**	18	active gene bodies	**A:** Cytoskeleton, centrosome, spindle, microtubule-based processes, MTOC, GTPase activity, organelle organization, membrane, cation transport, nucleolus, cell communication, signaling, transport – **Mitosis related, housekeeping functions**
	17	active gene bodies	**A:** DNA recombination, repair, ATP metabolism, GTPase activity, reproduction, M phase, RNA splicing, aging, cell adhesion, growth, apoptotic process, signaling, methylation, embryo development ending in hatching, gametogenesis, histone modification, ribosome, - **Maternal transcripts, Oogenesis, Housekeeping genes**		silent gene bodies	**S:** Immune system process, intracellular transport, membrane bounded vesicle-mediated transport, clathrin coated vesicle, lipid binding, defense response, response to stress, response to other organism – **Stress response**
		silent gene bodies	**S:** Methylation, ribosome biogenesis, ncRNA metabolism, tRNA metabolism, mRNA processing, regulation of translation - **Nutrient response**			
4	16		Overlap with states #3 and 5	19	silent TSS promoters, gene bodies	**S:** DNA damage response, meiosis, M-phase, gamete generation, reproduction, lipid biosynthesis, ribosome, endoplasmic reticulum, protein import, translation, zinc ion binding – **Gametogenesis, Meiosis**
	17					**A:** RNA biosynthesis, cell-cell signaling, regulation of hormone

	24				some active gene bodies	levels, alcohol metabolism, mitochondrial matrix, secretion, actin-filament based process
5	14 16	active TSS	Response to nutrient, locomotory behavior, contractile fiber, ion channel activity, cellular protein complex assembly, regulation of binding, cation transport, microtubule-based movement, fatty acid metabolism – **Nutrient response**	20	active gene bodies silent gene bodies	**A:** DNA replication, packaging, M-phase, chromosome organization, RNA splicing , anatomical structure,cellular metabolism,development, apoptosis, aging, response to hormone, chromatin organization, embryo development, gastrulation, male gamete generation, spermatogenesis **S:** MAPK cascade, ATPase activity, RNA processing, ncRNA processing, ribonucleoprotein complex biogenesis, RNA splicing, reproduction, M-phase, ectoderm development, growth, hormone metabolism, spermatogenesis – **Mitosis, spermatogenesis, development**
	17	active gene bodies	Overlap with states #3 and 4			
	24	active promoters and TSSes	Cell proliferation, developmental process, methylation, regulation of transport, of cell cycle and cellular metabolism, membrane organization, proteolysis, DNA metabolism, tRNA metabolism, translation, vesicle transport **– Housekeeping functions**	21	silent gene bodies	Cell development and differentiation, actin cytoskeleton, RNA metabolic process, nucleoplasm, nucleic acid binding, apoptotic process, programmed cell death, positive and negative induction and regulation of apoptosis, of cellular growth, of proliferation; homeostatic process, hydrolase, phospholipase and carboxylesterase activity - **Apoptosis**
	26	active promoters	Reproduction, M-phase, meiosis, DNA replication, growth, nucleolus, regulation of apoptosis, metabolism, gastrulation, hormone biosynthesis, embryonic morphogenesis, developmental process – **Oogenesis, maternal transcripts**			
6	27 28	silent gene bodies, TSS and TES	MAPK cascade, transmembrane receptor PTK signaling, hormone response, developmental growth, gastrulation, anatomical structure development, fatty acid metabolism, Immune system process, sex differentiation, metabolic processes – **Embryonic development**	7	active gene bodies and TESes	**A:** ATP metabolism, Golgi membrane, MAPK, Ras signaling, , tRNA metabolism, DNA recombination, repair, vesicle-mediated transport, cell-cell signaling, cell growth, ligase activity, ncRNA processing, spermatogenesis, histone modification, NTP synthesis, GTPase regulator activity **- Housekeeping functions and spermatogenesis**
				17	silent gene bodies	ATP binding, DNA binding, repair, proliferation, M-phase, GTPase, cellular metabolism,RNA metabolism, actin, chromatin organization, protein complex assembly, tissue development, embryonic development, organ development, regulation of cellular growth, larval development, **- Mitosis, metabolism, embryonic development**
7	3 4	silent promoters, TSS	Cell activation, TF binding, endocytosis, ectoderm development, developmental process, tube development, microtubule-based process, cell-cell signaling, tissue morphogenesis, muscle development, gastrulation - **Larval development**	4 6	active TSS	Overlap with states #6 and 8
	42	silent gene	Anatomical structure morphogenesis, cellular component biogenesis, protein complex biogenesis, M phase, mitosis,			

	43 44	bodies	growth, DNA packaging, gastrulation, chromatin organization, larval development, cell fate commitment, locomotory behavior, cell adhesion – **Larval development**	17	silent TSS	
8	22	active genes	DNA binding, DNA replication, embryo development, Golgi vesicle transport, MAPK cascade, Wnt receptor signaling pathway, cellular homeostasis, chromatin organization, negative and positive regulation of many processes, sex differentiation, cytoskeleton organization, nucleosome assembly, embryo development, organogenesis - **Maternal transcripts, Oogenesis**	4	active promoters	ATPase activity, chromatin assembly, muscle contraction, ncRNA metabolism, cilium, heat shock binding, hormone biosynthesis, lipid localization, reproductive process, microtubule-based process, mitosis and meiosis, DNA packaging, protein localization, cellular biosynthesis process, cellular development, centrosome, growth, heat shock, binding, hormone biosynthesis, male gamete generation, mitosis, meiosis, ncRNA metabolism, response to drug, nutrient, stress, ribosome, spliceosome, tissue development – **Spermatogenesis, nutrient response**
	23	silent promoters	DNA recombinations, M-phase, cell motility, chromatin organization, heat shock protein binding, hormone signaling, spermatogenesis, lipid metabolism, negative and positive regulation of many processes, meiosis, apoptosis - **Spermatogenesis**	6	active TSS TES and gene bodies	
9	37	silent promoters	M-phase, cell-cell signaling, locomotion, developmental growth, spermatogenesis, Wnt pathway - **Spermatogenesis**	9	silent promoters, TSS and TES	Spermatogenesis, gene regulation, sex differentiation, reproduction, response to hormone, mitotic cell cycle, ATP, GTP binding, actin, response to chemical, induction of apoptosis, organelle fission, phosphorylation, protein ubiquitination, endocytosis, Ras signaling, vitamin B6 binding, immune system process – **Spermatogenesis, Stress response**
	29	silent promoters	protein serine/threonine kinase signaling pathway, multicellular organism reproduction, response to steroid hormone, regulation of mitosis, protein phosphorylation - **Spermatogenesis**			
10	34 35	silent genes	Response to radiation, defense response, embryonic organ development, regulation of translation, response to biotic stimulus, small GTPase-mediated signal transduction. polysaccharide metabolid process – **Stress response, larval development**	12 13	silent	ectoderm development, cell adhesion, regulation of molecular function, developmental growth, muscle contraction, response to wounding and radiation – **Larval development, Stress response**
11	40	silent	RNA-dependent DNA replication, nitrogen compound metabolism	1	silent	RNA-dependent DNA replication
12				1	silent	RNA-dependent DNA replication
13	2	silent genes	Nuclear division, response to nutrient, hormone, drug, wound healing, transmembrane transport, regulation of hormones, nucleotide biosynthesis, nucleolus, MAPK cascade, negative regulation of cell proliferation, organelle fission – **Stress, nutrient response**	1	silent	RNA-dependent DNA replication
	6		ATP, NTP metabolic process, DNA metabolic process, immune response, response to nutrient, sulfur compound metabolic process, defense response - **Stress, nutrient response**	2	silent	DNA conformation change, NTP metabolic process, organic acid transport, hormone biosynthesis, positive regulation of differentiation, methylation

14	10	silent TSS	RNA-dependent DNA replication, DNA integration, response to wounding, neurotransmitter transport, regulation of Ras	3	silent	Reproduction, sex differentiation, spermatogenesis, larval development, sulfur compound metabolism, response to abiotic stimulus, stress, regulation of mitosis
				15	silent TSS and promoters	Wnt signaling, organ development, ectoderm development, anterior-posterior pattern specification, gastrulation, positive and negative regulation of signaling and gene expression, cell growth, tube morphogenesis, regulation of cell proliferation and apoptosis – **Embryonic development**
15	8	silent genes	M-phase, cell adhesion, muscle development,Negative regulation of cellular process,wound healing; Wnt signaling, cell growth, chromatin assembly; muscle cell, eye, gland, heart, epithelium development, polysaccharide metabolism, membrane invagination - **Larval development**	11	silent TSS	Wnt signaling, gastrulation, organ development, tube morphogenesis of an epithelium, cell growth, regulation of transcription, microtubule, regulation of cell size, cell migration – **Larval development, TFs**
	19	silent gene bodies	Cellular component biogenesis, dev. process involved in reproduction, sulfur compound metabolism, vesicle mediated transport, cell growth, protein import, regulation of secretion, regulation of cell size	17	silent gene bodies	overlap with states #6 and 7

The cluster numbers are derived from the dendograms in Fig. 3 in the ovary and testis, respectively. Transcriptionally active/silent regions are in green/red font, TF = transcription factor. Putative annotation of each cluster, where possible, is in bold font.

Supplemental Table S6. *Oikopleura dioica* homologs of human histone modifiers.

S6A. Homologs of human histone modification writers in *O. dioica.*

Histone Modifier	Targets	Expression ratio (log_2) ovary/testis	Functions (assigned in literature)
Histone acetyltransferases			
GCN5	H3K9ac, H3K14ac	NF	Conserved from yeast to humans in locus-specific transcriptional activation (Wang et al. 1997) as a subunit of SAGA and ATAC coactivator complexes [1]. Also acetylates histone H3 in gamma-H2A.X nucleosomes at sites of DNA damage [2].
PCAF (p300/CBP-associated factor)	H3K9ac, H4	NF	Paralog of Gcn5 responsible for nuclear receptor-independent co-activation by H3K9ac. Reviewed in [3].
ELP3	H3K9ac, H3K18ac, H4	1.66	HAT subunit of RNAP II elongator complex. Involved in transcription, cell cycle regulation and organizing chromatin during mitotic cycles [4].
CBP	H3K27ac, H3K18ac, H4ac	2.10	Global transcriptional activator of nuclear receptor-dependent genes [5]. Functional homolog of p300 [6,7].
p300	H3K27ac, H3K18ac, H4ac	2.28	Acetylates all 4 core histones and crotonylates histone 3 and 4 for transcriptional co-activation. Binds at promoters and enhancers [6–9].
Myst1 (hMOF, KAT8)	H4K16ac	0.38	Homolog of *Drosophila* MOF, part of MSL - dosage compensation complex [10] and NSL complex that regulates housekeeping genes [11]. NSL promotes MLL/SET-dependent H3K4me2-marking of some genes [12]. MOF interacts with MLL1 and they jointly establish and spread an active chromatin structure [13].
Myst2 (HBO1, KAT7)	H3K14ac	11.95	Evolutionarily conserved interaction with origin recognition complex (ORC). HBO1-mediated histone H4 acetylation plays a role in licensing replication origins and gene regulation [14].
Myst3 or 4 (hMOZ/KAT6A or MORF/KAT6B)	H3 and H4	10.50	Component of the MOZ/MORF complex [15]. Myst3 opposes BMI1 to control Hox gene transcriptional levels along anterior-posterior axis [16]. Myst4 protein is localized in mammalian gametes [17].
Tip60a (KAT5)	H3 and H4	10.37	Recruited by E2F transcription factors leading to promoter acetylation of E2F-responsive genes, hence affecting cell cycle progression [18]. Cell-type specific transcriptional activator/repressor [19].
Tip60b (KAT5)		0.83	

MGEA5 (NCOAT)	H4K8ac, H3K14ac	-0.82	Bifunctional protein *O*-GlcNAcase and HAT [20]. E2F1 negatively regulates MGEA5 in Rb1-dependent manner [21].
SRC1 (Ncoa1)		NF	Facilitates formation of stable pre-initiation complex and transcriptional activation of steroid receptor responsive genes [22].
ACTR (Ncoa3)		NF	Associates with other HATs (CBP/p300/PCAF etc.). Chromatin remodelling in response to hormone signalling [23].
Histone methyltransferases			
SETD1B (dSet1, *Drosophila*; set-2, *C. elegans*)	H3K4	0.22*	Responsible for bulk of H3K4me3 in *Drosophila*. Performs majority of transcription-coupled H3K4me at active genes, presumably through co-transcriptional recruitment [24]. Deficiencies in the H3K4me3 complex of ASH-2, WDR-5 and SET-2 extend lifespan in *C. elegans* [25].
MLL1	H3K4me3	NF	TrxG protein activating Hox genes in a cell-specific manner [26]. Interacts with Ash1 in mammals [27]
MLL3/4 (trr in *Drosophila,* set-1/12/16 in *C. elegans*)	H3K4me1, H3K4me2	1.64	Transcriptional coactivator, required for enhancer activation, cell-type specific gene expression and cell differentiation. MLL4 deletion decreases enhancer H3K4me1/2, H3K27ac, Mediator and RNAPII levels [28]
MLL5 (trx in *Drosophila*)	H3K4me1,2	1.19	Inhibition of MLL5 results in G1 and G2/M phase cell cycle arrest. Stimulates E2F1 gene expression via binding to HCF1 and facilitates G1/S phase progression [29].
Ash1 (lin-59 in *C. elegans*)	H3K36me1,2, H3K4me3, K9, H4K20	NF	Maintains retinoic acid-induced transcription of Hox genes by counteracting Polycomb silencing by methylating H3K36 independently of transcriptional elongation during embryonic development in worm, fly and human [27,30–32].
SETD1A	H3K4	NF	Induces miRNAs that target downstream effectors of p53, as well as cell cycle regulators in mammals [33]
SETDB1 (ESET, eggless in *Drosophila*, met-2 in *C. elegans*)	H3K9me1,2	11.97	Part of HP1alpha-CAF1-SETDB1 complex involved in depositing H3K9me in pericentric heterochromatin during DNA replication [34]. Targeted by factor recruited by KRAB zinc-finger proteins to euchromatin, for HP1-mediated silencing of euchromatic genes [35]. Complex with MBD1 and CAF1-HP1 couple DNA methylation and H3K9me3 to propagate heterochromatin during replication[36]. In *C. elegans*, SPR-5 and MET-2 function cooperatively to reestablish an epigenetic ground state required for the continued immortality of the C. elegans germ line [37].
SETDB2	H3K9me3	9.68	Contributes to H3K9me3 in interspersed repetitive elements and centromeric repeats. Role in chromosome condensation and segregation during mitosis [38].
Suv39H1 (set-25 in *C. elegans*)	H3K9me3	0.70	H3K9me3 creates interaction site for HP1 to promote heterochromatin formation in centromeres[39]. Disruption of Suv39H1 leads to aberrant mitosis. SUV39H1 along with SIRT1 mediates silencing of rDNA loci in response to energy deficiency [40].
Suv39H2	H3K9me3	11.98	Testis-specific in mouse, accumulates on sex chromosomes (XY body) which undergo transcriptional silencing during meiotic prophase I, may impart an epigenetic imprint to the male germ line [41].

EHMT1 GLP1	H3K9me2, H3K27me1	10.35	Methyltransferase that targets euchromatic regions. Part of a complex with Suv39h1, GLP1 and SETDB1[42]. Induces DNA methylation and transcriptional repression [43,44].
EHMT2 G9a	H3K9me1, H3K9me2, H3K27me1	9.82	Catalyzes mono and dimethylation of H3K9 and H3K27 with high specificity [45]. Part of a large multimeric complex of Suv39h1, GLP1 and SETDB1[42].
EZH1 Enhancer of zeste homolog 1	H3K27me1, H3K27me2, H3K27me3	11.41	Catalytic subunit of Polycomb repressor complex PRC2/EED-EZH1 involved in maintaining transcriptional repressive state of genes over successive cell generations [46]. Low levels of activity, but efficiently represses transcription, compacts chromatin and is ubiquitously expressed in mouse [47].
EZH2 (mes-2 in *C. elegans*)	H3K27me1, H3K27me2, H3K27me3, H3K9me	9.82	Catalytic subunit of PRC2/EED-EZH2 complex that may serve as recruiting platform for DNA methyltransferases [48]. Expressed in proliferating tissues. Responsible for large-scale changes, onset of differentiation and loss of plasticity in C. elegans [49].
SETD2	H3K36me3	11.09	Interacts with hyper-phosphorylated RNAPII [50]. Influences splicing [51]. Prevents cryptic intragenic transcription initiation by recruitment of an HDAC in yeast and FACT complex recruitment in human [52].
NSD-like (mes-4 in *C. elegans*, dMes4 in *Drosophila*)	H3K36me1,2	0.87	Regulates gene expression by stimulating transition of RNAPII from initiation to elongation-competent state [53,54]. H3K36me2 peaks adjacent to promoters in *Drosophila* [55]. Responsible for H3K36me2 in *C. elegans* germ line.
SETMAR	H3K36me2	nearly silent	Mediates NHEJ repair of DNA damage (dsb). It forms an open chromatin conformation and is responsible for integration of exogenous DNA. This gene aroused from the fusion of a H3 methylase with a mariner family transposase; exists as a fusion gene only in anthropoid primates, other organisms lack mariner transposase domain [56,57].
SMYD 1 and 3	H3K4me	silent	Embryonic histone methyltransferases. *C. elegans* homolog set-30 may establish and maintain H3K4me2 on spermatogenesis genes [58].
SETD3	H3K4, H3K36	silent	Embryonic histone methyltransferase. Regulates muscle differentiation [59].
SETD8 (set-1 in *C. elegans*)	H4K20me1	0.60	H4K20me1 helps load pre-RC on origin of replication and plays a role during initiation of DNA replication [60]. Functions with condensin-like *C. elegans* DCC to repress transcription of X-linked genes [61]. Required for further methylations of H4K20 which antagonize H4 acetylation by Myst1 and pauses RNAP II [62].
Suv4-20H1 (Suppressor of variegation 4-20 homolog 1)	H4K20me2 (of H4K20me1)	11.18	Functions in pericentric and telomeric heterochromatin, to establish constitutive heterochromatin [63].
Suv4-20H2	H4K20me3 (of H4K20me1)	11.33	Stably associates with pericentric heterochromatin via interaction with HP1, resulting in compaction of heterochromatin. Involved in initial loading or maintenance of cohesion subunits and in rDNA antisense lncRNA-mediated global chromatin compaction and establishment of quiescence [64].
Dot1L	H3K79me1-3	1.89	Regulates cell cycle progression, may be a specific mark of Wnt target genes. Accumulates on aging histones as a cell aging timer [65,66].

PRDM9 (set-17 in *C. elegans*)	H3K4me1-3, H3K36me3	-10.55	Meiotic prophase H3K4 and H3K36 tri-methyltransferase essential for meiotic progression and activation of meiotic prophase genes [67–69]. Contributes to transgenerational inheritance in *C. elegans* [70].
Histone kinases			
Aurora B	H3S10P, H3S28P	-0.15	H3S28P in early prophase required for proper chromosomal condensation [71].
MSK1_a	H3S10P (interphase), H3S28P	2.73	H3S28P that initiates methyl-acetyl switch at H3K27 (methylated by Polycomb repressive complex, phosphorylation causes loss of PRC2 interaction) to de-repress target genes [72]. H3S28P also activates stress response genes [73].
MSK1_b		2.27	

S6B. Homologs of human histone erasers in *O. dioica.*

Histone modifier	Targets	Expression ratio (log_2) ovary/testis	Functions (assigned in literature)
Histone deacetylases			
SIRT1 (NAD+ - dependent)	H4K16ac, H3K9ac	2.61	Involved in formation of facultative heterochromatin. Mammalian SIRT1 interacts directly with, recruits and deacetylates K266 in SET domain of SUV39H1, and these activities independently elevate SUV39H1 activity to increase H3K9me3 [74]. SIRT1 along with SUV39H1 mediates silencing of rDNA in response to energy deficiency [75].
SIRT2/3	H4K16ac, H3K56ac	10.60	Deacetylates H4K16 during mitosis which is crucial for chromatin condensation [76]. Deacetylates BuBR1 which increases lifespan [77].
SIRT6	H3K9ac, H3K56ac	10.01	Loss of SIRT6 causes premature lethality and aging-related degeneration. SIRT6 is also involved in DNA repair [78]. Mediates the cell cycle-dependent deacetylation of H3K56 at telomeres [79].
SIRT7	H3K18ac	silent	Binds to promoters to promote transcriptional repression. Target genes (linked to tumor suppression) defined in part by interaction with cancer-associated factor ELK4 [80]. Involved in CDK1-cyclin B dependent repression of rDNA transcription at mitosis onset [81].

HDAC1/2	H3K56ac, H4?	2.45	Deacetylation of histone tails results in chromatin compaction and the loss of binding sites for transcriptional machinery components that have bromodomains (e.g., TAFII1). Essential for mouse embryogenesis [82].
HDAC3	H3, H4	11.05	Plays role in cell cycle progression (required for H3S10P) and DNA damage control. Along with p300, causes deacetylation and repression of the c-myc promoter which leads to transcriptional repression and inhibits premature escape of cells from G1 phase [83].
Histone demethylases			
PHF8	H3K9me1,2 H4K20me1, H3K27me2	0.47	Involved in G1/S transition in conjunction with E2F1, HCF-1 and SETD1A, in part, by removing repressive H4K20me1 mark from a subset of E2F1-regulated promoters [84]. Recruited to promoters via its PHD domain interaction with H3K4me2/3. Coactivator of RNAP I-mediated rDNA transcription [85].
KDM1A (LSD1) (spr5 in *C. elegans*)	H3K4me1,2 H3K9me1,2	0.13	Belongs to flavin monoamine oxidase family, conserved from *S. pombe* to human [86]. De-represses androgen-receptor-dependent transcription by removing H3K9me [87]. Regulates transgenerational inheritance in *C. elegans* [58].
KDM1B (LSD2)	H3K4me1,2, H3K9me2	10.40	Associates with H3K36me3 on transcribed gene bodies and demethylates H3K4me2. Contributes to intragenic dynamics of H3K4me2/H3K9me2. LSD2 depletion results in increased H3K4me2 and decreased H3K9me2 [88].
KDM2B/2A	H3K36me2, (H3K4me3)	11.60	Conserved from yeast to humans [89]. Regulates rRNA genes by demethylation of H3K36me2 at promoters under starvation[90]. As part of the PCGF/PRC1 complex bound to non-methylated DNA recruits PRC2 for gene repression [91]
KDM3A	H3K9me1, H3K9me2	11.88	Upregulates mammalian Y chromosome sex-determining gene *Sry* [92]. Hormone-dependent recruitment to androgen-receptor target genes, resulting in H3K9 demethylation and transcriptional activation. In spermatogenesis regulates expression of genes such as PRM1 and TMP1, required for sperm chromatin condensation [93].
KDM4D	H3K9me3, H3K9me2, H3K4me2	1.98	Has neither a PHD nor TUDOR domain. Catalyzes demethylation of H3K9me3 at enhancer regions leading to their activation [94]. Catalyzes H3K4me2 to H3K4me1. Participates in DNA repair by NHEJ and HR [95].
KDM5A/B/C/D (**JARID1 family**: rbr-2 in *C. elegans*, lid in *Drosophila*)	H3K4me3	11.26	Represses homeotic genes by removing H3K4me3[96]. Acts in coordination with Suv39H1 homolog in yeast in establishment of heterochromatin. In euchromatin, associates with Set1 and Lsd1 to function as their structural link and to ensure H3K4 hypermethylation and H3K9 hypomethylation of active genes [97]. Opposes set-2 in regulating the lifespan extension in *C. elegans* [25]. Involved in progression from G2 to M phase. E2F1 is a downstream target in KDM5B pathway [98].
KDM6A (UTX) **KDM6B**	H3K27me	11.15 12.38	X-chromosomal genes that escape inactivation. H3K27me3 controls the expression of Hox genes by PRC1 recruitment and in germ cells participates in epigenetic reprogramming though KDM6 not required for demethylation of these regions [99,100]. Regulates lifespan in *C. elegans* [101].

NO66	H3K4me3, H3K36me3	11.44	Regulates osteoblast differentiation by demethylating H3K4 and H3K36, to inhibit SP7/OSX-mediated promoter activation [102]. Recruited by PHF19 to transcribed regions together with PRC2 during ESC differentiation [103]. A ribosomal oxygenase in nucleolus important for translation regulation [104].
KDM7_a	H3K9me2, H3K27me2, H4K20me1	silent	Removes dimethyl repressive marks and activates transcription[105]. Demethylation of the promoter and further activation of FGF4 gene by KDM7A regulates neuronal differentiation.
KDM7_b		silent	
KDM8_a	H3K36me2, H3K36me2	11.88	Required for G2/M progression [106]. Specifically demethylates H3K36me2 repressive mark, acting as a transcription activator. Regulates Cdkn1a expression and cell proliferation in embryonic development [107].
KDM8_b		silent	
Histone Phosphatases			
PP1-alpha catalytic subunit_a	H3S10P, H3S28P, H3T3P	-12.16	PP1α-mediated dephosphorylation of H3S10P allows deacetylation of H4K5ac/K8ac by HDAC1/2/3, leading to release of chromatin-bound BRD4, and subsequent recruitment of P-TEFb to enhance elongation and expression of inducible genes [108]. LAB-1 may act at the onset of meiosis in a manner akin to Shugoshin, by recruiting PP1 phosphatase to counteract Aurora B kinase, thereby ensuring sister chromatid cohesion [109].
PP1-alpha catalytic subunit_b		0.06	

Homologs were identified using human protein sequences from Uniprot and protein BLAST against the *O. dioica* proteome: “NF” indicates that no homolog was found in the *O. dioica* genome using this approach. Homology was validated using InParanoid [110] and/or comparison of functional domain compositions. HAT, histone acetyltransferase; RNAP II, RNA polymerase II; HDAC, histone deacetylase complex; *SET domain spliced out of *O. dioica* SETD1B testis transcript.

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