

Supplementary Table 2

ChIA-PET interaction data summary

Factor	EED		EZH2		SUZ12		PRC2 (combined)	
Number of replicates	6		7		11		24	
Total reads pairs	1,575,374,571		1,034,753,420		2,507,372,657		5,117,500,648	
non-redundant, non-chimeric	208,931,828	13%	97,936,086	9%	268,046,232	11%	574,914,146	11%
Total binding peaks	31,366		42,189		25,467		23,368	
Peaks with interactions	10,789	34%	15,483	37%	11,678	46%	15,428	66%
Interaction clusters	146,066,534		57,294,283		200,505,313		397,500,613	
Significant cis-interactions (FDR<0.05, p<0.05)	63,317	0.04%	50,819	0.09%	104,822	0.05%	261,440	0.07%
Interactions with PRC2 binding	12,130		19,302		28,310		54,173	
Interactions with PRC2 binding (single anchor; SA)	7,937	13%	10,718	21%	20,614	20%	40,544	16%
Interactions with PRC2 binding (both anchors; BA)	4,193	7%	8,584	17%	7,696	7%	13,629	5%
Interaction Types	BA	SA	BA	SA	BA	SA	BA	SA
Intragenic loops	1332	1799	3390	3033	2380	3714	3686	8925
	(32%)	(23%)	(39%)	(28%)	(31%)	(18%)	(27%)	(22%)
promoter anchored	1915	3573	3980	4717	4305	11626	8,175	21,584
	(46%)	(45%)	(46%)	(44%)	(56%)	(56%)	(60%)	(53%)
P-P	951	483	1,991	587	2,381	1,425	4,694	2,998
P-I	593	1,820	1,248	2,541	1,060	5,791	1,800	10,710
P-G	371	1,270	741	1,589	864	4,410	1,681	7,876
non-promoter anchored	946	2,565	1214	2968	1011	5274	1768	10035
	(22%)	(32%)	(14%)	(28%)	(13%)	(26%)	(13%)	(25%)
I-I	427	1,184	669	1,459	449	1,875	737	4,201
G-G	189	443	169	478	202	1,124	356	1,921
G-I	330	938	376	1,031	360	2,275	675	3,913

Replicates were combined and processed for interaction callings. Interactions were further examined for binding peak support. We report interactions with both anchors (BA) and single anchor (SA) support, respectively. Data for each factor were further combined and processed as a PRC2 interactions.

Supplementary Table 6

Gene Ontology analysis: Top 20 enriched biological processes for PRC2 interactions-tethered genes (5825 PRC2-associated genes in relative to 24,692 non-interacting genes)

GO term	Description	FDR q-value	Enrichment (N, B, n, b)
GO:0032502	developmental process	2.16E-140	1.65 (21172,4680,4642,1692)
GO:0048856	anatomical structure development	1.29E-133	1.80 (21172,3273,4642,1292)
GO:0048869	cellular developmental process	2.47E-99	1.75 (21172,2861,4642,1096)
GO:0009653	anatomical structure morphogenesis	2.35E-96	2.09 (21172,1463,4642,672)
GO:0051239	regulation of multicellular organismal process	1.96E-95	1.74 (21172,2815,4642,1073)
GO:0048731	system development	6.42E-94	2.55 (21172,771,4642,431)
GO:0007275	multicellular organism development	9.33E-94	2.10 (21172,1402,4642,647)
GO:0050793	regulation of developmental process	1.55E-91	1.79 (21172,2449,4642,959)
GO:0030154	cell differentiation	4.62E-86	1.83 (21172,2108,4642,847)
GO:2000026	regulation of multicellular organismal development	1.11E-82	1.87 (21172,1891,4642,775)
GO:0045595	regulation of cell differentiation	6.73E-78	1.90 (21172,1687,4642,703)
GO:0048518	positive regulation of biological process	1.77E-74	1.43 (21172,5348,4642,1673)
GO:0048522	positive regulation of cellular process	4.90E-73	1.46 (21172,4789,4642,1529)
GO:0048513	animal organ development	3.12E-66	1.97 (21172,1281,4642,553)
GO:0007267	cell-cell signaling	8.51E-60	2.61 (21172,464,4642,266)
GO:0023052	signaling	3.20E-59	2.47 (21172,547,4642,296)
GO:0051094	positive regulation of developmental process	4.53E-59	1.87 (21172,1386,4642,569)
GO:0060284	regulation of cell development	6.54E-58	2.08 (21172,935,4642,426)
GO:0051960	regulation of nervous system development	1.86E-57	2.09 (21172,904,4642,415)
GO:0051240	positive regulation of multicellular organismal process	2.14E-57	1.78 (21172,1633,4642,638)

Enrichment (N, B, n, b) is defined as follows:

N - is the total number of genes

B - is the total number of genes associated with a specific GO term

n - is the number of genes in the top of the user's input list or in the target set when appropriate

b - is the number of genes in the intersection

Enrichment = $(b/n) / (B/N)$

Supplementary Table 11

Regulatory features in the PRC2-bound silencers.

	Features	log2 Fold Enrichment	Z score (1000X simulation)
Ensembl Regulatory Build (PMID:25887522)	Open chromatin	1.05	11.58
	TF binding	1.06	5.68
	Enhancer	-1.76	-6.86
TF binding (PMID:18555785)	n-Myc	4.4	26.05
	Smad1	4	14.68
	ZFX	3.8	26.32
	Pou5f1	3.6	17.9
	Klf4	3.5	25.7
	c-Myc	3.5	8.54
	Esrrb	3.4	37.51
	Tcfcp2l1	3.2	33.65
	STAT3	3.1	10.27
	Sox2	3	14.23
	E2F1	2.8	17.1
CTCF	2.6	28.21	
Nanog	2.5	14.74	
Sequence composition	CGI	6.8	176.37

Enrichment of open chromatin, transcription factor binding sites and CpG islands were assessed in the PRC2-bound silencers.