

Figure S1: Novel motifs identified among different Ubx data sets. **(A)** Table of motifs that served as references to select novel Ubx binding motifs. **(B)** Novel Ubx binding motifs identified by the STREME sub-routine in the MEME suite using different data sets (2kb_common, meso_ONLYpeaks, neuro_ONLYpeaks) as input. Motifs with red labeled numbers were selected for closer analysis. Green boxes highlight the Ubx-like motif.

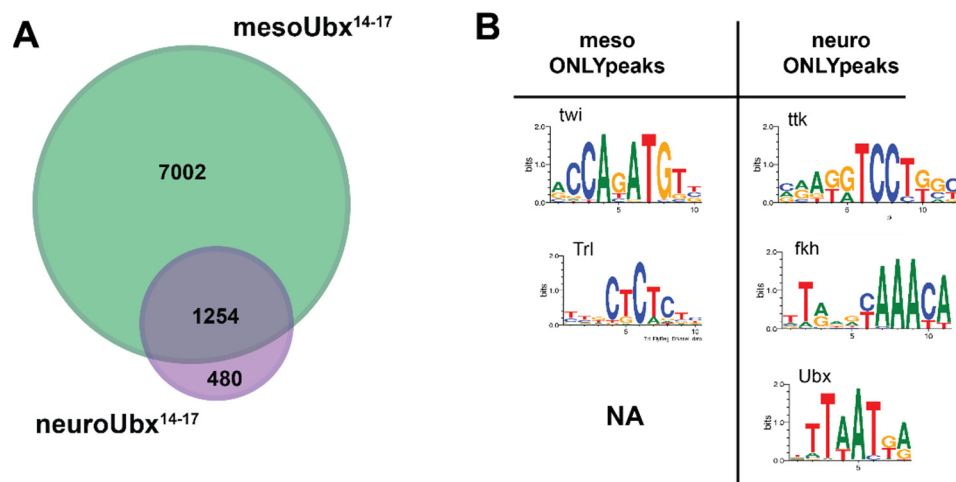


Figure S2. Analysis of the Ubx binding behavior during the differentiation stage (stage 14-17). **(A)** Venn diagram of Ubx peaks associated genes in the mesodermal and neuronal tissue, showing a substantial overlap of co-bound and potentially co-regulated genes (common genes). **(B)** Motif search based on an Analysis of Motif Enrichment (AME within the MEME suite) using the sequences from two categories meso_ONLYpeaks and neuro_ONLYpeaks derived from the common gene pool. The classical Ubx motif is not found in meso_ONLYpeaks. NA: not available.

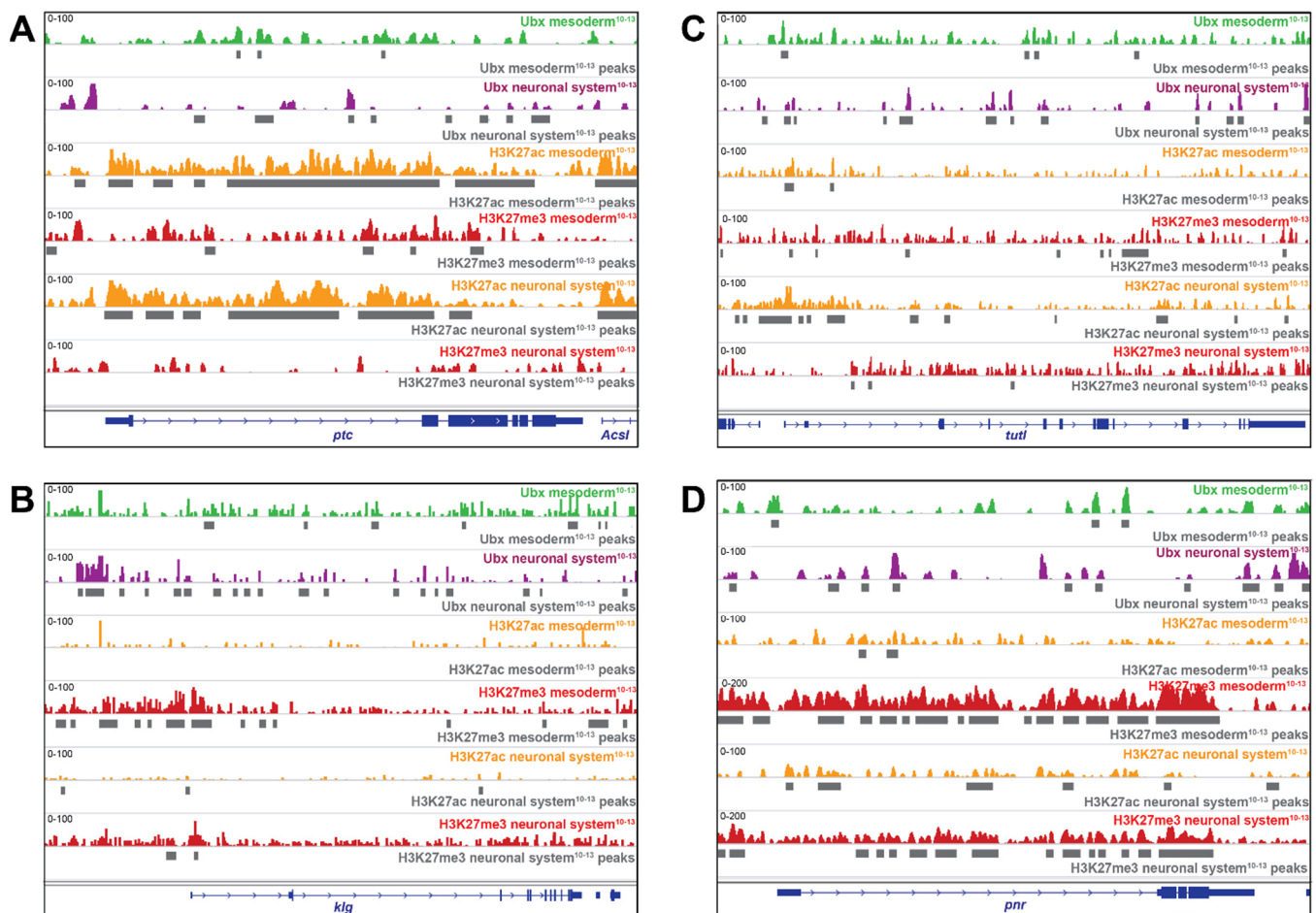


Figure S3. Genome view of selected examples to Figure 4. **(A)** Acetylation marks in the mesodermal and neuronal reads within the *patched* (*ptc*) locus. Scale: Ubx and histones 1-100. **(B)** Enriched methylation marks in mesodermal reads within the *klingon* (*klg*) locus. Scale: Ubx and histones 1-100. **(C)** Enriched acetylation marks in neuronal reads within the *turtle* (*tutl*) locus. Scale: Ubx and histones 1-100. **(D)** Methylation marks in neuronal and mesodermal reads within the *pannier* (*pnr*) locus. Scale: Ubx 1:100, acetylations 1-100, methylations 1:200. Genome viewer annotations: Green: Ubx mesodermal reads stages 10-13, purple: Ubx neuronal reads stages 10-13, orange: H3K27ac mesodermal or neuronal reads stages 10-13, red: H3K27me3 mesodermal or neuronal reads stages 10-13, gray boxes: respected accepted peaks, blue: coding region.

Table S1. Characterization of the three different categories in Figure 2. Results were obtained from the DiffBind analysis.

	mesoSpec	common genes	neuroSpec
Category of genes (Enrichment according to WEADE)	Metabolism Trafficking transport Differentiation	Differentiation Stimulus Signalling pathways	Metabolism Differentiation Stimulus
Number of peaks	2589 (single: 931, multiple: 1676)	11772 (single: 1062, multiple: 10710)	4690 (single: 1936, multiple: 2754)
Location of peaks	Upstream: 42,31 Inside: 25,82 Downstream: 31,87	Upstream: 29,99 Inside: 49,23 Downstream: 20,78	Upstream: 25,53 Inside: 57,75 Downstream: 16,72
Biological GO-terms (top three hits)	Stress response to cadmium ion Epithelial to mesenchymal transition Negative regulation of membrane potential	Mesodermal fate commitment Neuroblast development Negative chemotaxis	Anion homeostasis Basement membrane assembly TOR signalling
molecular GO-terms (top three hits)	Juvenile hormone response element binding Adenosine kinase activity Oxidized DNA binding	Cell adhesion molecule binding DNA-binding transcription activator activity Actin binding	ABC-type xenobiotic transporter activity Xenobiotic transmembrane transporter activity Nucleoside binding