

Figure S1

Head malformations in *Tasp1*^{-/-} mice in mixed genetic background (129SvJ:C57Bl/6). **(A)** Skulls of *WT* and *Tasp1*^{-/-} newborns (129SvJ:C57Bl/6) (N2), stained with alizarin red, show a marked difference in size and dimensions. The average ratios of skull height to its length are shown. ***p* < 0.01, unpaired two-tailed Student's *t*-test. **(B)** Regions of the jaw and tongue of E14.5 *WT* and *Tasp1*^{-/-} embryos are shown by H&E in sagittal sections. Note the difference in size of the tongues denoted by yellow asterisks.

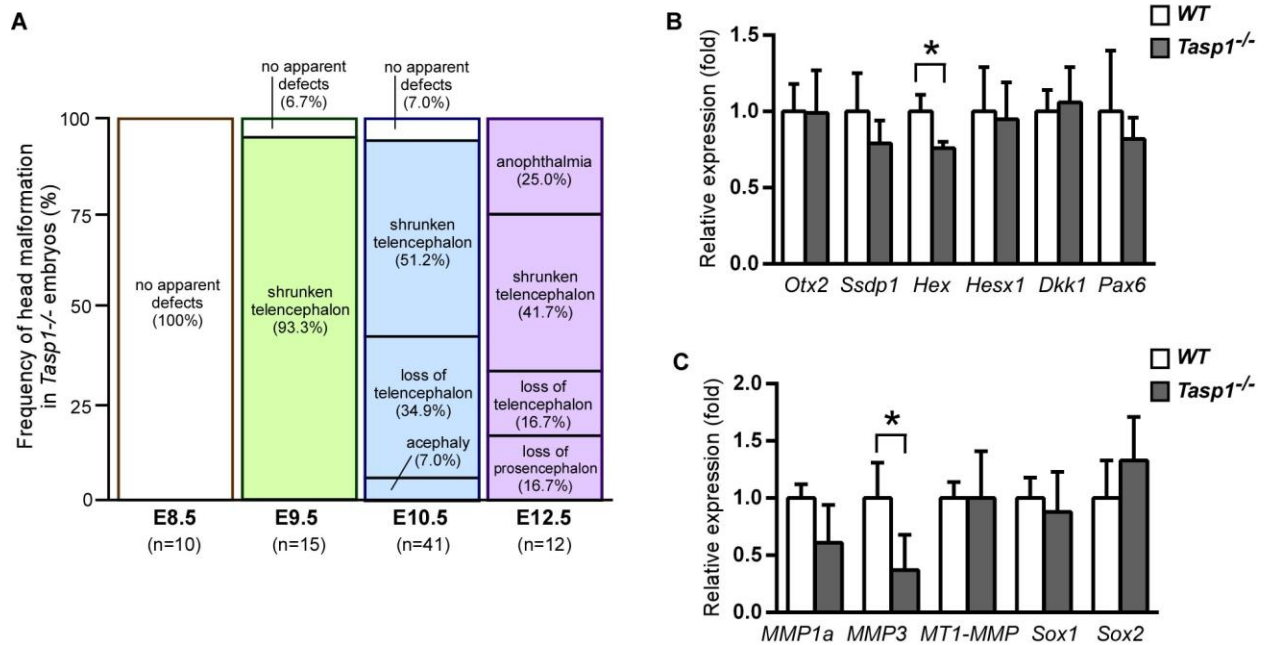


Figure S2

Craniofacial malformations in *Tasp1*^{-/-} mice during embryogenesis. **(A)** Frequencies of the various head malformations observed in *Tasp1*^{-/-} embryos at E8.5-E12.5. **(B)** Expression of key genes associated with head formation. Quantitative RT-PCR analyses of the indicated genes were performed using RNA isolated from *WT* and *Tasp1*^{-/-} E9.5 embryo head. n=3-6 (*TFIIA*^{nc/nc}) and n=3 (*WT*). Error bars represent SD. *p < 0.05, unpaired two-tailed Student's t-test. **(C)** Quantitative RT-PCR analyses of *MMPs* and *Sox* genes for *WT* and *Tasp1*^{-/-} E10.5 embryo head RNA. n=3-5 (*TFIIA*^{nc/nc}) and n=3-4 (*WT*). Error bars represent SD. *p < 0.05, unpaired two-tailed Student's t-test.

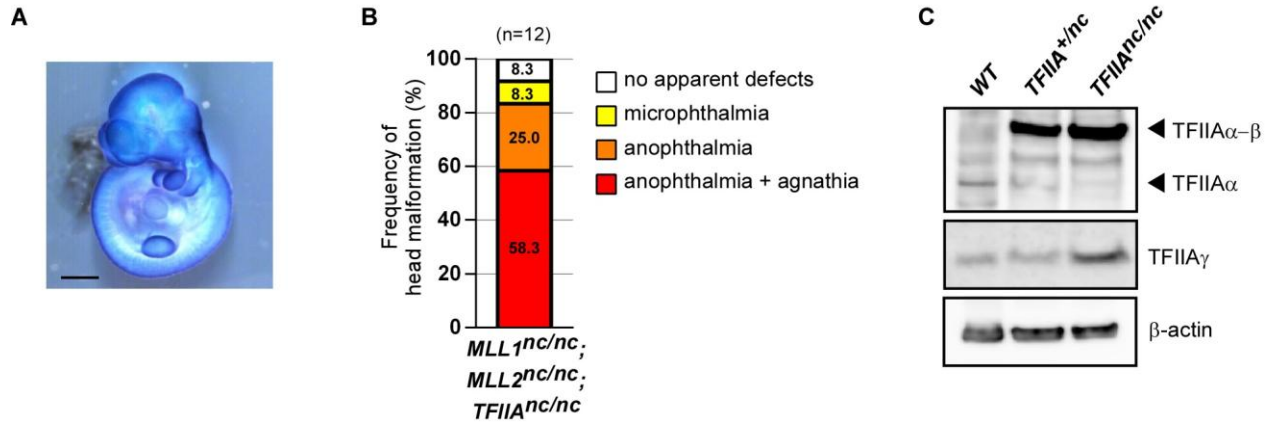


Figure S3

(A) Whole mount in situ hybridization with *TFIIA* α - β antisense probes on E10.5 WT embryo. (B) The frequencies of head malformations in E14.5 *MLL1*^{nc/nc}; *MLL2*^{nc/nc}; *TFIIA*^{nc/nc} embryos. (C) Immunoblots detecting *TFIIA* α - β , *TFIIA* α , *TFIIA* γ , and β -actin in lysates from WT, *TFIIA*^{+nc}, and *TFIIA*^{nc/nc} E10.5 embryo heads. In contrast to *TFIIA* α - β , *TFIIA* γ is not markedly stabilized in the *TFIIA*^{+nc} lysate.

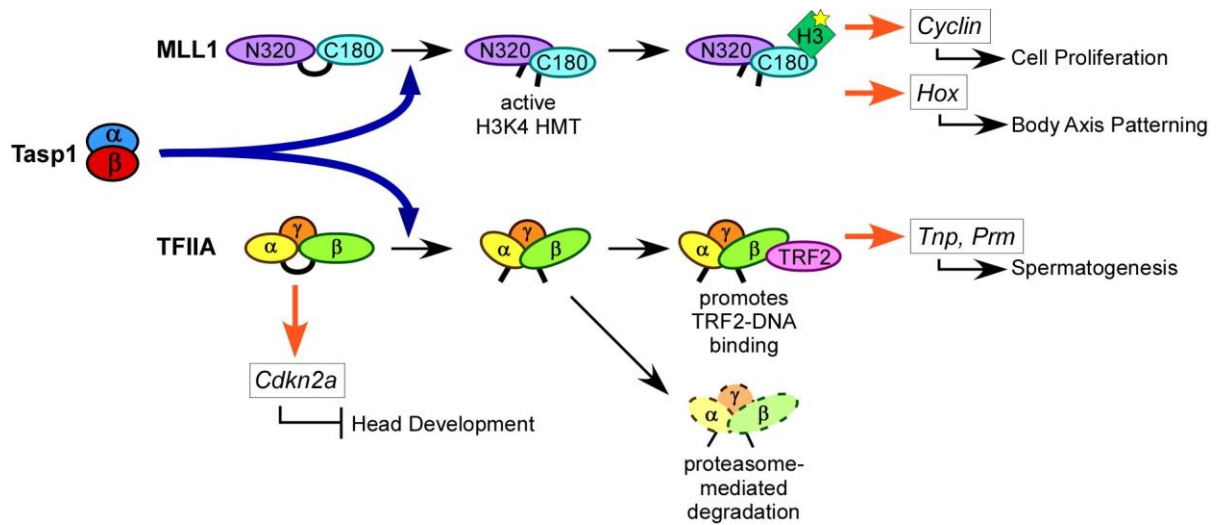


Figure S4

Summarized diagram of the biological functions of Taspase1 in embryogenesis. Taspase1-mediated proteolysis of MLL1 promotes maturation of MLL1's histone methyltransferase activity, which in turn, leads to upregulation of *Cyclin* and *Hox* genes via histone H3 lysine-4 trimethylation. In testes, Taspase1-mediated proteolysis of TFIIA promotes targeting of TRF2 to the promoters of spermiogenic genes, *Tnp* and *Prm*, to drive spermatogenesis. During head morphogenesis, this Taspase1-mediated proteolysis of TFIIA induces TFIIA susceptibility to proteasome-mediated degradation, thereby limiting transcriptional activation of *Cdkn2a*.

Gene set	Size	NES	NOM p-val
RACCYCDPATHWAY	21	1.61	0.000
CELL_CYCLE_KEGG	76	1.57	0.000
HSA04115_P53_SIGNALING_PATHWAY	57	1.57	0.000
CELLCYCLEPATHWAY	20	1.55	0.000
CALCINEURINPATHWAY	18	1.54	0.000
HSA05219_BLADDER_CANCER	36	1.48	0.000
HSA05218_MELANOMA	66	1.46	0.000
HSA05214_GLIOMA	58	1.45	0.000
RHOPATHWAY	27	1.45	0.101
CARM_ERPATHWAY	24	1.43	0.080
HSA04150_MTOR_SIGNALING_PATHWAY	42	1.42	0.095
G1PATHWAY	23	1.42	0.080
G2PATHWAY	19	1.40	0.000
CCR3PATHWAY	20	1.31	0.204
ATMPATHWAY	17	1.29	0.181
DEATHPATHWAY	26	1.27	0.191
HSA03022_BASAL_TRANSCRIPTION_FACTORS	28	1.25	0.083
HSA05220_CHRONIC_MYELOID_LEUKEMIA	71	1.22	0.201
HSA05223_NON_SMALL_CELL_LUNG_CANCER	48	1.22	0.107
HSA00592_ALPHA_LINOLENIC_ACID_METABOLISM	15	1.19	0.224

Table S1

GSEA list of the top 20 overrepresented gene sets in expression signals of *Taspl*^{-/-} embryo heads. Gene set sizes, normalized enrichment scores (NES), and nominal p-values (NOM p-value) are included. Gene sets related to cell proliferation are shown in bold.

Mouse <i>p16Ink4a</i> F	ATTGGGCGGGCACTGAATCTC
Mouse <i>p16Ink4a</i> R	TCTGTCTGCAGCGGACTCC
Mouse <i>p19Arf</i> F	GTTCTTGGTCACTGTGAGGATTCAGC
Mouse <i>p19Arf</i> R	CCTCTTCTCAAGATCCTCTCTAGCCTC
Mouse <i>p21Cip1</i> F	CCTGGTGATGTCCGACCTGTTC
Mouse <i>p21Cip1</i> R	CCTCTTCTCAAGATCCTCTCTAGCCTC
Mouse <i>p27Kip1</i> F	GGTCTCAGGCAAACCTCTGAGGACC
Mouse <i>p27Kip1</i> R	AGCTGTTTACGTCTGGCGTCAAG
Mouse <i>CyclinD1</i> F	CGTATCTTACTTCAAGTGCCTGCAGAAG
Mouse <i>CyclinD1</i> R	CAGGTTCCACTTGAGCTTGTTTAC
Mouse <i>CyclinE1</i> F	GGATGAGAGCAGTTCTTCTGGATTGG
Mouse <i>CyclinE1</i> R	GACACAATGGTCAGAGGGCTTAGAC
Mouse <i>CyclinA2</i> F	CACTGACACCTCTTGACTATCCAATGG
Mouse <i>CyclinA2</i> R	GCTGAAGCTTCCCTCTTAACACAGAC
Mouse <i>Otx2</i> F	TATCTAAAGCAACCGCCTTACG
Mouse <i>Otx2</i> R	AAGTCCATACCCGAAGTGGTC
Mouse <i>Ssdp1</i> F	CCACCTCACAATCCCAGCAG
Mouse <i>Ssdp1</i> R	CCTCGGGGAGGGTTCATTC
Mouse <i>Hex</i> F	CGGACGGTGAACGACTACAC
Mouse <i>Hex</i> R	CGTTGGAGAACCCTCACTTGAC
Mouse <i>Hesx1</i> F	TGAGAGCATTTTAGGACTGGACC
Mouse <i>Hesx1</i> R	GGGTGGGTTGCCATCTTTCT
Mouse <i>Dkk1</i> F	CTCATCAATTCCAACGCGATCA
Mouse <i>Dkk1</i> R	GCCCTCATAGAGAACTCCCG
Mouse <i>Mmp1a</i> F	GATGCTATAACTACATTTAGGGGAGAGGTGT
Mouse <i>Mmp1a</i> R	CTTCATAAGCAGCGTCAAGTTTAACTGGAAG
Mouse <i>Mmp3</i> F	GGAGAACATGGAGACTTTGTCCCTTTTG
Mouse <i>Mmp3</i> R	TTGGCTGAGTGGTAGAGTCCC
Mouse <i>MT1-MMP</i> F	CAGTATGGCTACCTACCTCCAGG
Mouse <i>MT1-MMP</i> R	GCCTTGCCTGTCACTTGTAACCC
Mouse <i>Sox1</i> F	ATACCGCAATCCCCTCTCAGACG
Mouse <i>Sox1</i> R	GCTATGTACAACATCCGACTCCTCTTCC
Mouse <i>Sox2</i> F	GCGGAGTGGAACCTTTGTCCG
Mouse <i>Sox2</i> R	CGGGAAGCGTGTACTTATCCTTCTTC
Mouse <i>Cdkn2a</i> upstream (ChIP) F	CTATGGCCCAGTTTGAGCTC
Mouse <i>Cdkn2a</i> upstream (ChIP) R	GCTGAGATGATTCGGTGGAT
Mouse <i>p19Arf</i> TSS (ChIP) F	AAGCTTTCCTCCGCGACT
Mouse <i>p19Arf</i> TSS (ChIP) R	CATCTTTGCTCCACGCCATCT
Mouse <i>p16Ink4a</i> TSS (ChIP) F	TTCAGGGCAAATAGCGCCACCTAT
Mouse <i>p16Ink4a</i> TSS (ChIP) R	TGGGTCCCTCCTTCTTCTCTGA
Mouse <i>p21Cip1</i> TSS (ChIP) F	CCACTGGACCTAGCAATTCACACGTATTT
Mouse <i>p21Cip1</i> TSS (ChIP) R	AGAAGTAGGAGTCACCGTCCTGTTTACC

Table S2

The oligonucleotide sequences utilized in quantitative RT-PCR analysis. F, forward; R, reverse.