

Figure S1. Top candidate genes identified by RNA-Seq screen (red) converge onto the Hippo signaling pathway (turquoise). Kibra activates Hippo signaling by interactions with mer and ex (Genevet et al., 2010). Activation of Hippo signaling prevents yki from entering the nucleus and turning on transcriptional targets, including kibra. All other candidate genes instead activate yki mediated transcription by either interacting directly with its transcriptional coactivator sd/TEAD2 (sox21b ortholog SOX12 (Bhattaram et al., 2010)) or by inhibition higher up in the signaling cascade (Fan et al., 2013; Ribeiro et al.). β -arrestin (arr2) and PHGDH have not been shown to directly inhibit Hippo signaling, but they are known interactors of the inhibitors PP2A and aPKC (PKCzeta) (Beaulieu et al., 2005; Ma et al., 2013). LDHA (Imp13) has not been shown to act on Hippo signaling, but instead may be a transcriptional target (Xiang et al., 2015).

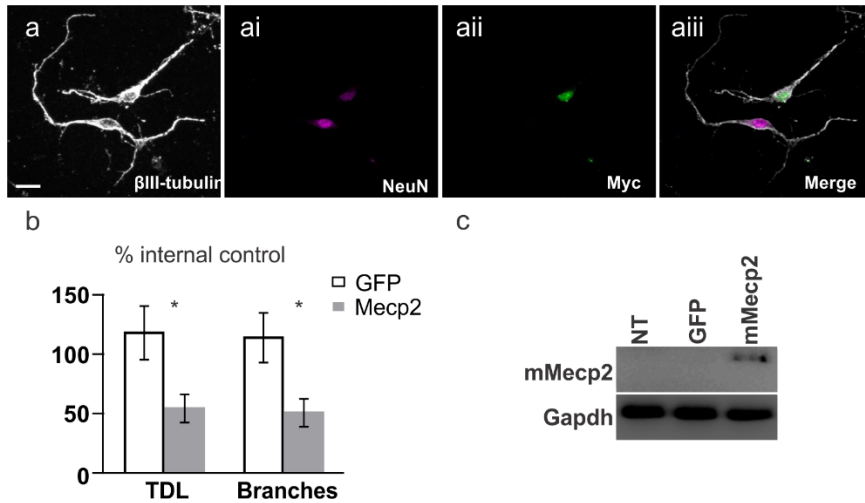


Figure S2. Overexpression of mMeCP2 using AAV causes the same dendritic phenotype as electroporation method. a. Representative image of AAV-mMeCP2-myc transduced neuron in at 4DIV in culture shows localized nuclear expression (a ii). b. Quantification of total dendritic length (TDL) and number of branches following AAV transduction ($*p < 0.05$, Bonferroni t-test after 2-way ANOVA, $F_{1,36} = 13.09$, $p < 0.001$, $n = 10$ cells per group). c. Representative Western blot showing mMeCP2 overexpression following in primary cortical neurons following AAV-mMeCP2-myc transduction. mMeCP2 is expressed at low levels during early postnatal cortical development (Kishi and Macklis, 2004); thus, mMeCP2 was only detected with AAV induced overexpression. Scale bar represents 20 μ m.

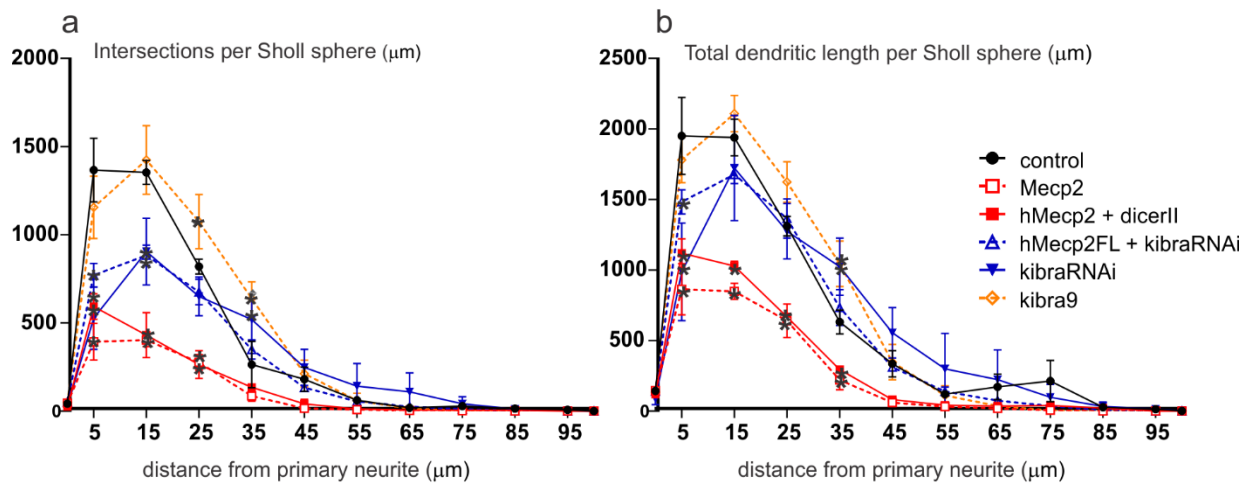


Figure S3. Sholl analysis of *Drosophila* MN5 dendritic morphology with targeted genetic manipulations. a. Quantification of the number of intersections or total dendritic length per 10µm Sholl sphere (* $p < 0.05$, Bonferroni t-test after two-way ANOVA, $F_{5,192} = 38.65$, $p < 0.0001$, $n = 3-7$ cells per group). b. Quantification of total dendritic length per Sholl sphere (* $p < 0.05$, Bonferroni t-test after two-way ANOVA, $F_{5,192} = 31.35$, $p < 0.001$, $n = 3-7$ cells per group). The entire primary neurite of MN5 was defined as the tree origin for Sholl analysis.

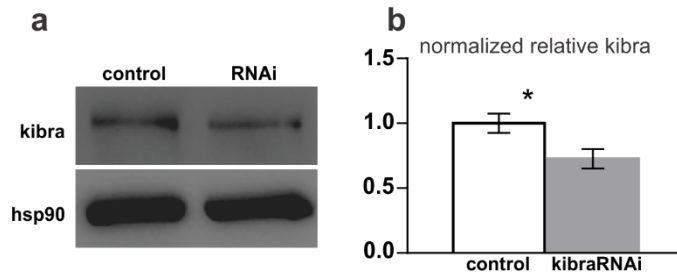


Figure S4. *kibra*RNAi moderately decreases dkibra levels in *Drosophila* brain. a. Representative Western blot for dkibra following pan neuronal *kibra* knockdown. b. Quantification of Western blot analysis (* $p < 0.05$ unpaired t -test, $t_{23} = 2.59$, $n = 12-13$ per group).

Table S1.**a. List of genes differentially expressed with pan neuronal human MECP2 expression in the adult fly brain**

Flybase ID	Human orthologs	log2- Fold Change	FDR corrected p	Mouse array matches
Genes with identified human orthologs				
arr2	ARRB2, ARRB1, SAG, ARR3 PNLIP, PNLIPRP1, PNLIPRP3,	1.610	0.001	ARRB2 in hyp., SAG in hipp. (9wk)
CG5966	PNLIPRP2	3.377	0.004	PNLIPRP2 in hipp. (4wk)
pepck	PCK2, PCK1	1.676	0.004	PCK2 in hyp.
rh2	COMMD2, OPN4	1.377	0.007	OPN4 in hipp. (4wk)
pi3k92e	PIK3CD, PIK3CB, PIK3CA, PIK3CG	1.385	0.008	PIK3CG in hyp. & cb.
CG11486	PAN3	1.580	0.008	PAN3 in hipp. (4 & 9 wk)
cka	STRN4, STRN, STRN3	2.022	0.013	STRN4 in hyp.
sox21b	SOX14, SOX21, SOX12	1.464	0.024	SOX 12 in cb.
dysc	DFNB31, PDZD7	1.242	0.040	PDZD7 in hyp. & hipp.
ppt2	PPT2, EGFL8	1.716	0.042	PPT2 in hyp.
arpc1	ARPC1A, ARPC1B	2.546	0.042	ARPC1A in hyp.
kibra	WWC1 (KIBRA), WWC2	1.217	0.049	WWC1 in cb.
CG3328	MYRF, MYRFL	1.743	0.001	
CG6287	PHGDH	1.722	0.001	
hr4	NR6A1	2.706	0.003	
impL3	LDHA, LDHB, LDHAL6A	2.988	0.025	
CG7332	FAM188A	1.278	0.027	
sec31	SEC31A, SEC31B	1.428	0.049	
CG18095	LRRTM3	6.330	0.050	
CG3625	AIG1, ADTRP	-1.490	0.011	
Genes without identified human orthologs				
irc		1.971	0.000	
CG13722		3.990	0.002	
CG11697		2.115	0.005	
CG14982		1.570	0.006	
mtk		5.463	0.015	

CG32240		7.373	0.024
drs		4.017	0.033
CG15784		3.527	0.042
CG10332		5.878	0.049
totA		-3.743	0.000
totC		-7.476	0.040
fok		-1.250	0.040

b. List of genes differentially expressed with hR106W expression, but not hMECP2FL

Flybase ID	Human orthologs	log2- Fold Change	FDR corrected p	Mouse array matches
Su(Ste):CR42418		-2.921	0.000	
bt	TTN	-1.695	0.016	

c. List of genes differentially expressed with both hMECP2 and hR106W expression

Flybase ID	Human orthologs	log2- Fold Change	FDR corrected p	Mouse array matches
socs16D	SOCS7	1.705	0.000	SOCS7 in hyp.
CG12241	SGSM3	1.842	0.001	
CG7582	TMEM86A, TMEM86B	1.543	0.012	
CR40712		-2.624	0.000	

SUPPLEMENTARY MATERIAL REFERENCES

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