

# Potential of Small Molecule Inducers in Cell-Based Therapeutics



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# Muscle Wasting Disorder

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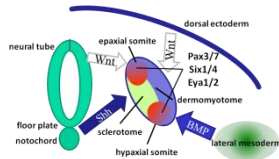
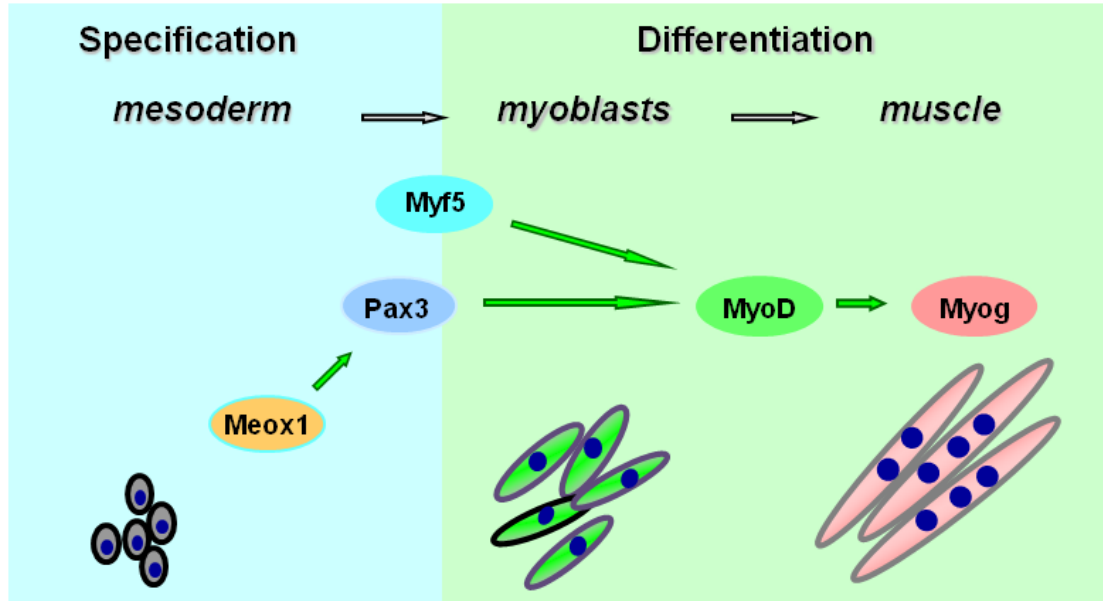


**Aging**  
**Cancer**  
**AIDS**

**Congestive Heart Failure**  
**Chronic Obstructive Pulmonary Diseases**

**Degenerating**  
**Cachexia inducing**  
**Mobility / Neurogenic**

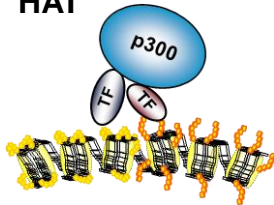
# Myogenic Differentiation



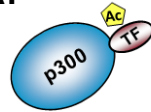


# Transcriptional Coactivator p300

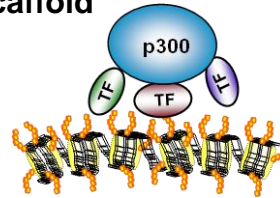
HAT



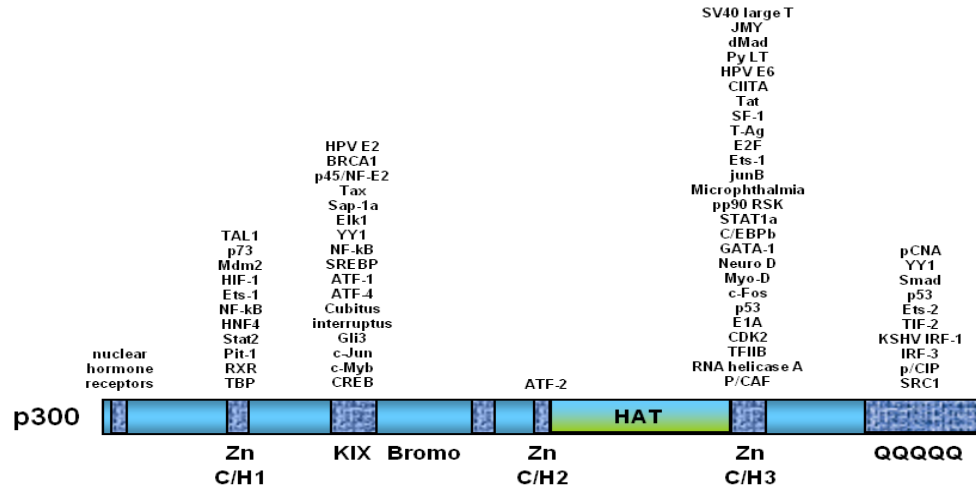
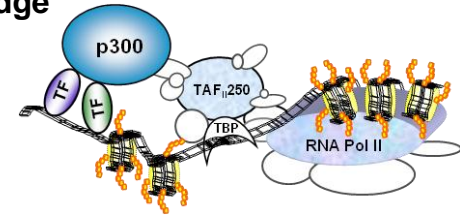
FAT



Scaffold

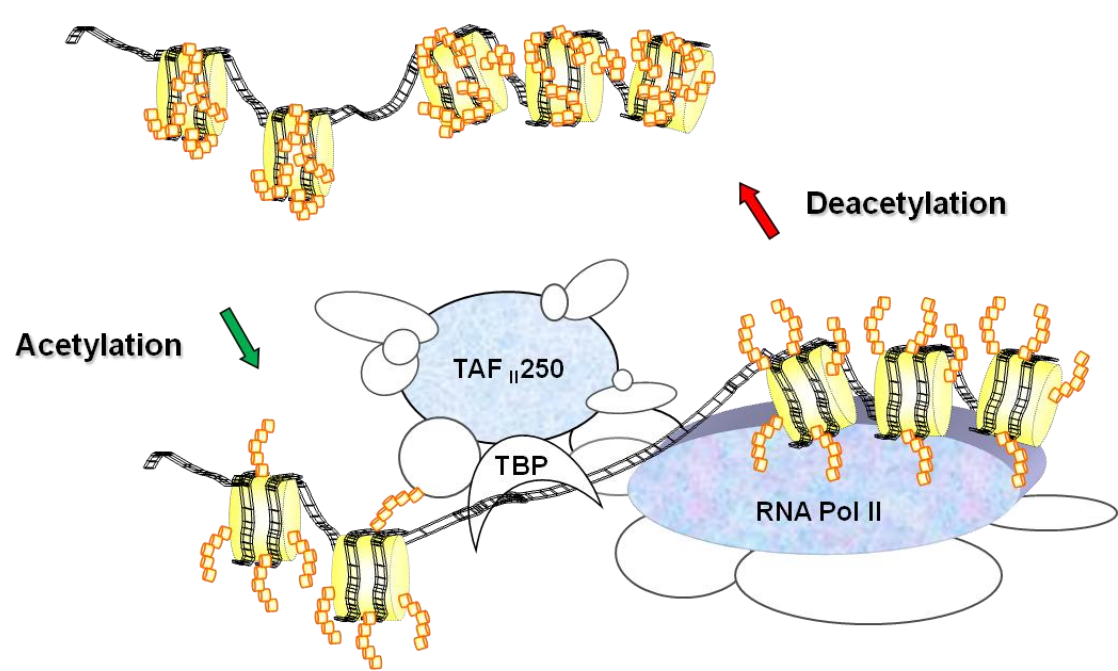
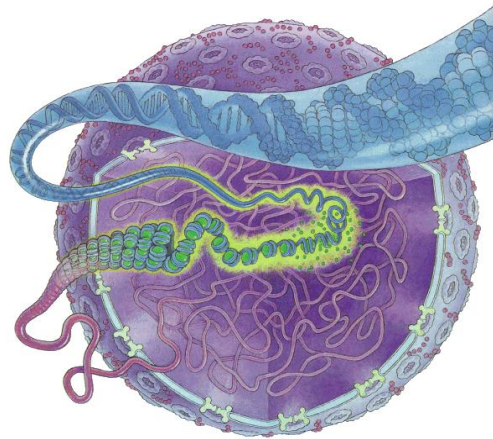


Bridge

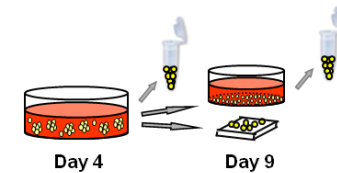
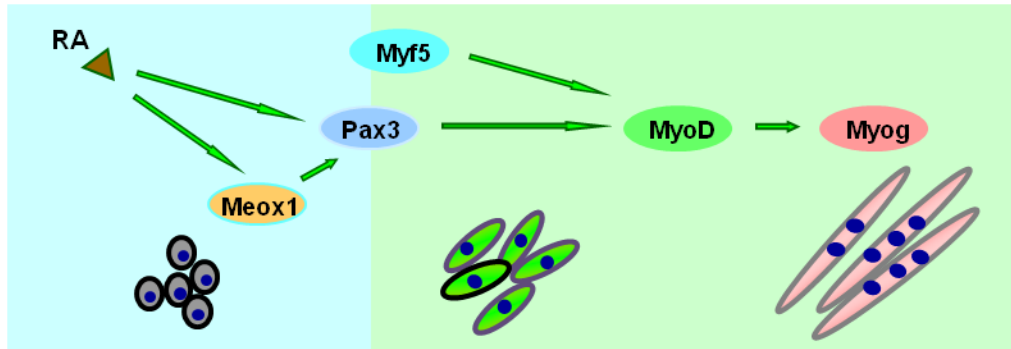
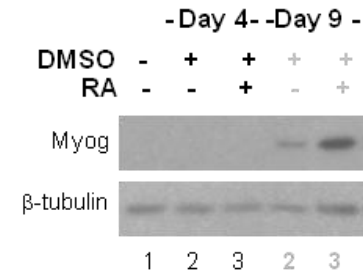
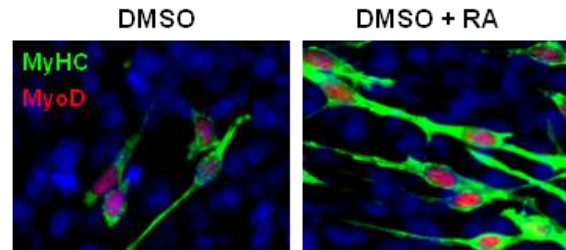
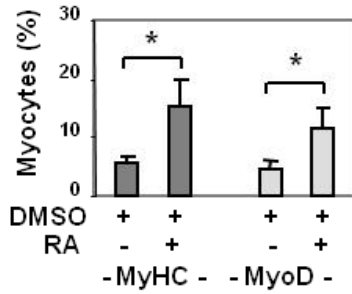




# Histone Acetylation & Gene Activation

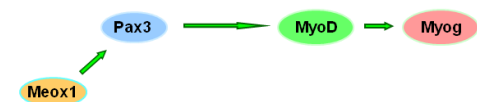
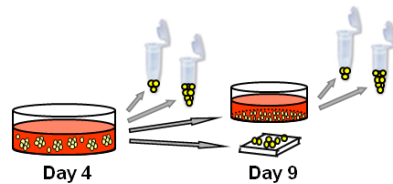
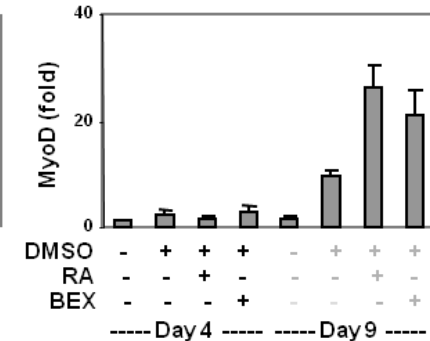
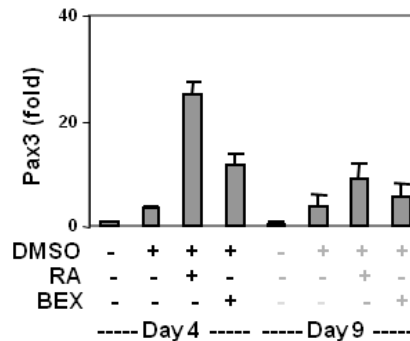
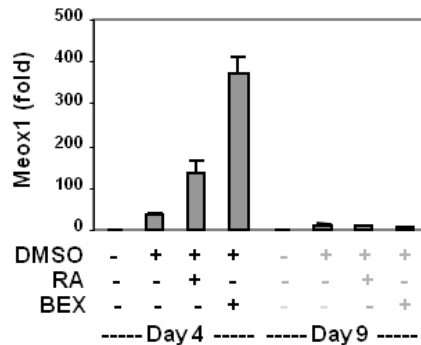
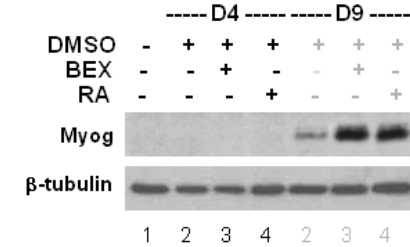
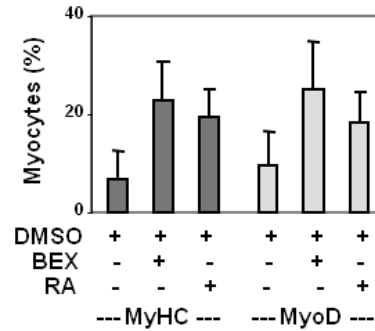
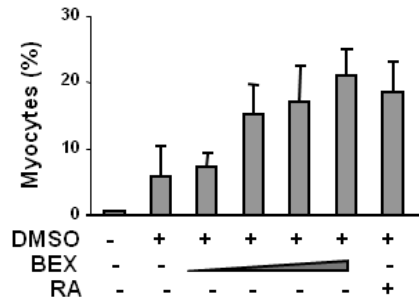
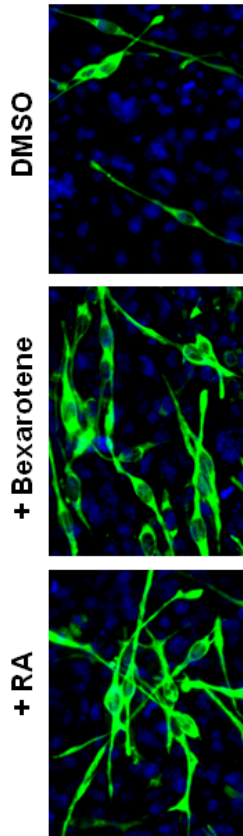


# Small molecule inducers

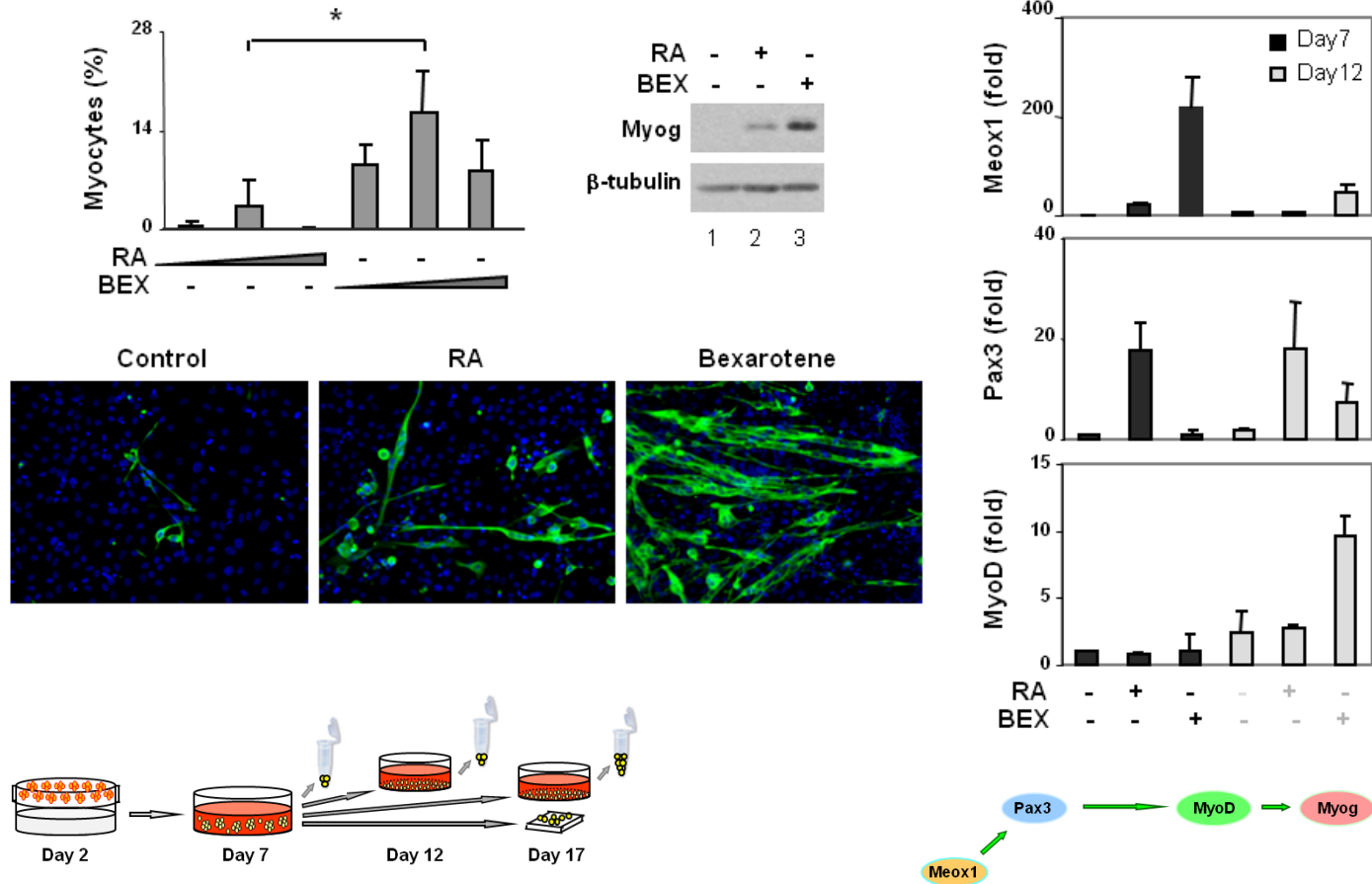




# Bex @ myogenic differentiation



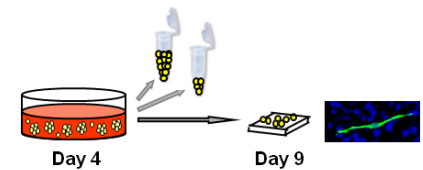
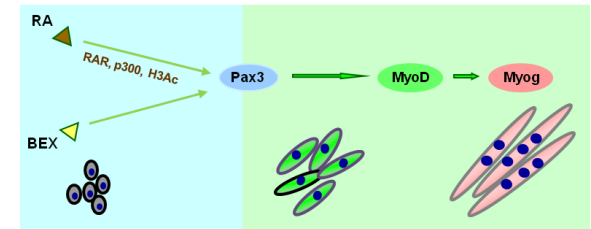
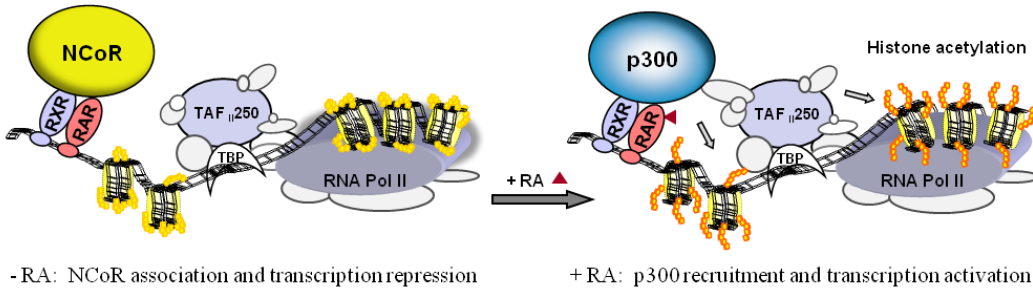
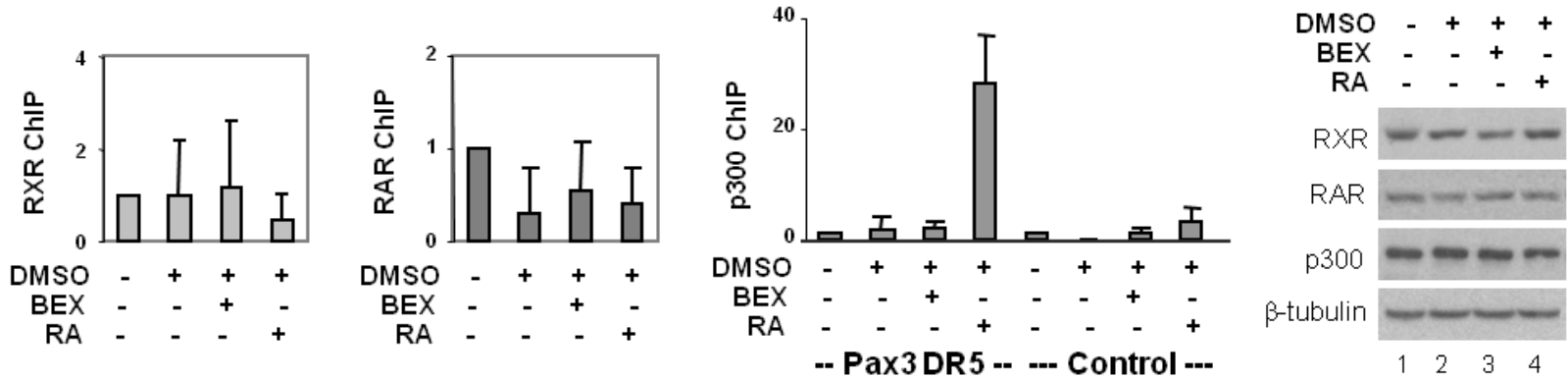
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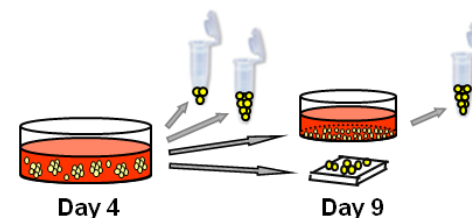
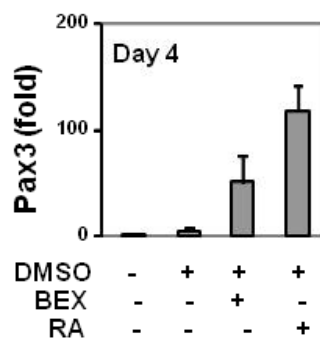
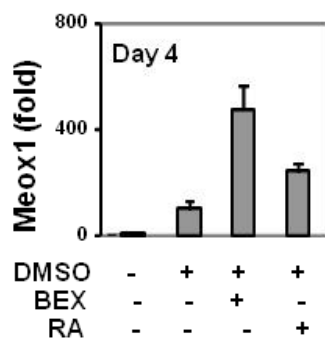
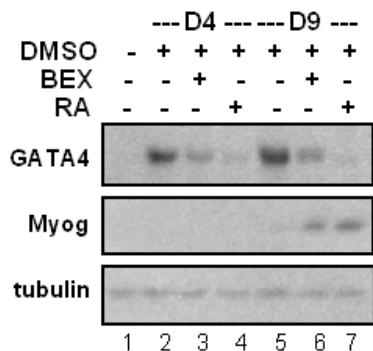
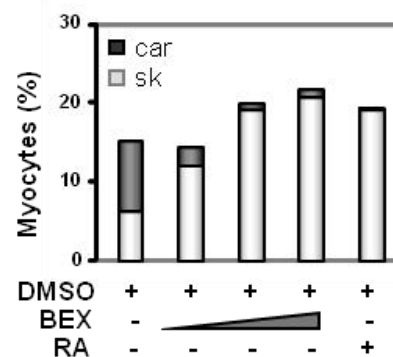
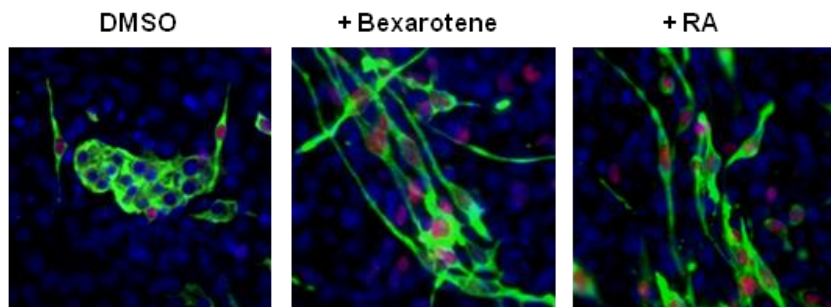




# RA signaling @ a Pax3 DR5 locus

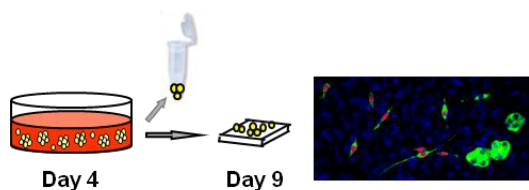
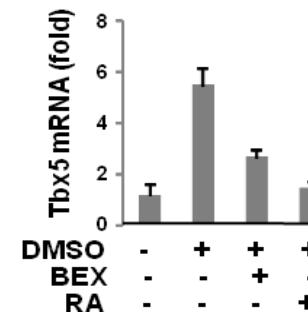
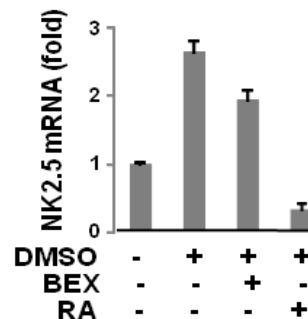
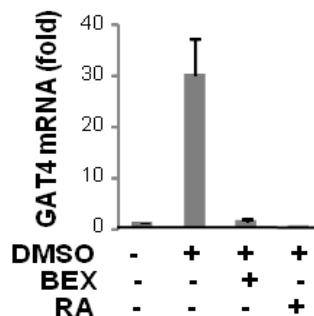
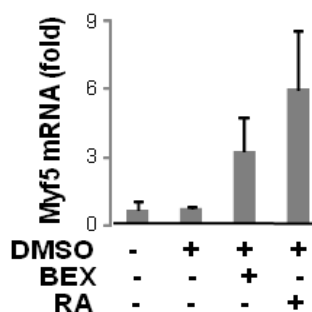
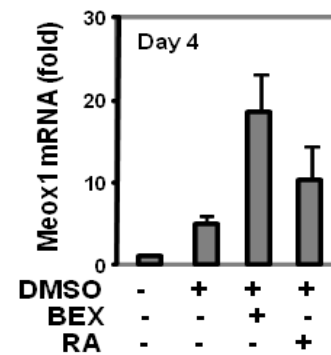
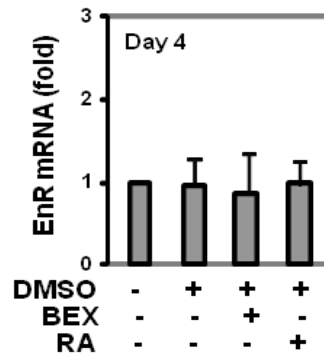
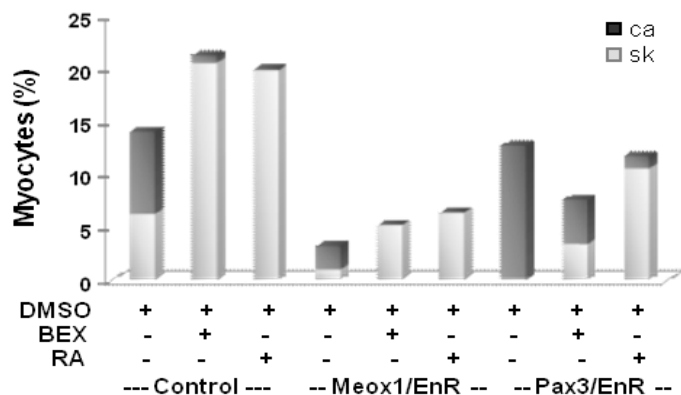


# Cardiac and skeletal conversion



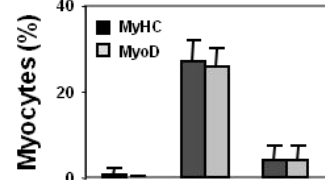
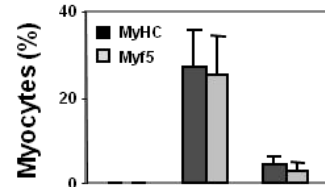
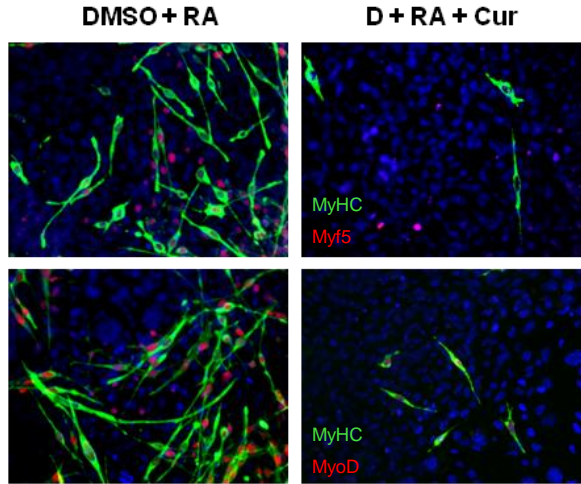


# Pax3 in lineage specification

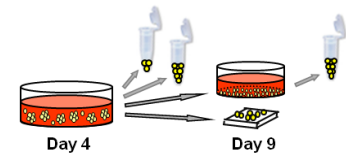
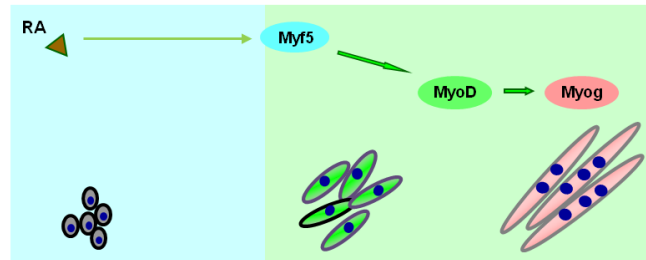
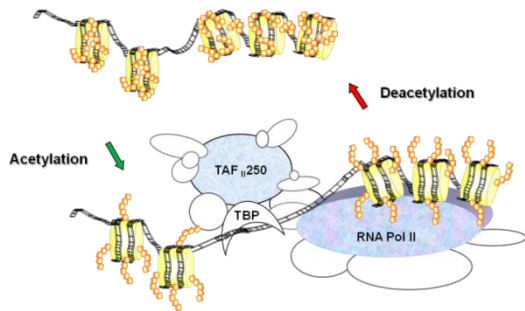
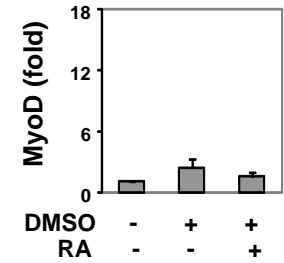
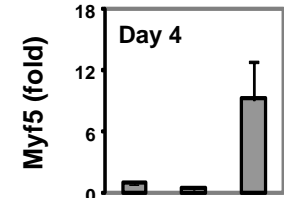
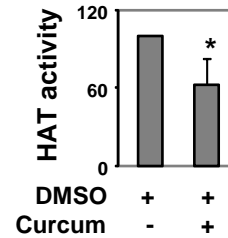
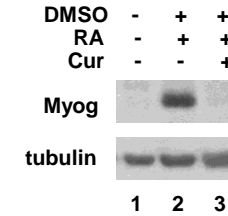




# Cur @ myogenic differentiation

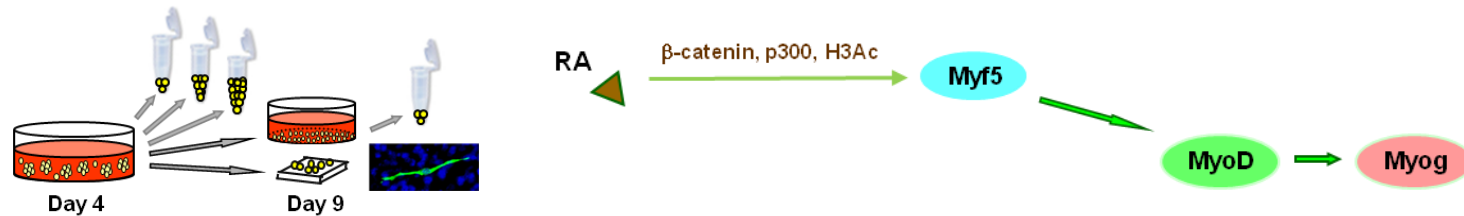
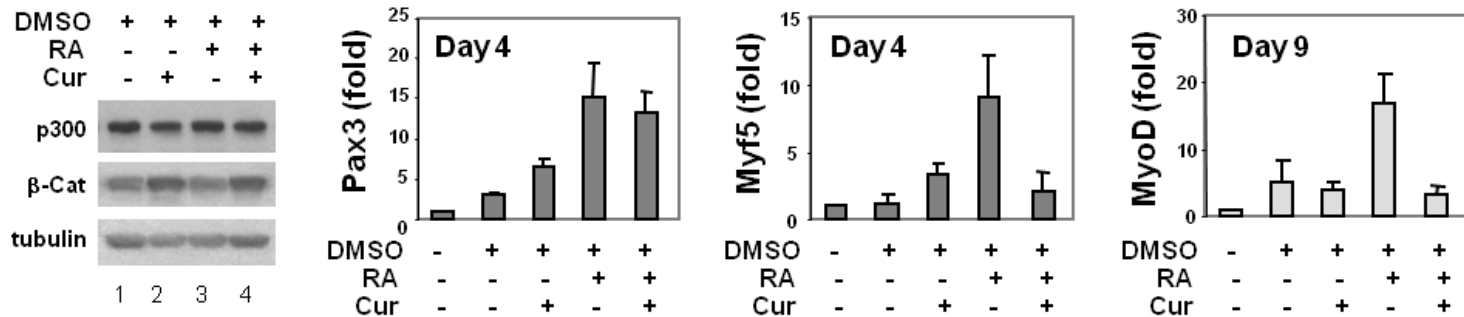
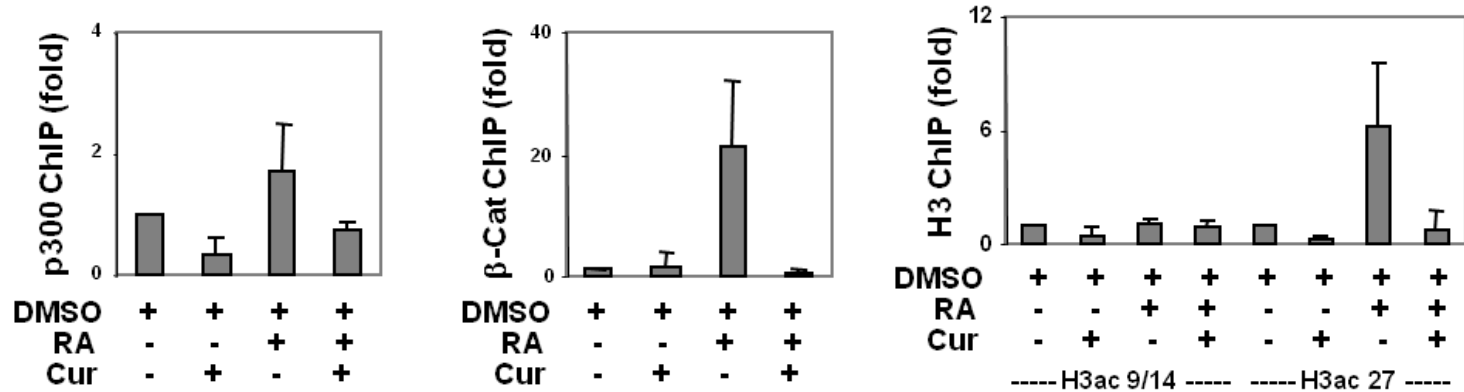


DMSO	-	+	+
RA	-	+	+
Cur	-	-	+

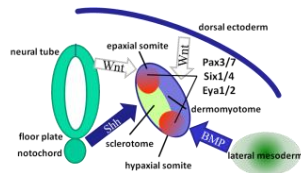
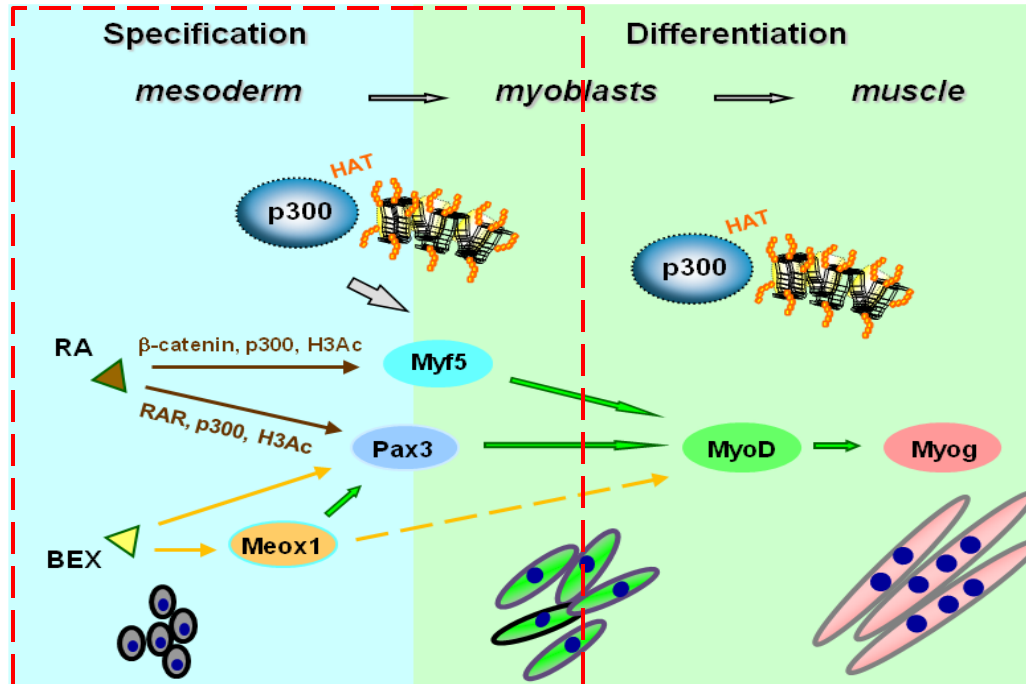




# The Myf5 Early Enhancer



# Mechanisms of Specification



Chen and Li, *Cell & Bioscience* 2013

Francetic and Li, *Transcription* 2011

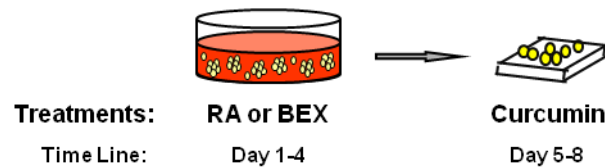
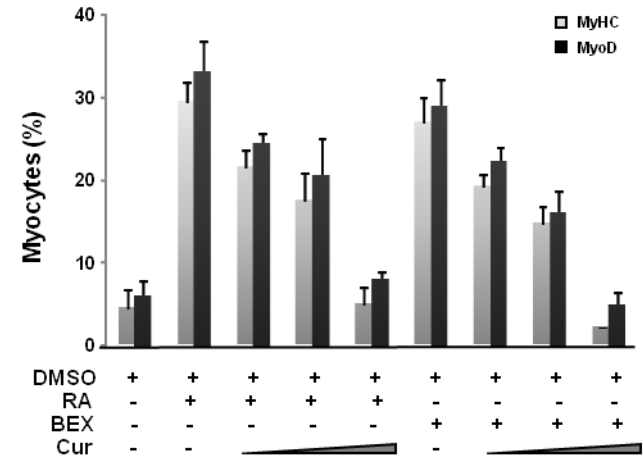
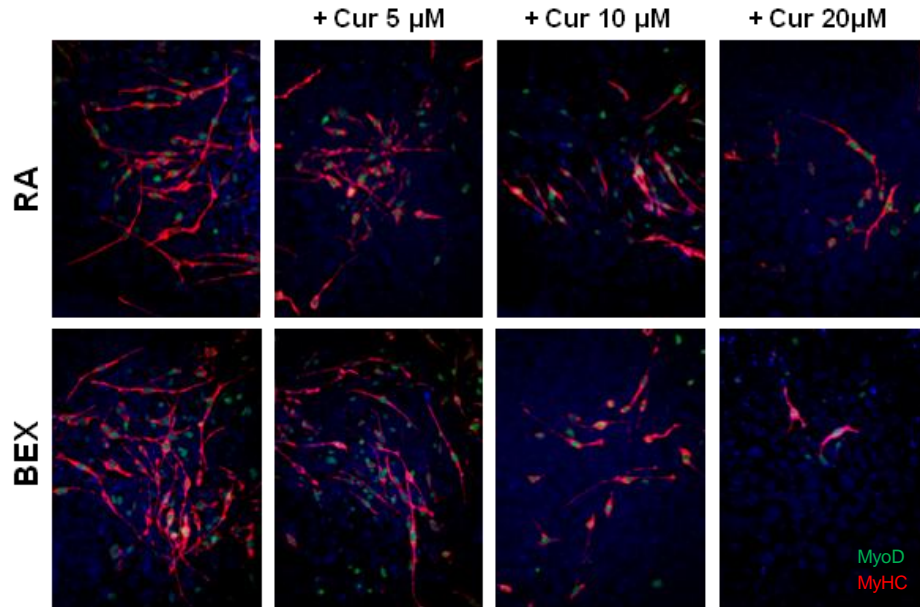
Le May et al. *JBC* 2011

Francetic et al. *Mol Biol* 2012

Li et al. *Sci Rep* 2013

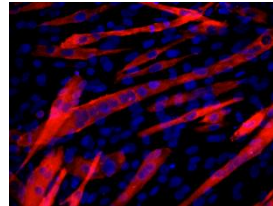
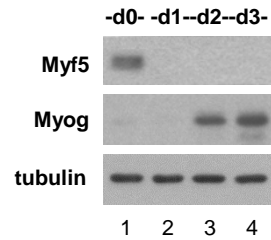


# Cur @ MyoD gene expression

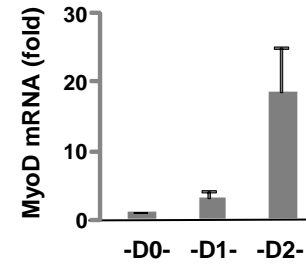




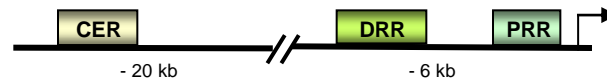
# Myoblast differentiation



Day 3

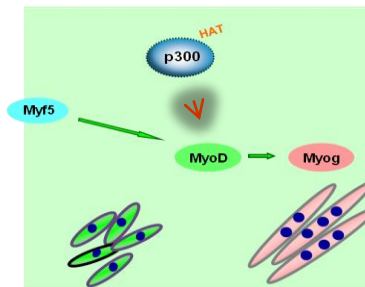
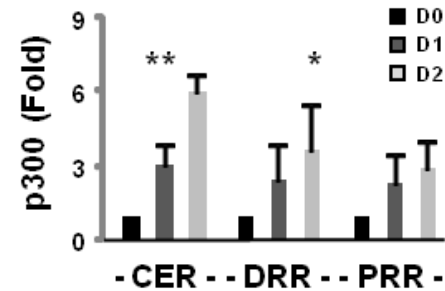
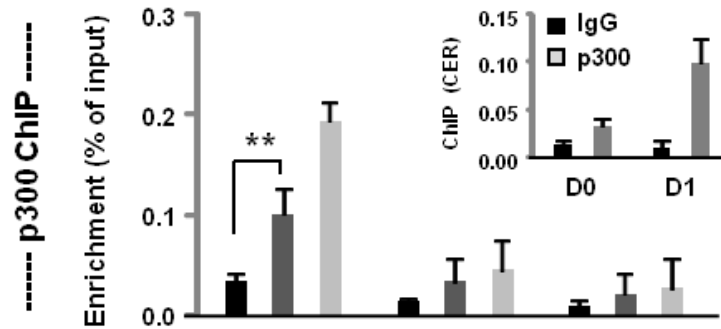


## *Myod1* locus



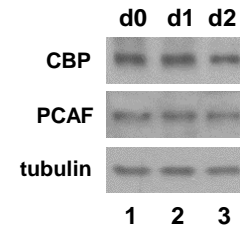
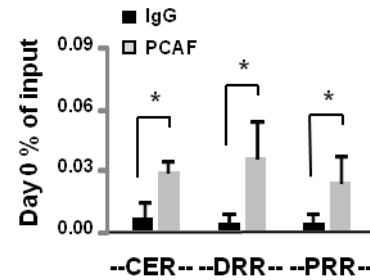
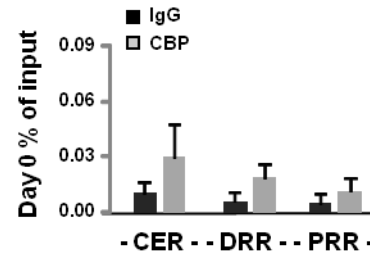
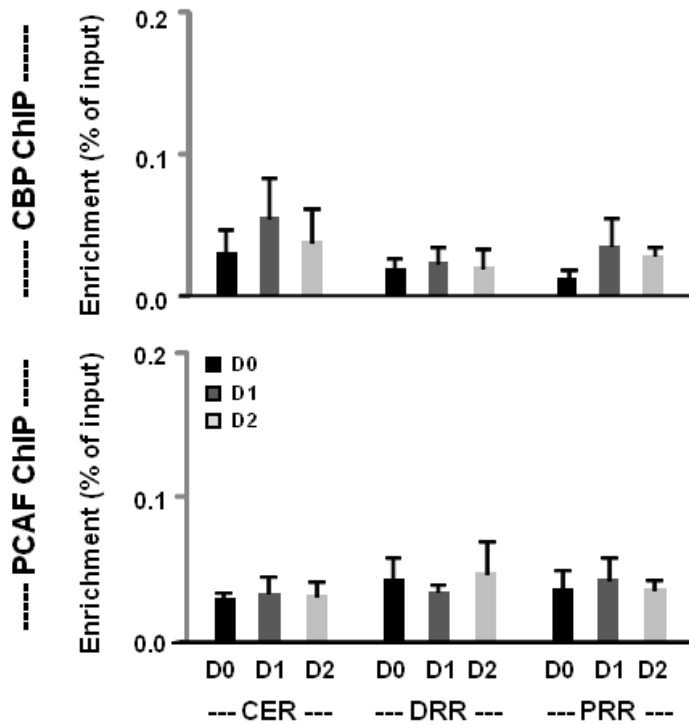


# Stepwise p300 association

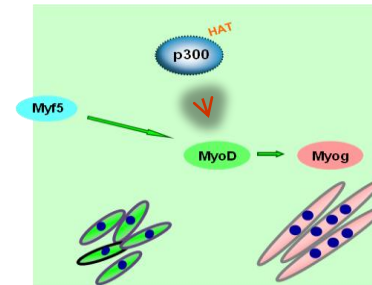
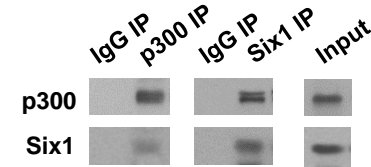
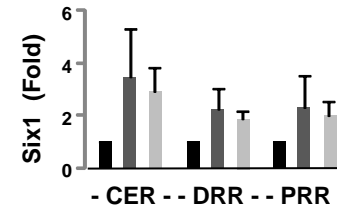
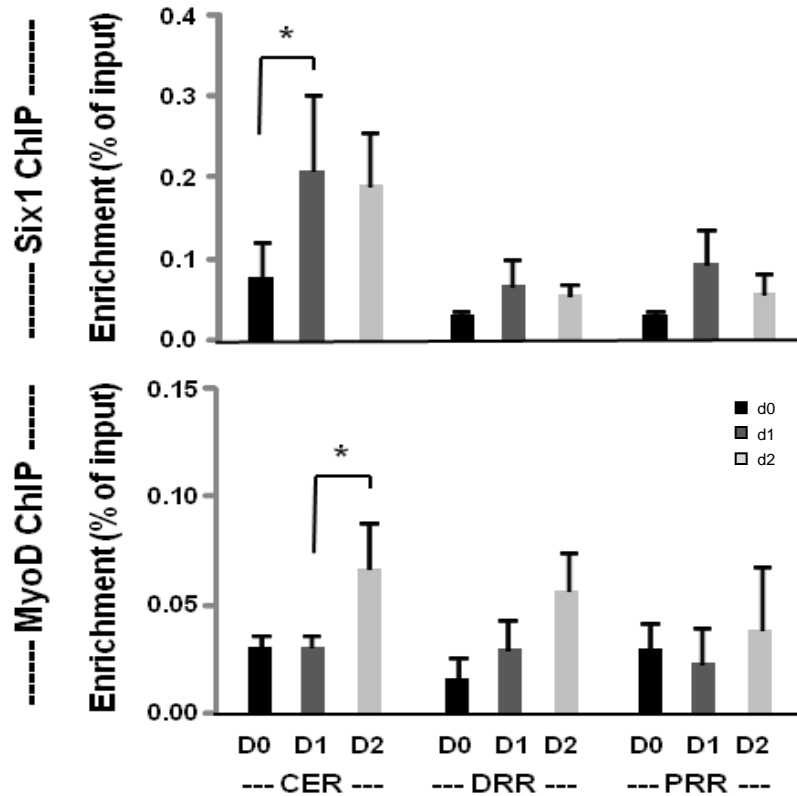




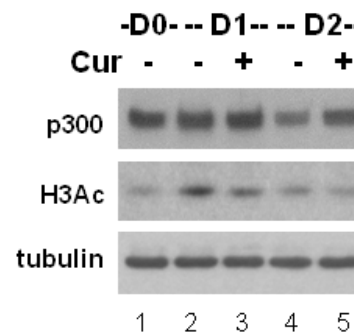
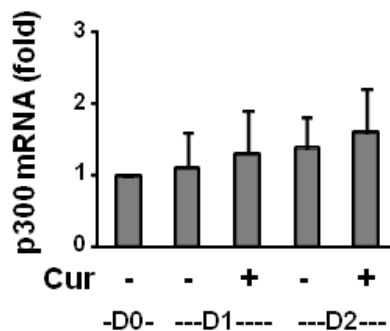
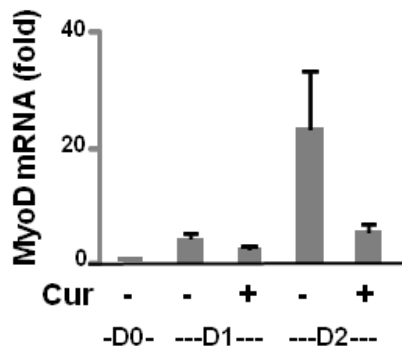
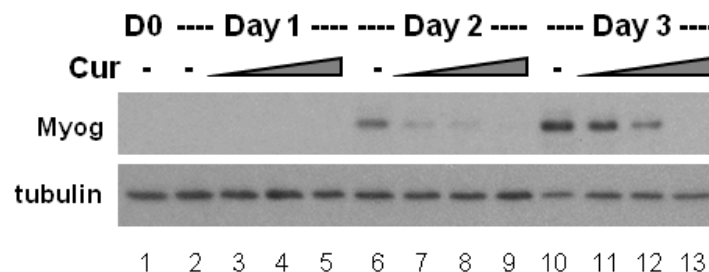
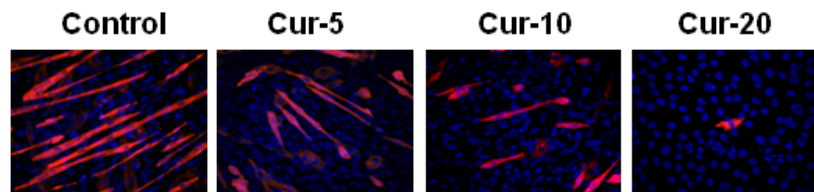
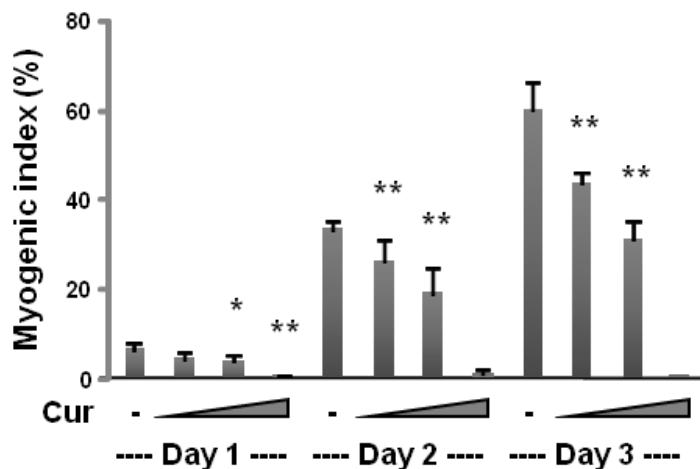
# Association of other HATs



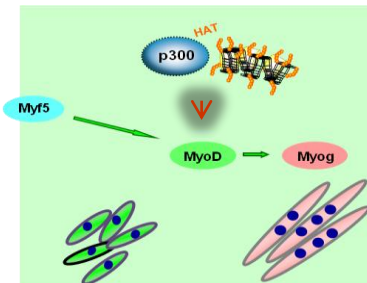
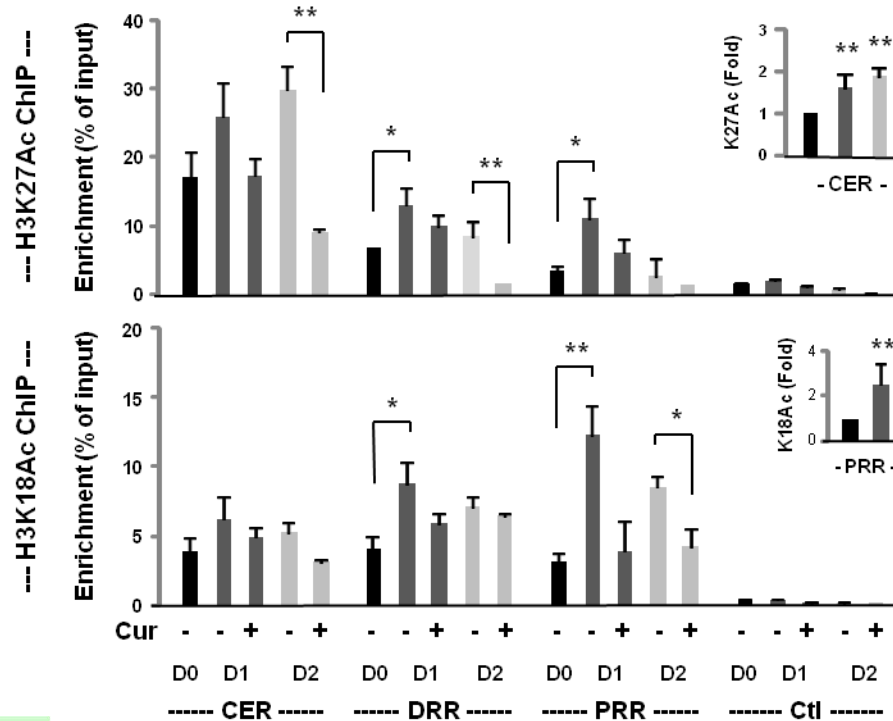
# Putative p300 recruiters



# HAT activity in myogenesis

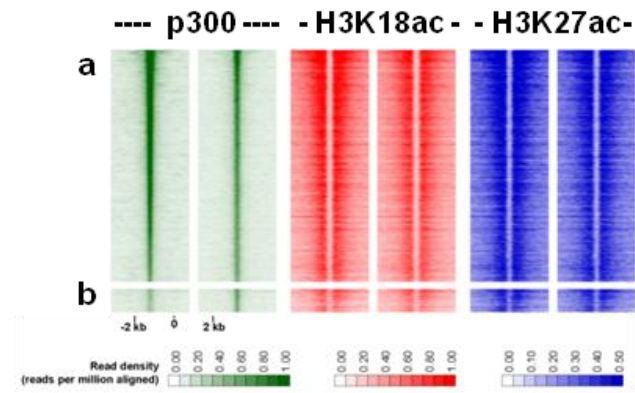
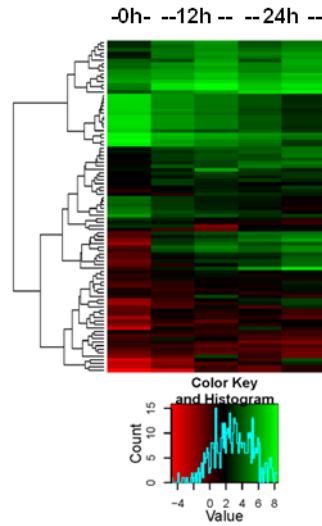


# H3K27 & H3K18 acetylation



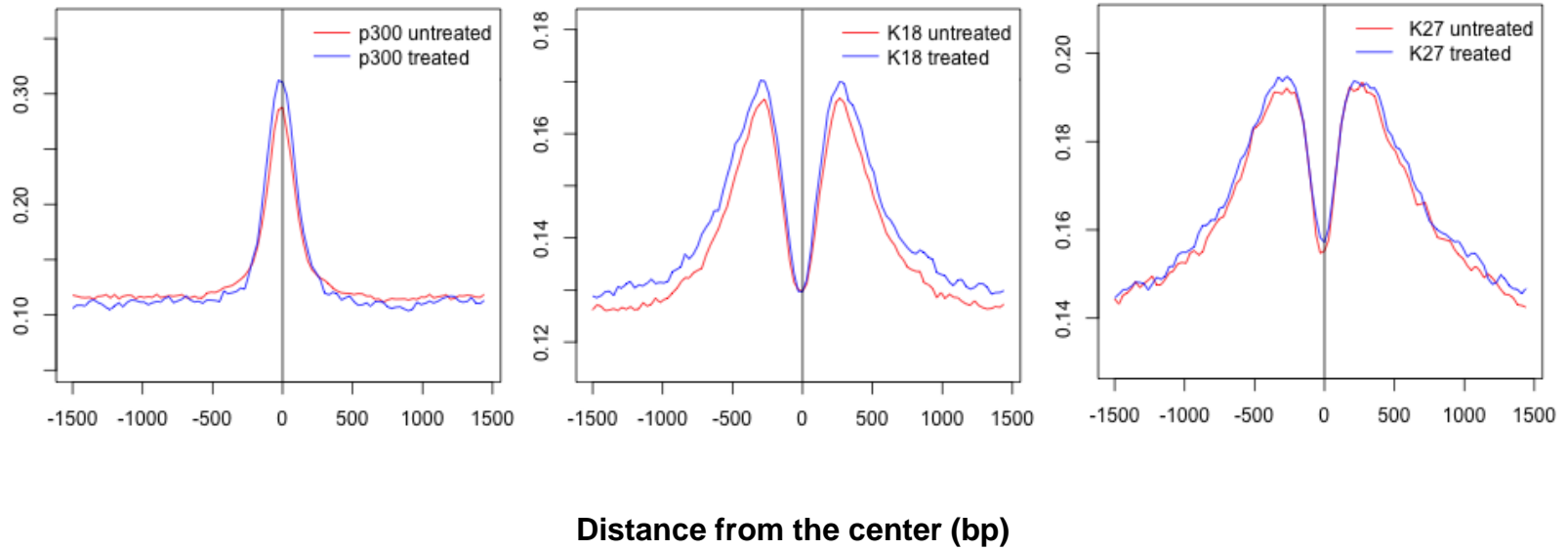


# RNA-seq & ChIP-seq



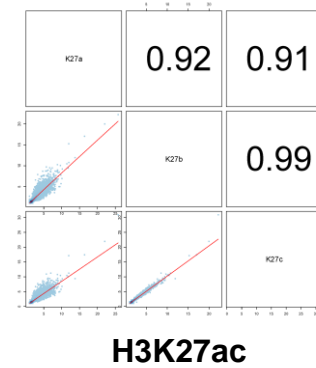
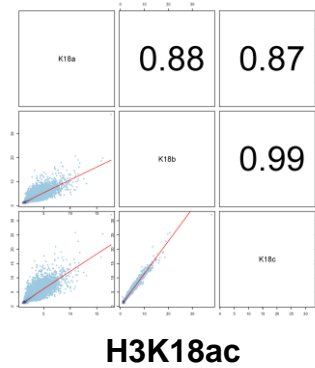
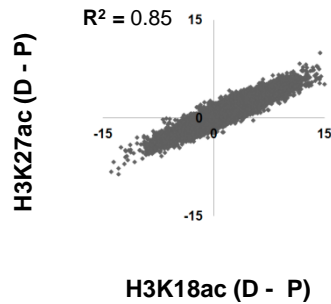
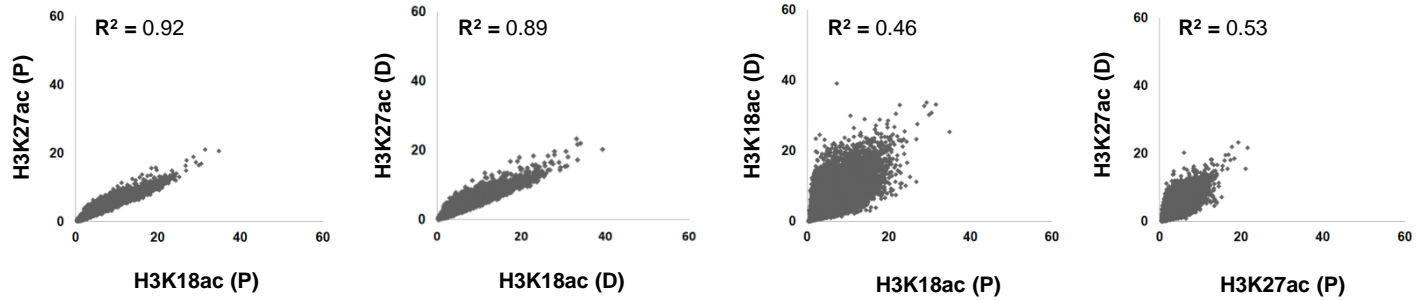


# Average phastCons





# Correlation of the ChIP signals

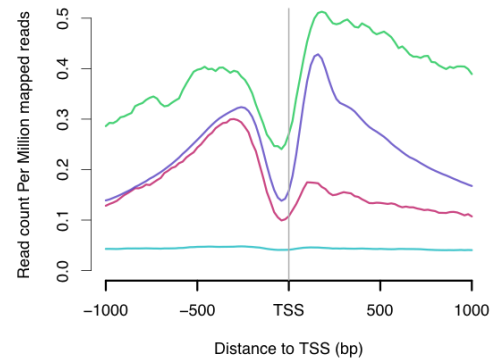
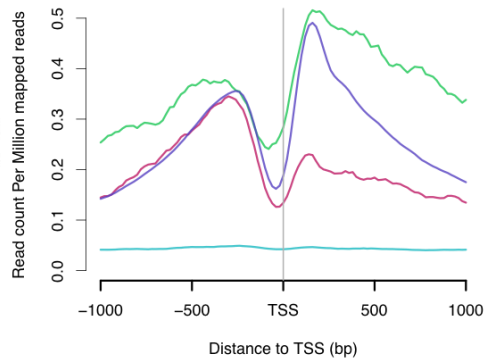
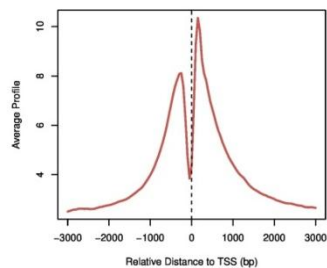
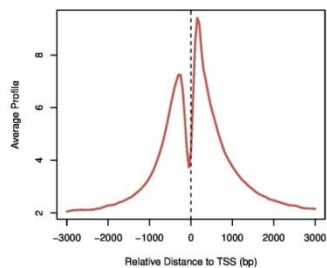




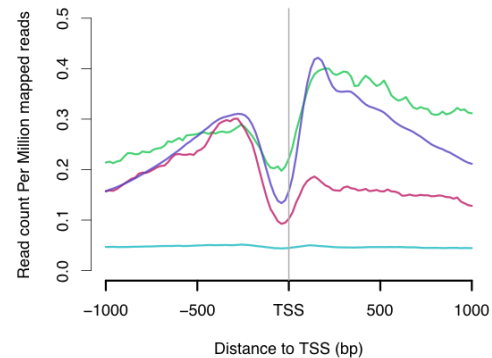
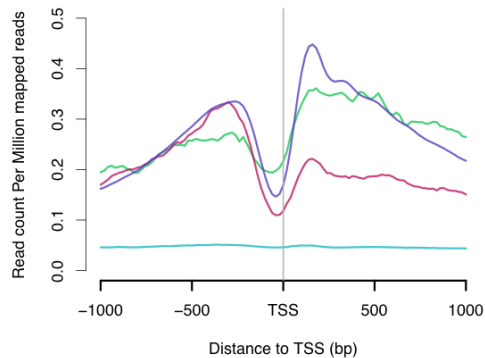
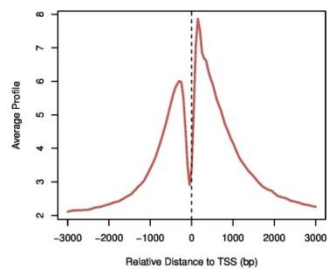
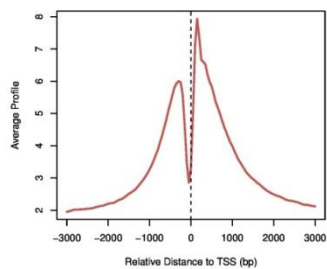


# ChIP signals around TSSs


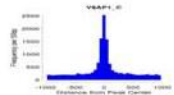
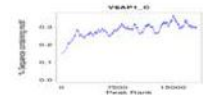

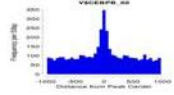
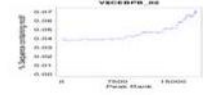

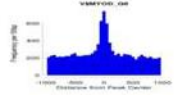
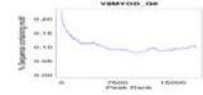

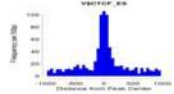
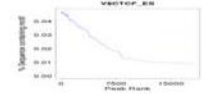

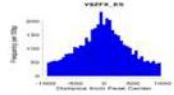
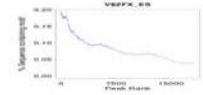
## H3K18ac



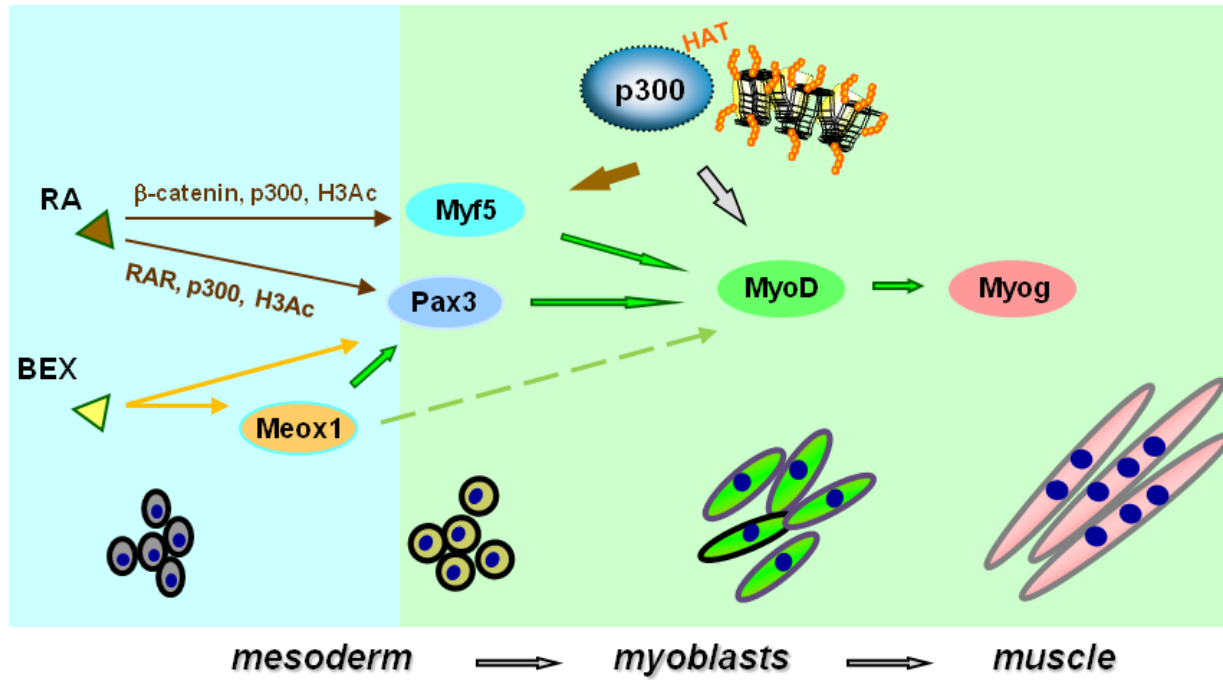
## H3K27ac



# Motif analysis

Family	Logo	Distribution of motifs relative to the center of the p300 peak	%Sequence with motif	P-value
AP1				0
CEBPB				7.58E-9
EBOX				0
CTCF				1.18E-9
Zfx				0.000301

# Conclusions



Chen and Li, *Cell & Bioscience* 2013

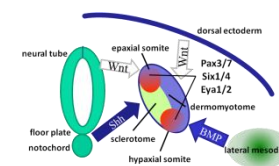
Francetic and Li, *Transcription* 2011

Le May et al. *JBC* 2011

Francetic et al. *Mol Biol* 2012

Hamed et al. *Sci Rep* 2013

Li et al. *Sci Rep* 2013





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