

A network of long noncoding RNAs are
modulated by inflammatory signalling in
vascular endothelial cells

Nadiya Khyzha

PhD Candidate

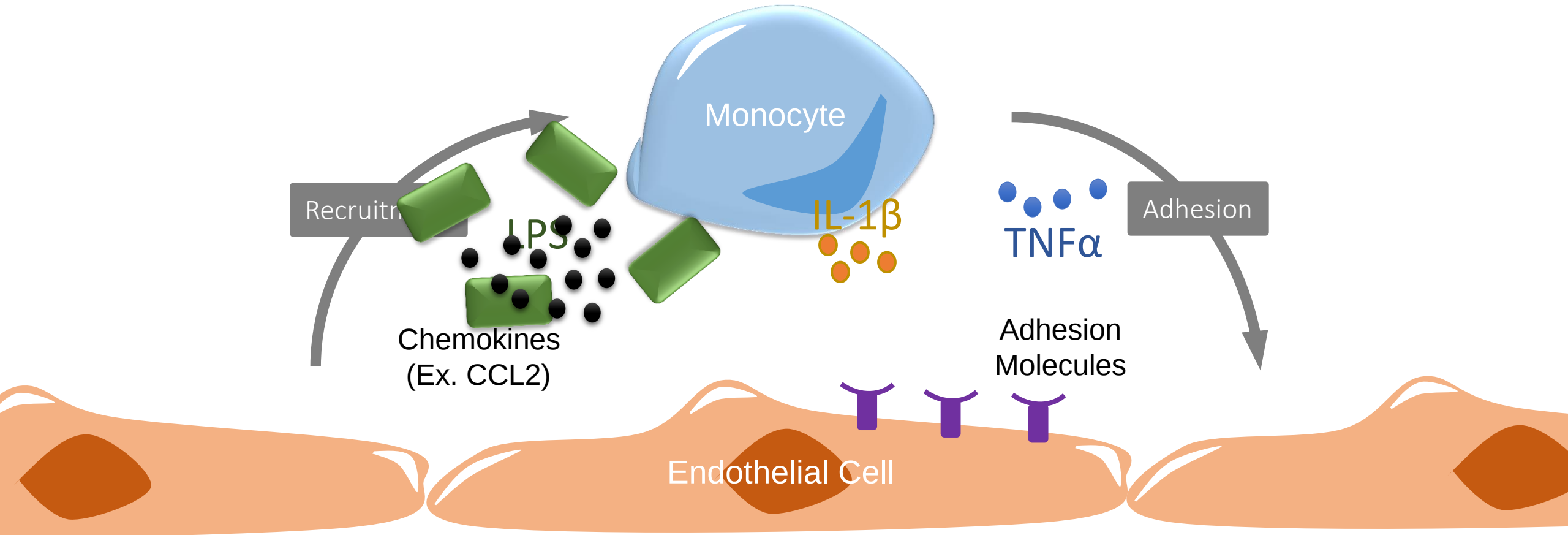
University of Toronto

Toronto General Research Institute

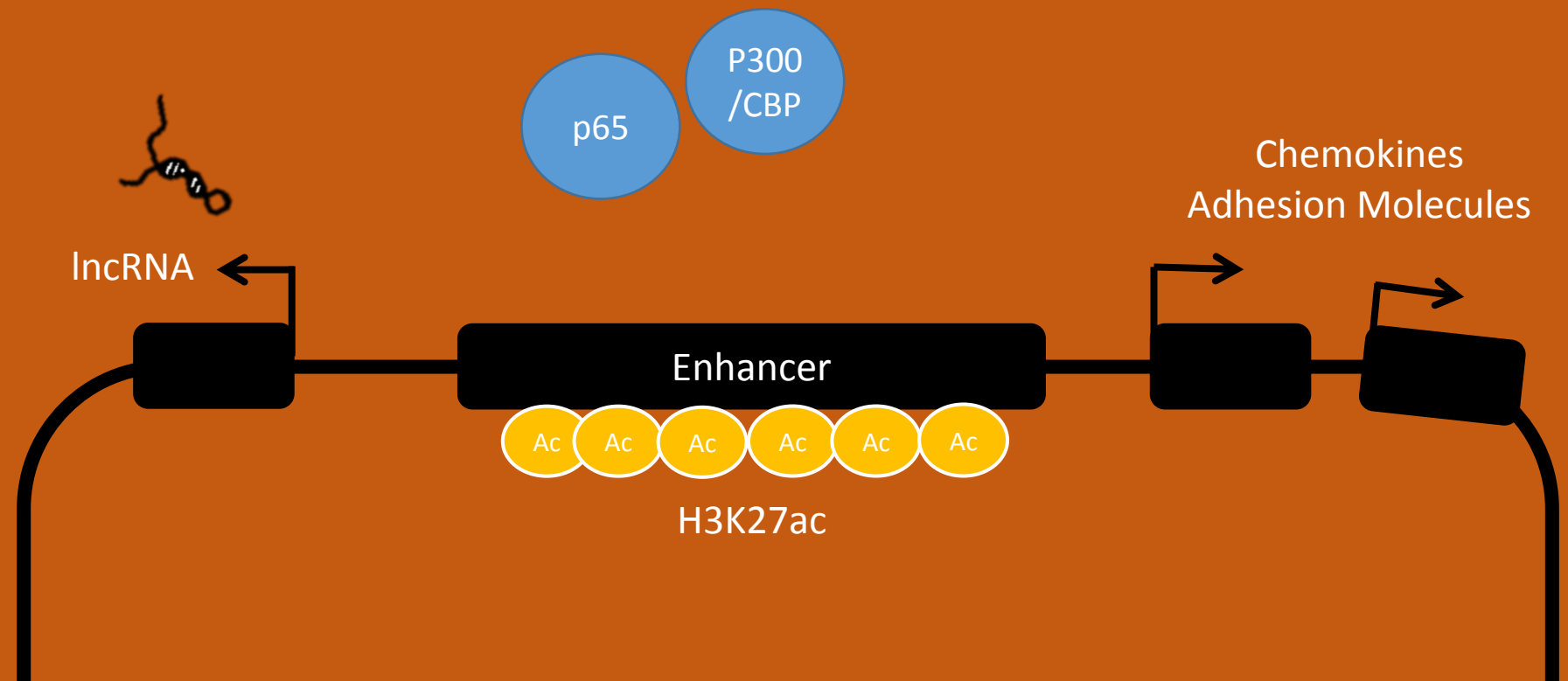
Supervisor: Dr. Jason Fish

March 31, 2017

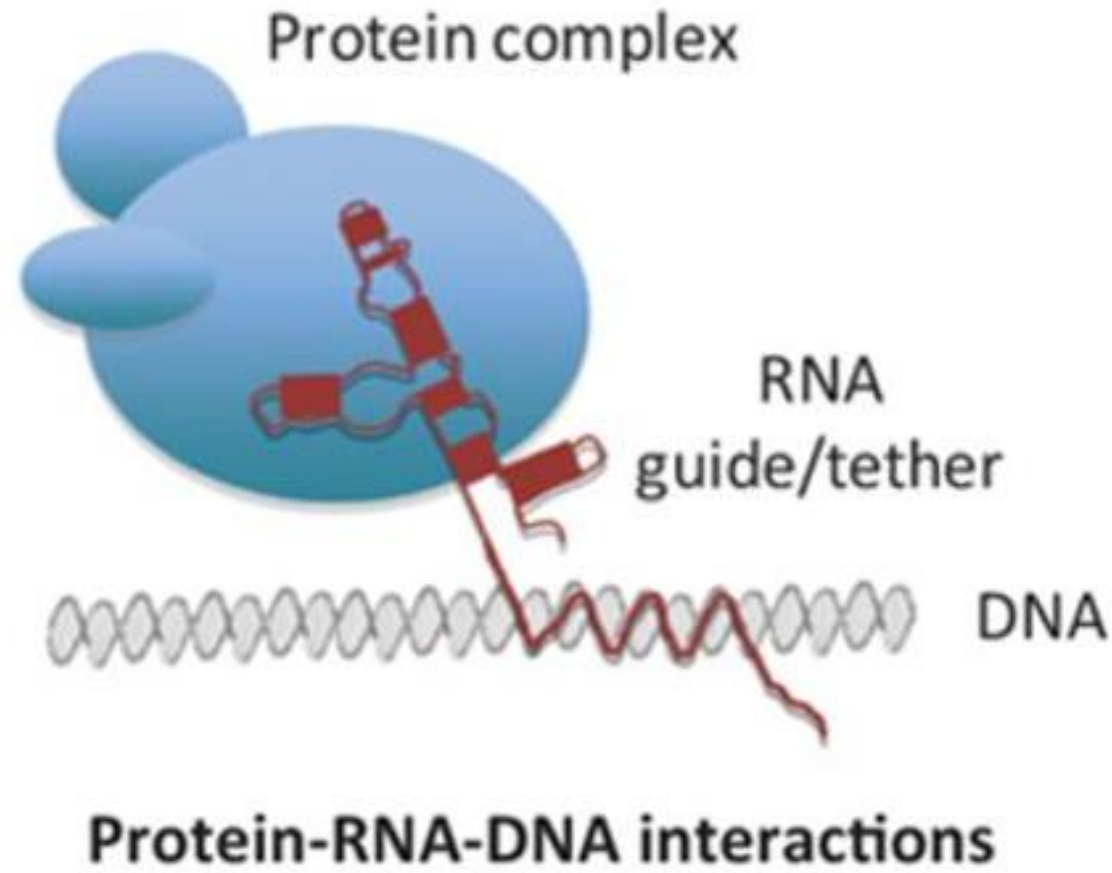
Vascular Endothelial Cell Activation



(Ghosh & Hayden, *Immunology Reviews*, 2012)
(Huang et al, *Mol Cell Biol*, 2009)

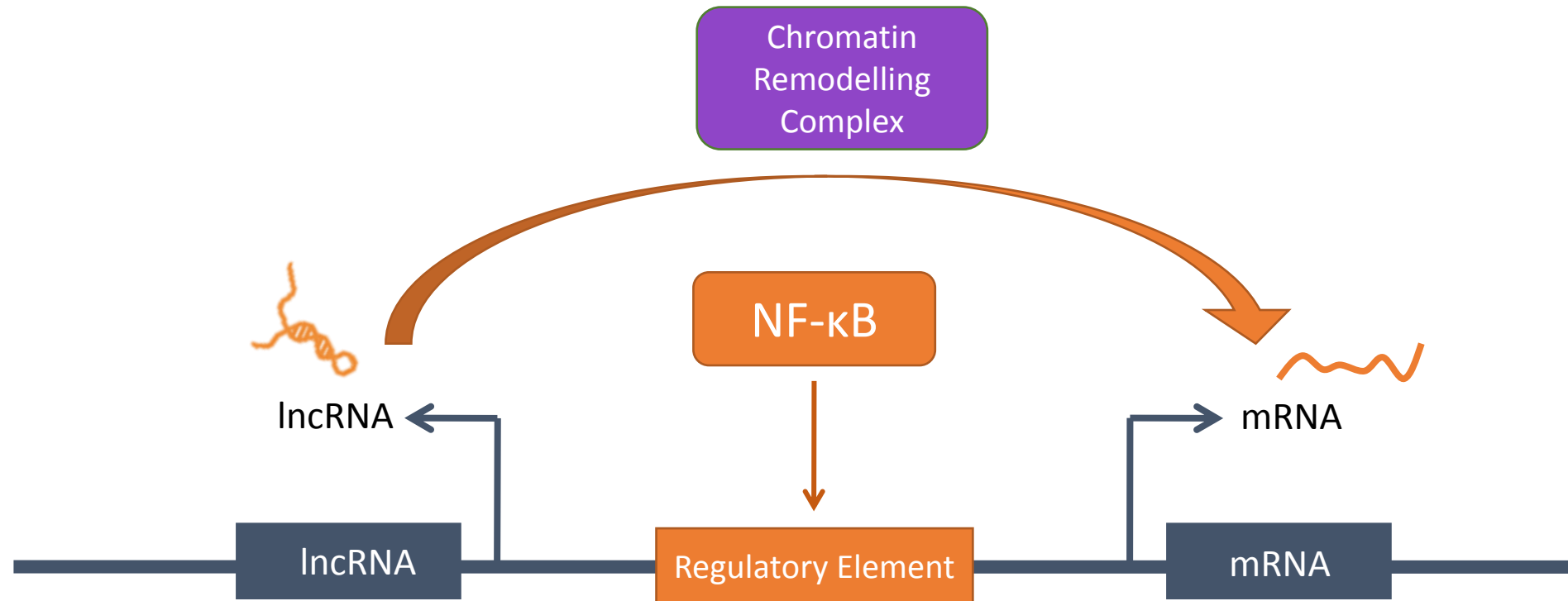


Long Noncoding (lnc) RNA

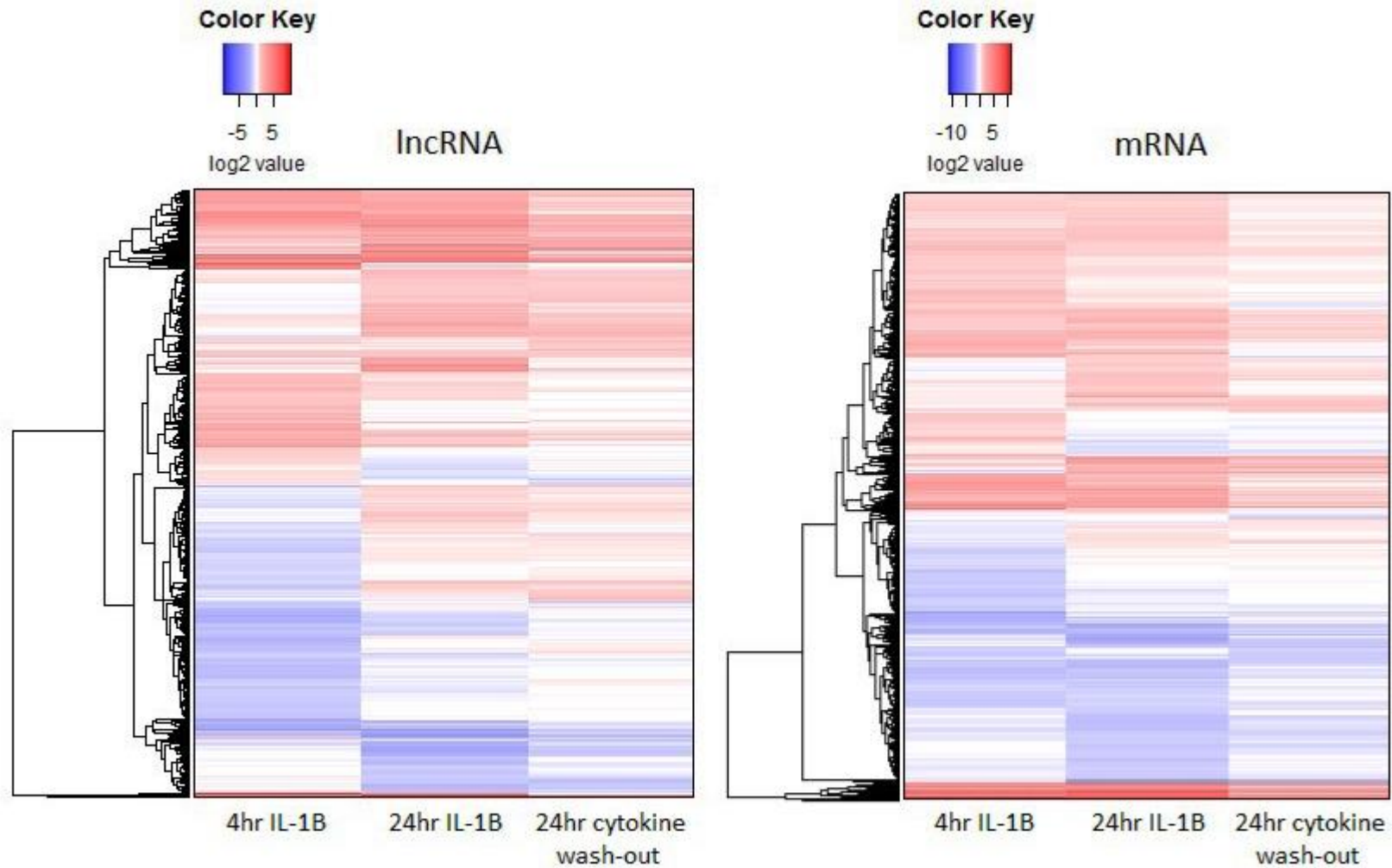


- Noncoding transcripts >200nt
- Shown to act in cis to regulate neighbouring transcripts

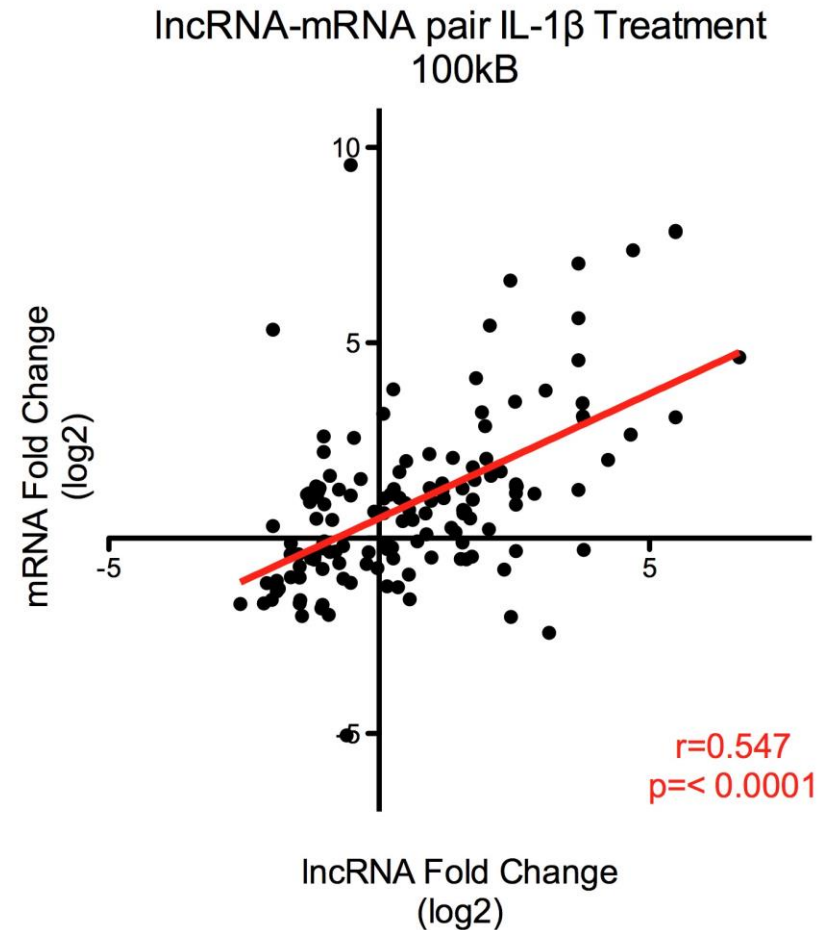
Hypothesis



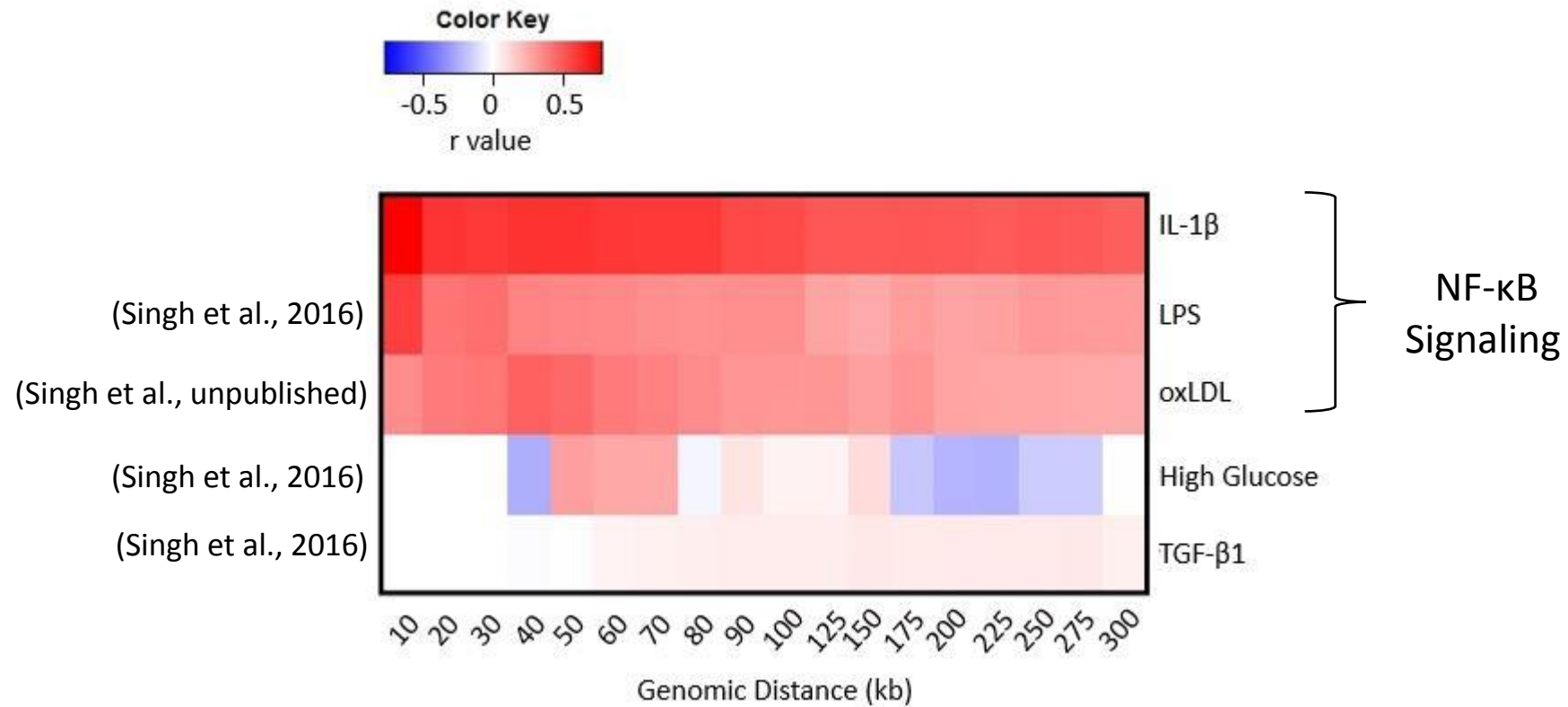
Identifying IL-1 β neighboring lncRNA-mRNA pairs



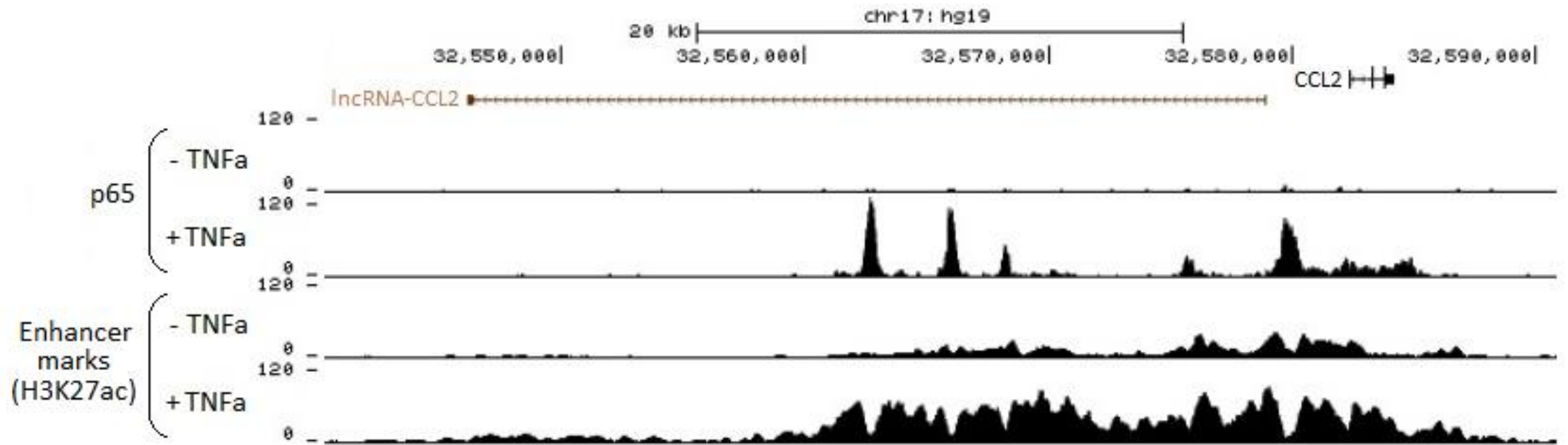
lncRNA-mRNA pairs are correlated in expression



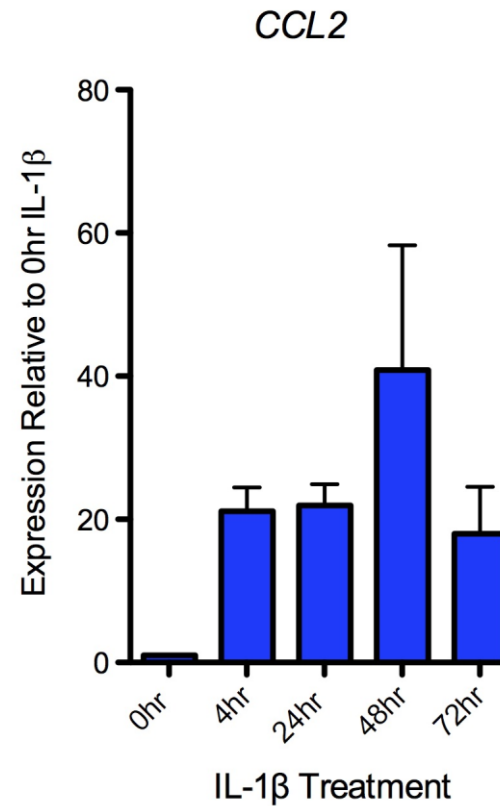
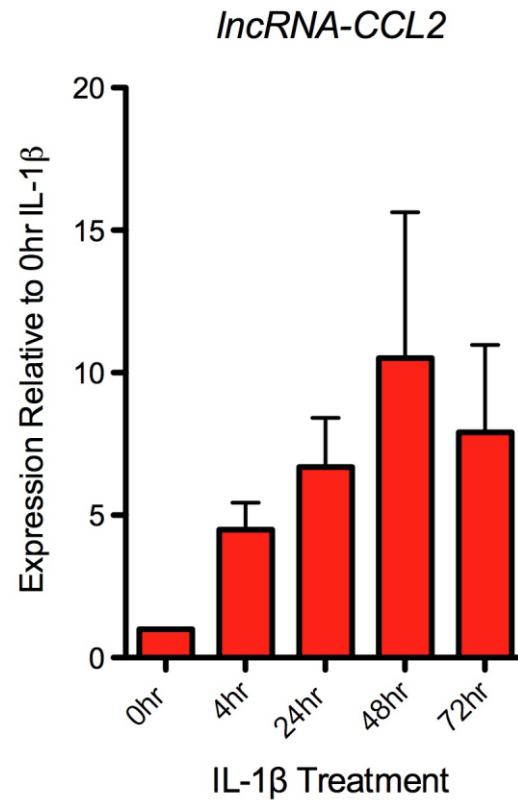
NF- κ B regulated lncRNA-mRNA pairs are correlated in expression



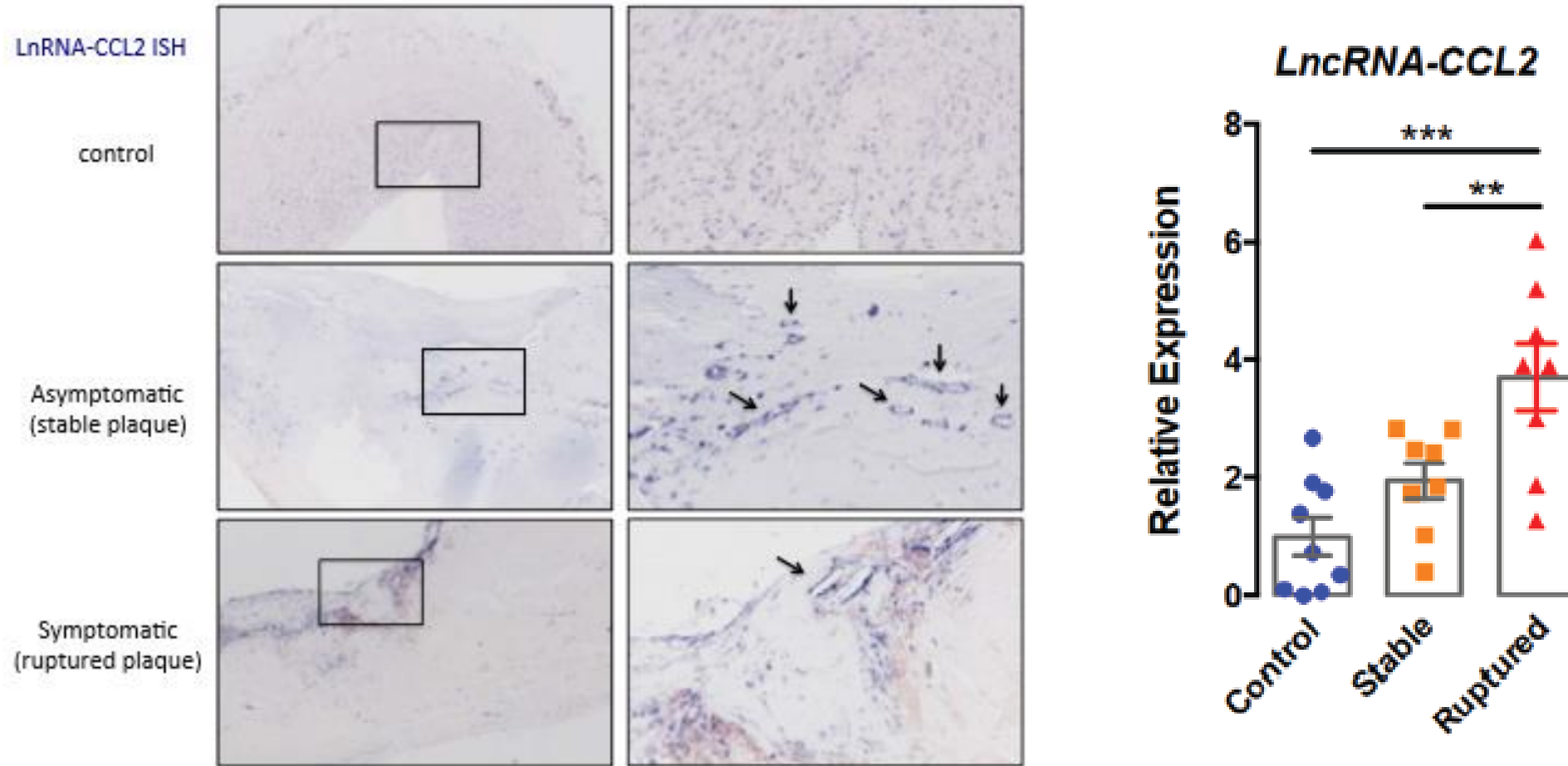
Genomic loci of *lncRNA-CCL2* and *CCL2*



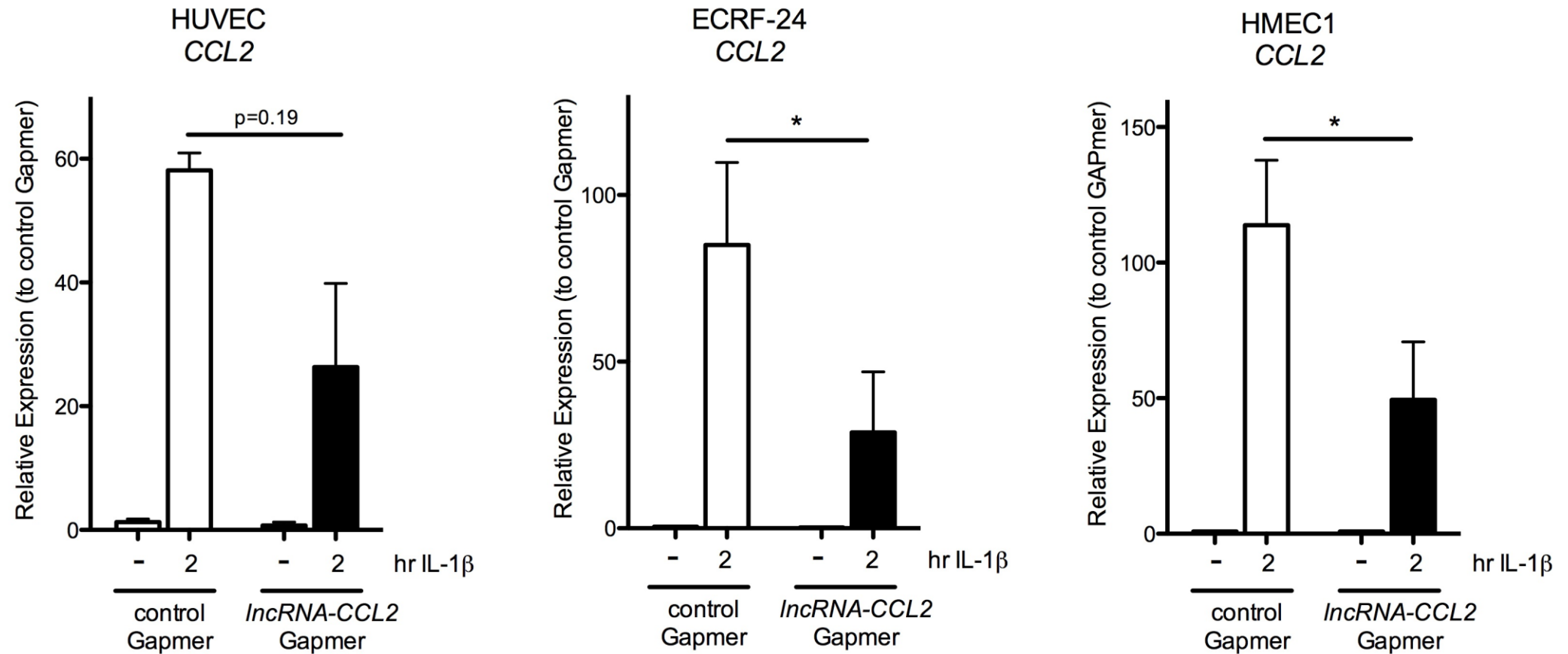
IncRNA-CCL2 and *CCL2* expression follows a similar IL-1 β kinetic



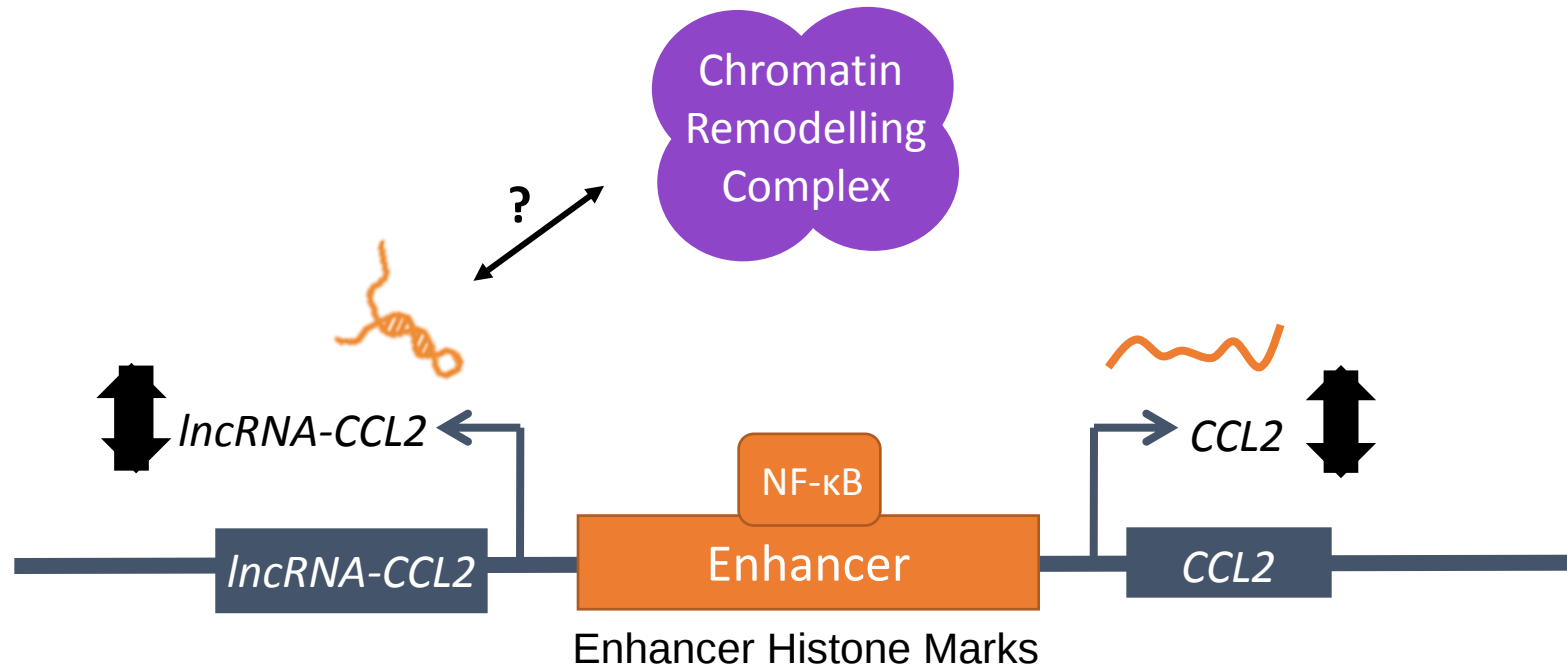
lncRNA-CCL2 is elevated in symptomatic human plaques



lncRNA-CCL2 knockdown results in decreased *CCL2* expression



Mechanism



Acknowledgements

Fish Lab

Dr. Jason Fish

Melvin Khor

Emilie Boudreau

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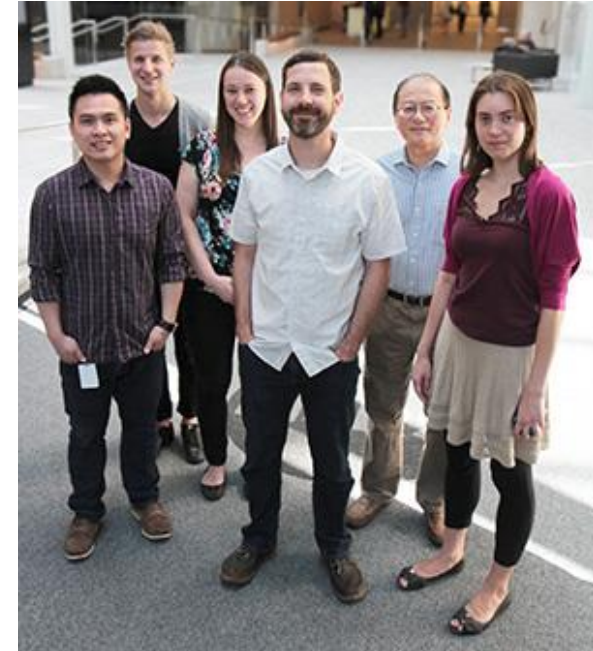
Collaborators

Toronto Hospital for Sick Children

Dr. Michael Wilson

Karolinska Institute

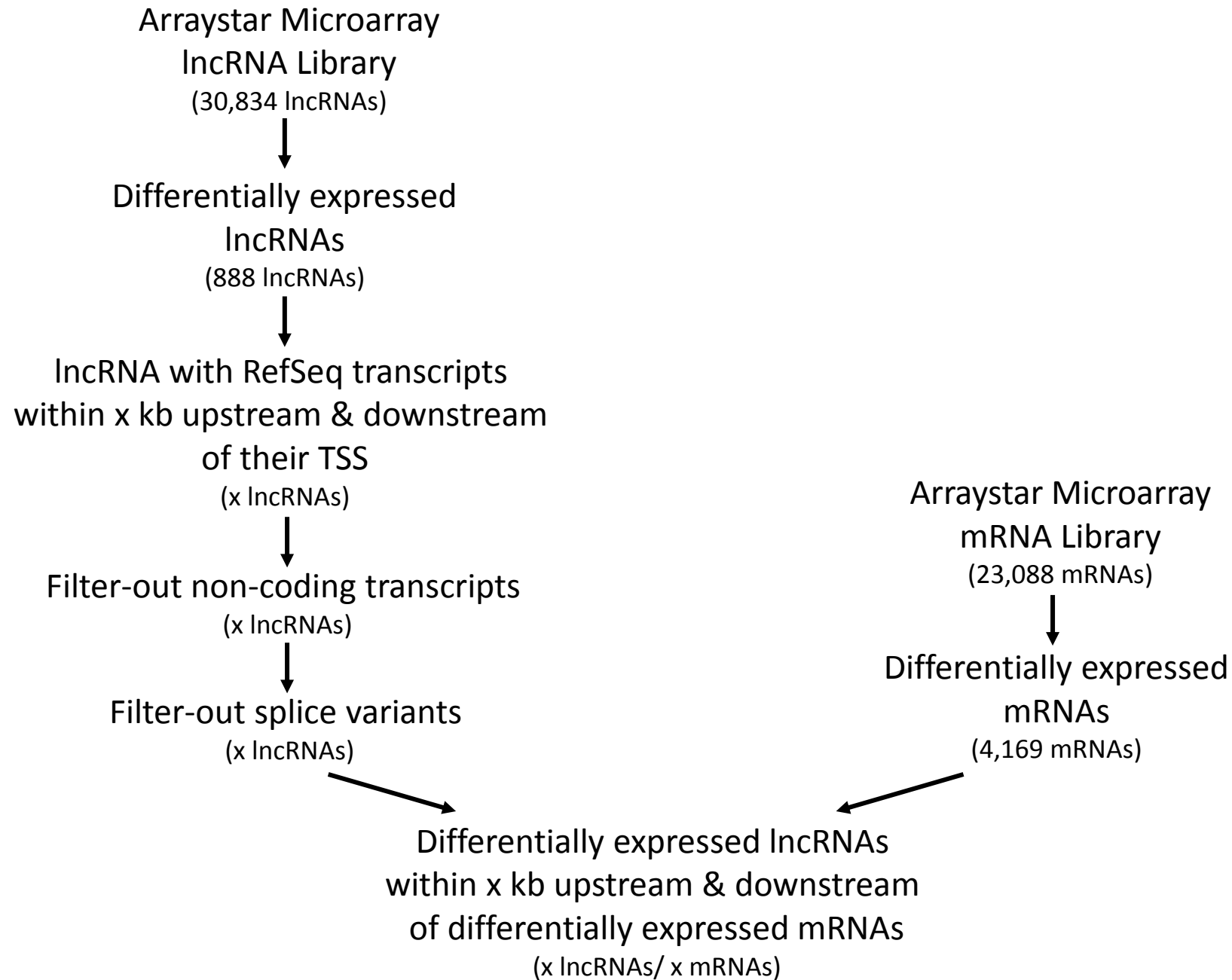
Dr. Lars Maegdefessel



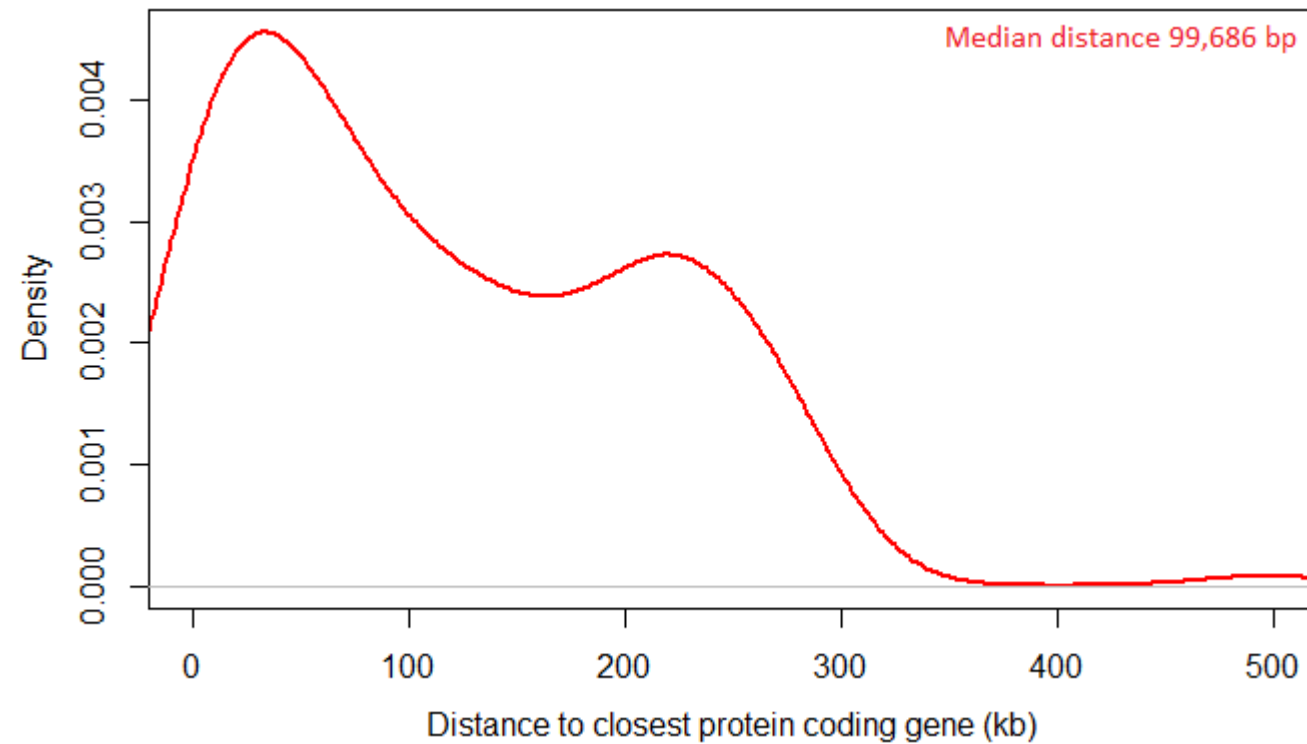
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Supplementary Slides



Distribution of distances between lncRNA-mRNA pairs

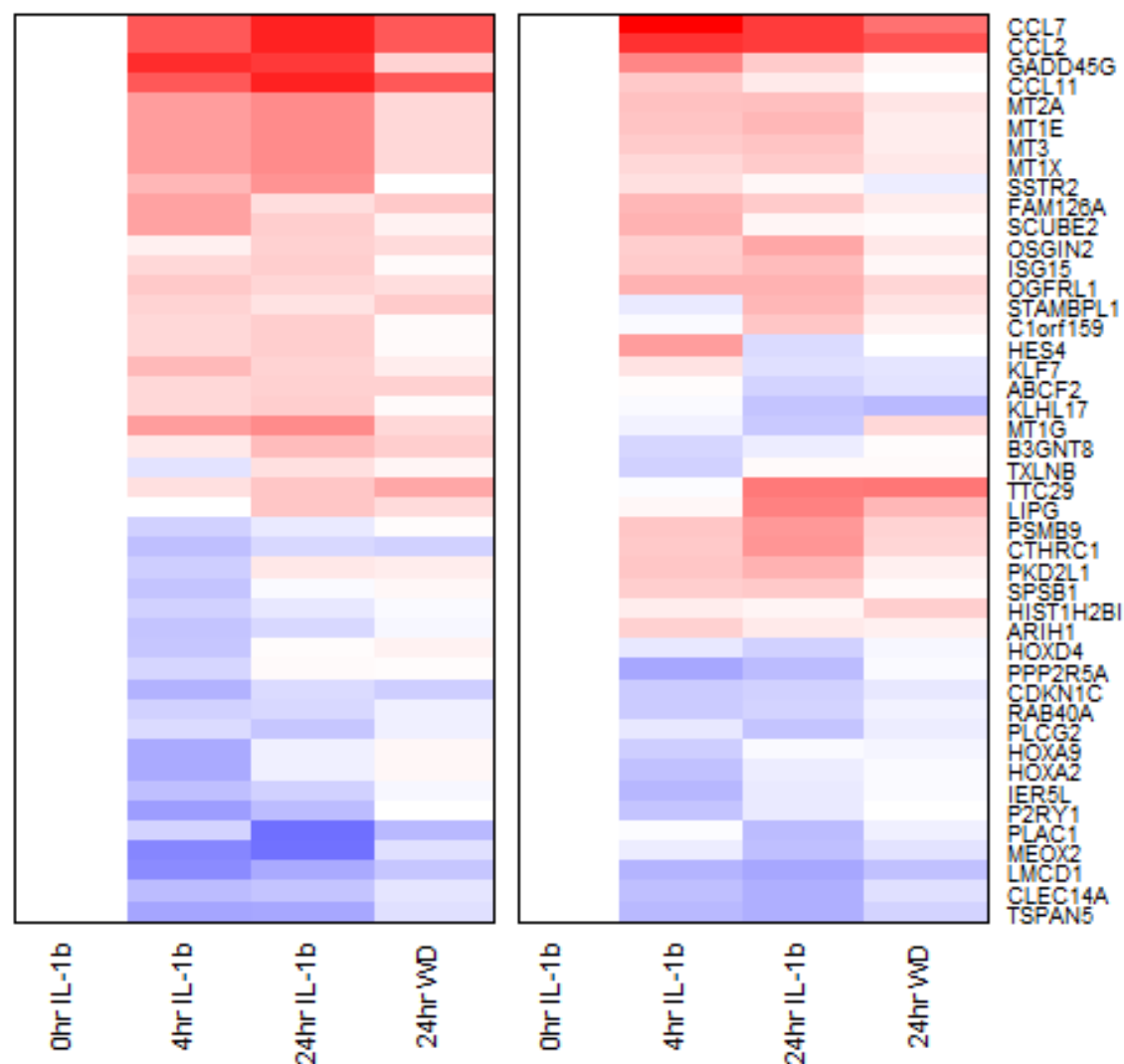


	Presence		Absence		
Feature	Pearson r	# samples	Pearson r	# samples	p-value
p65	0.4352	14	0.6018	127	0.4654
H3K4me3	0.5930	131	0.2444	10	0.2627
H3K27ac	0.6191	125	0.0822	16	0.0278
CTCF	0.4479	110	0.7242	31	0.0404

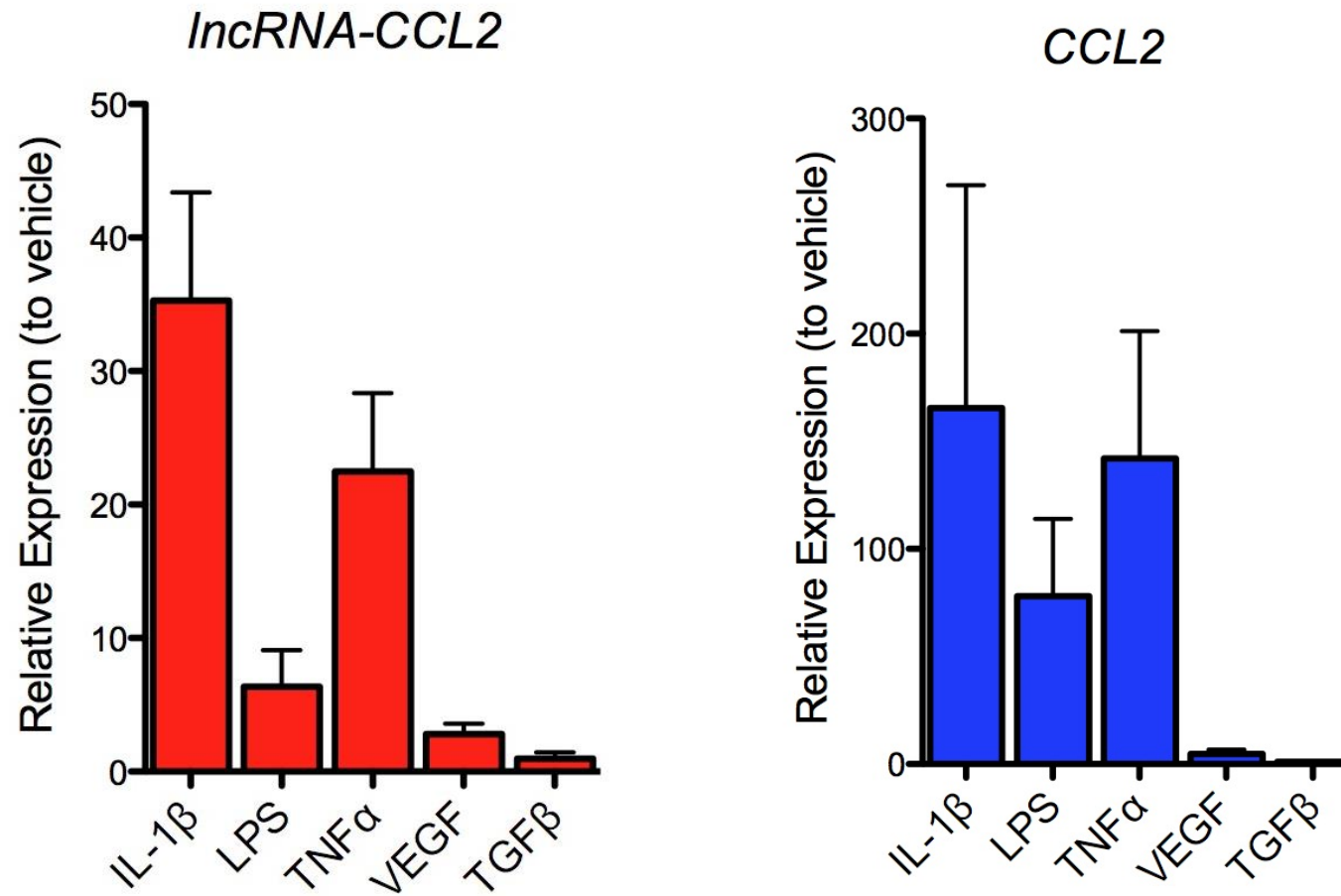
Color Key

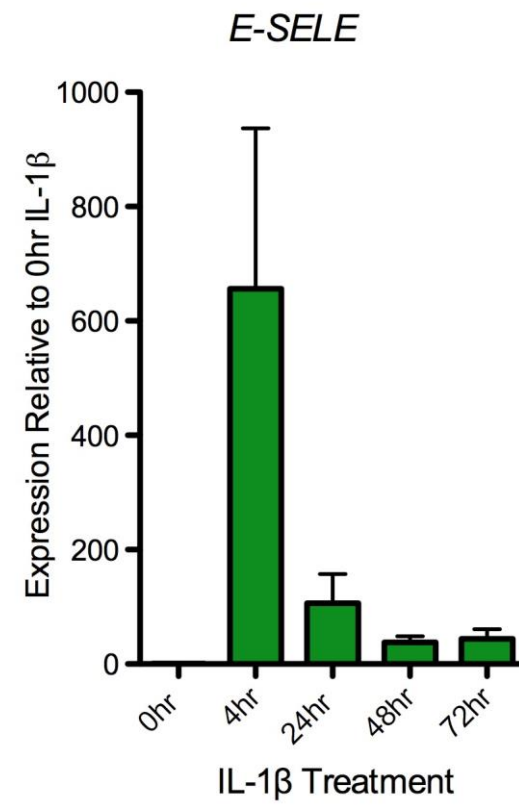
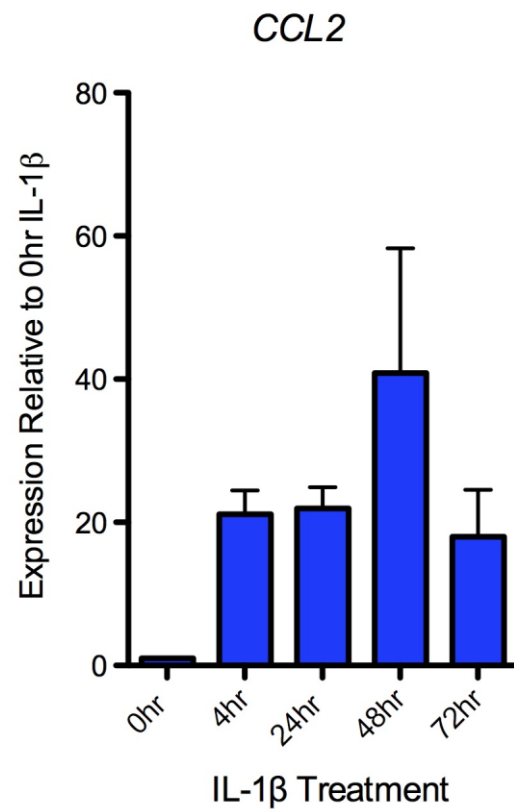
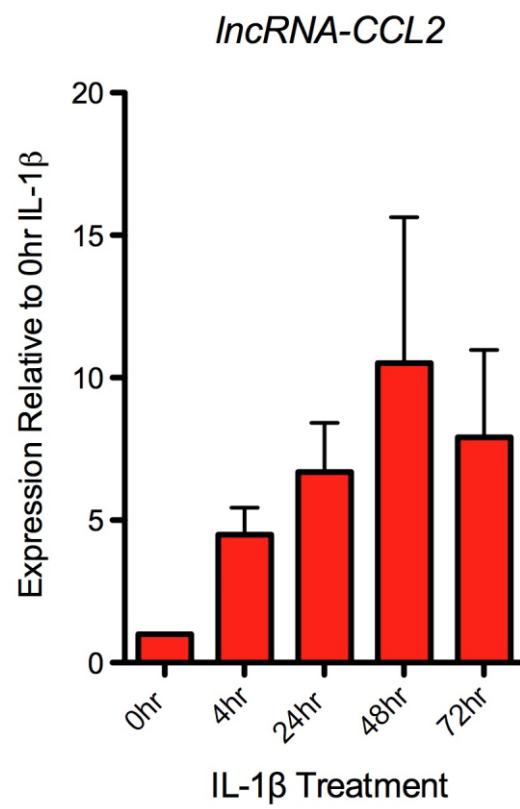


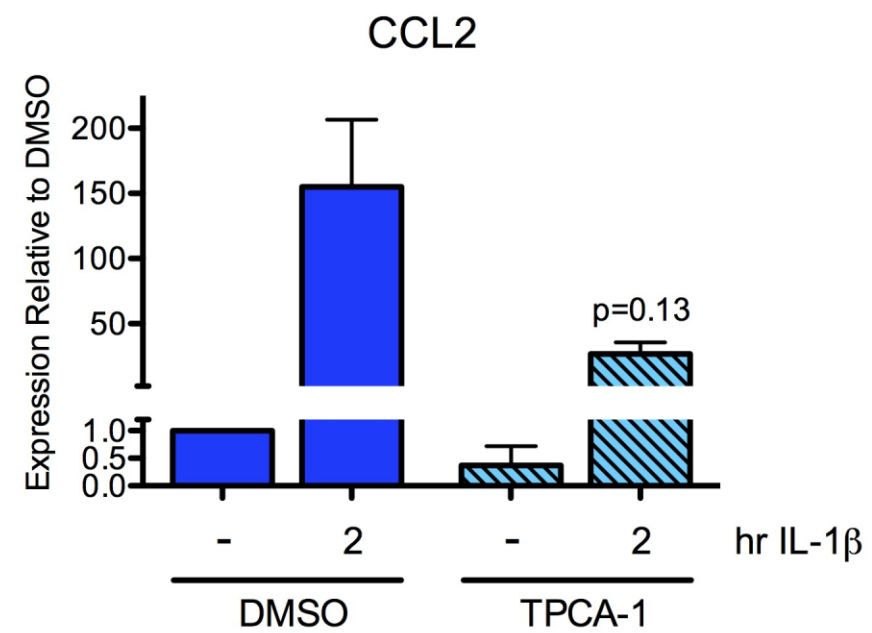
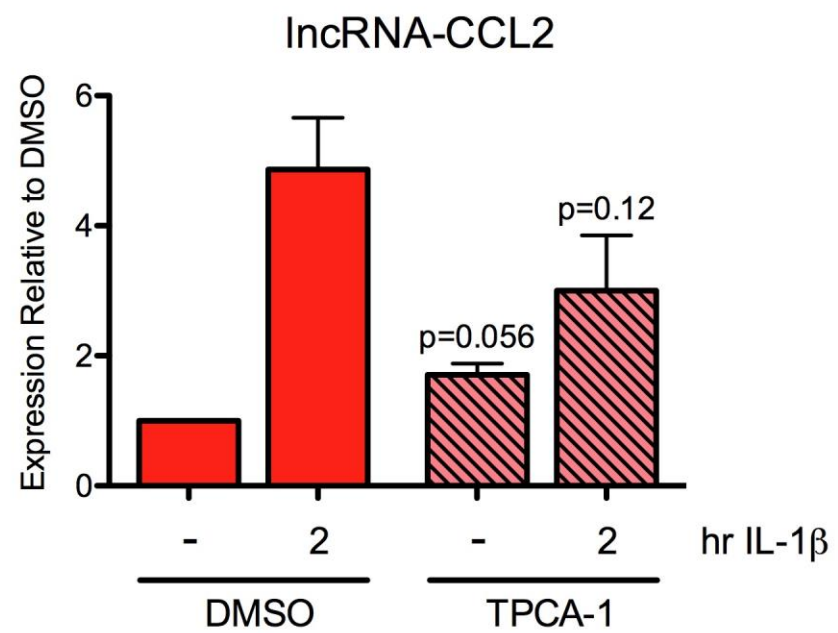
-4 2
log2 value

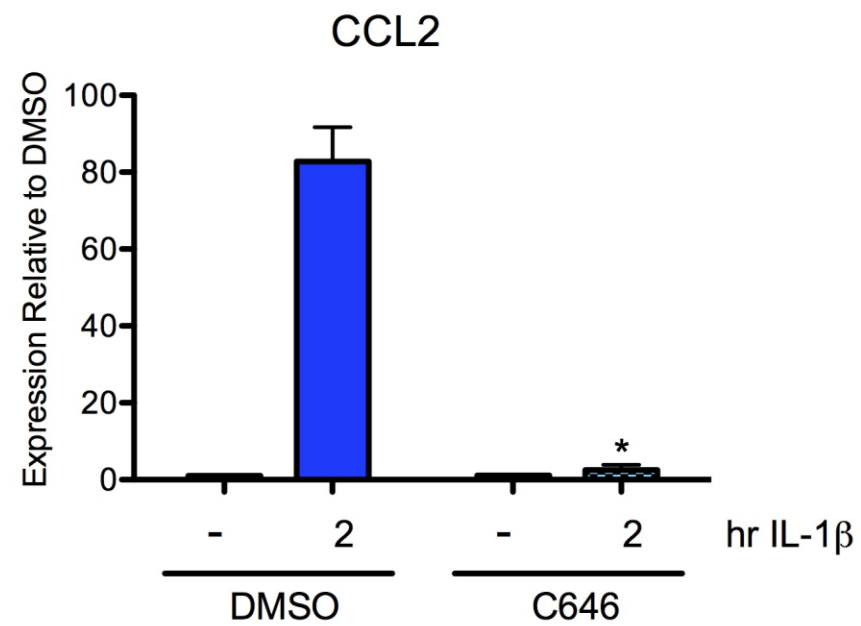
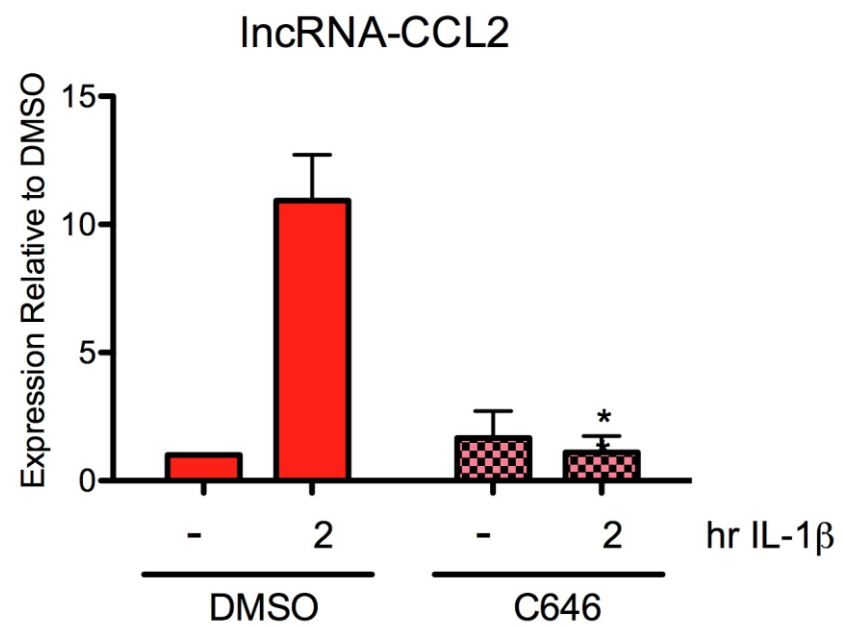


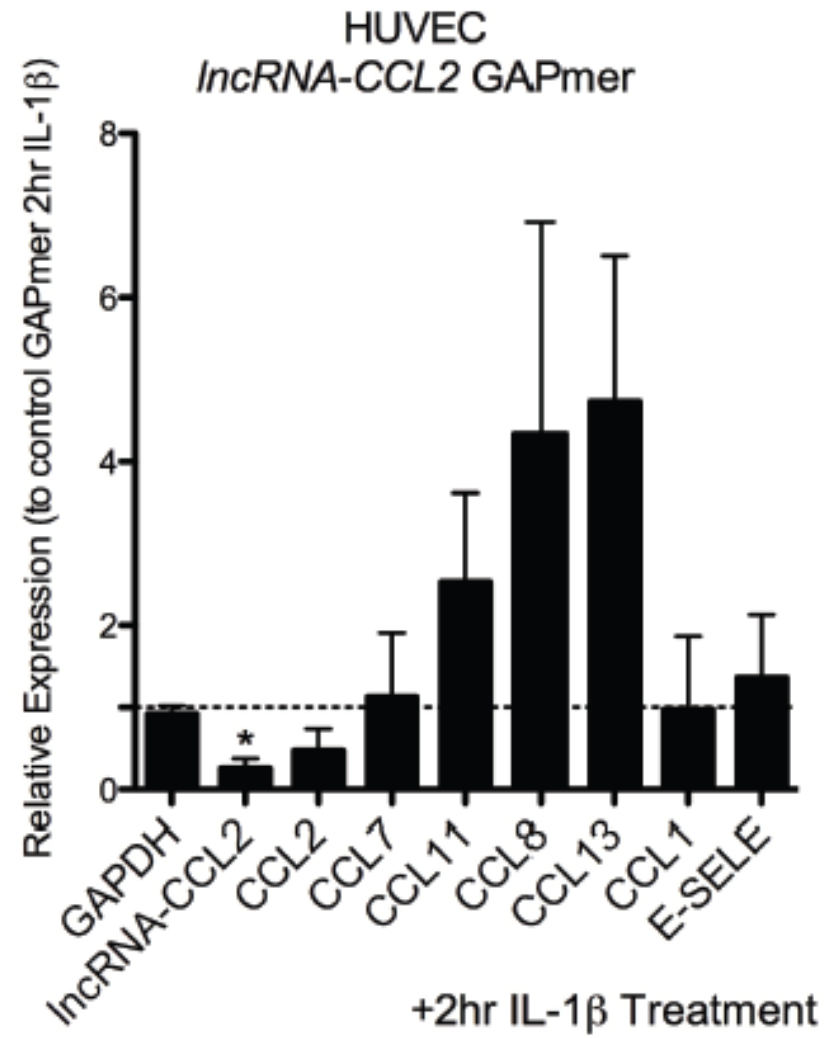
lncRNA-CCL2 and *CCL2* are regulated by inflammatory stimuli



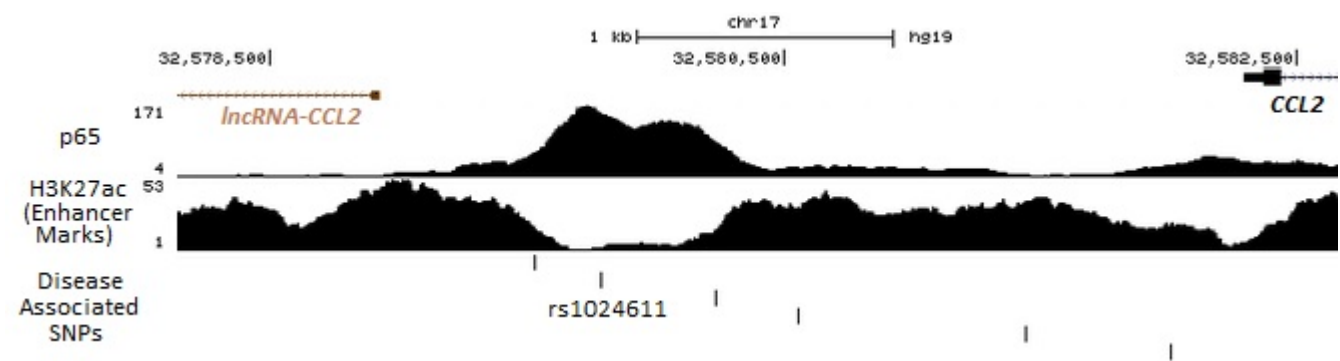






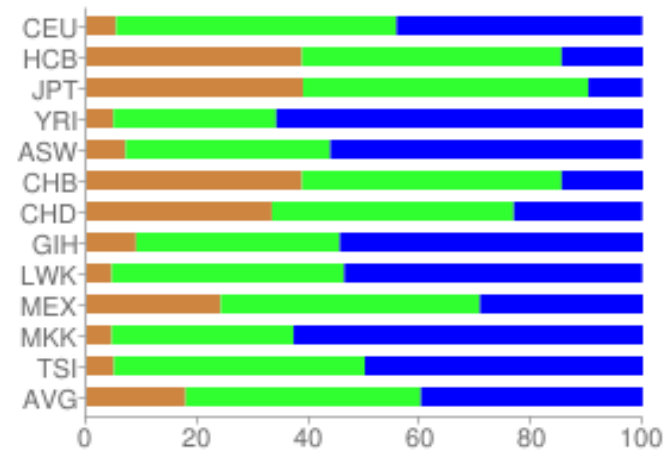


Rs1024611 (-2578A>G) SNP

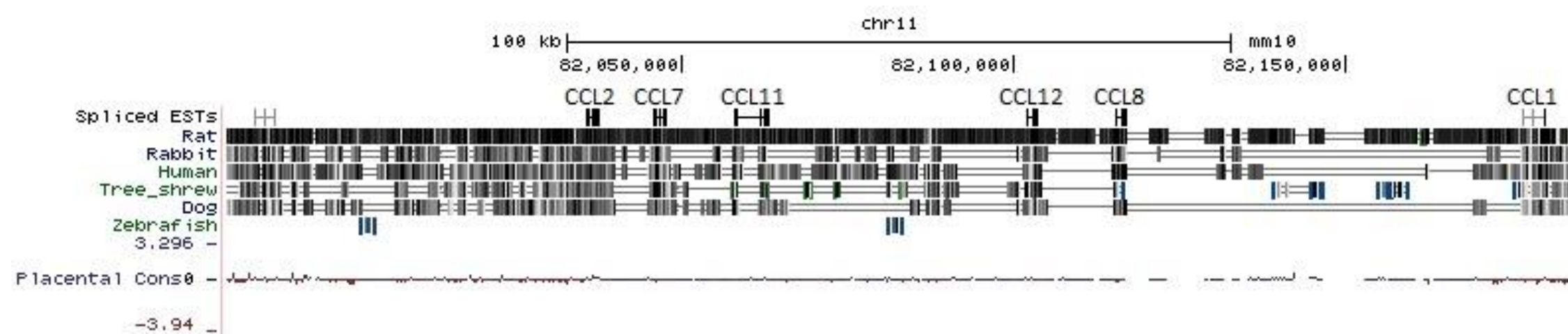


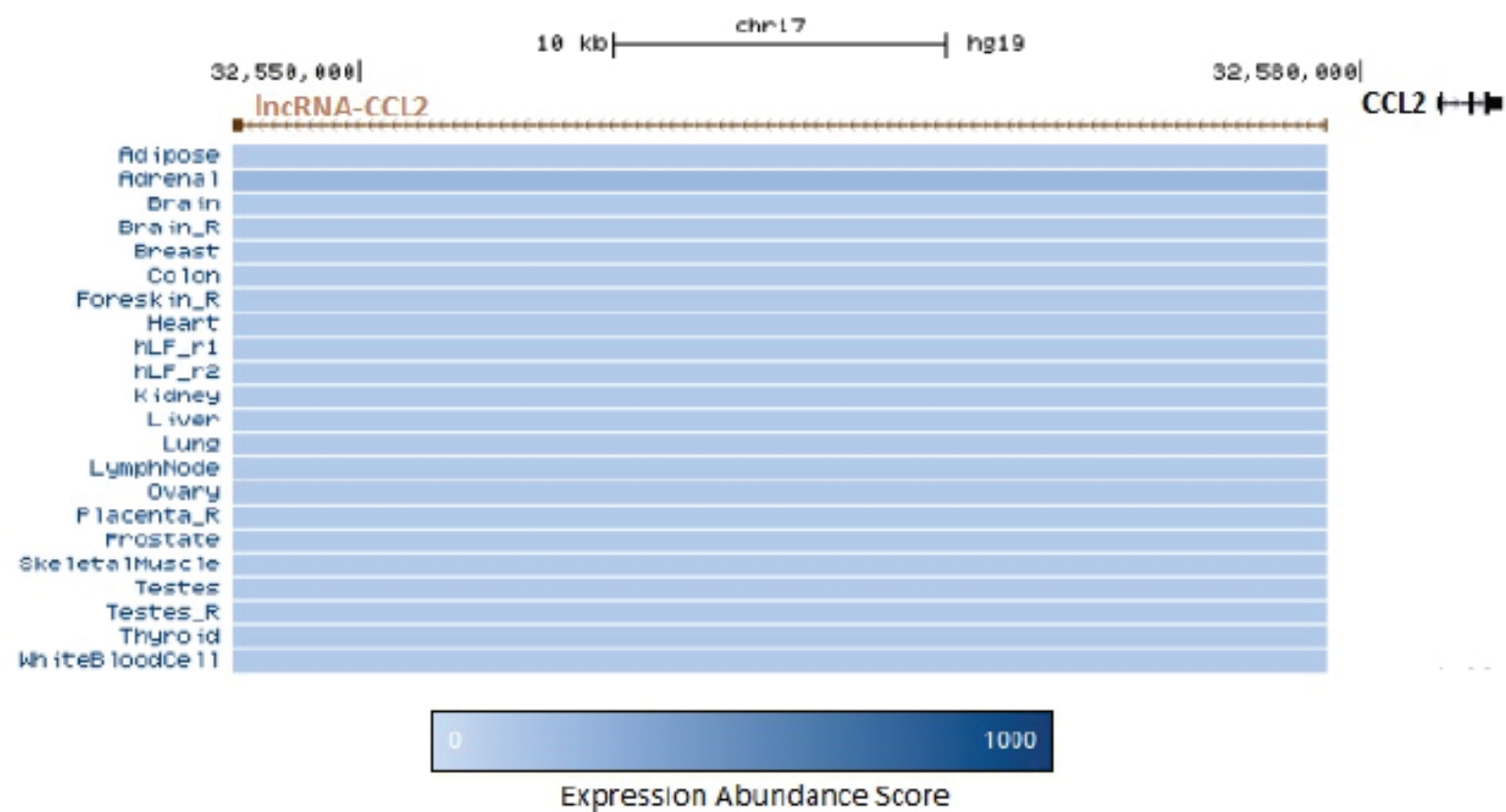
? (C;C) (C;T) (T;T) 28

Geno	Mag	Summary
(C;C)	2.2	increased risk of exercise induced ischemia, Increased CCL2 levels; increased rate of HIV progression
(C;T)	2	increased risk of exercise induced ischemia
(T;T)	0	normal risk

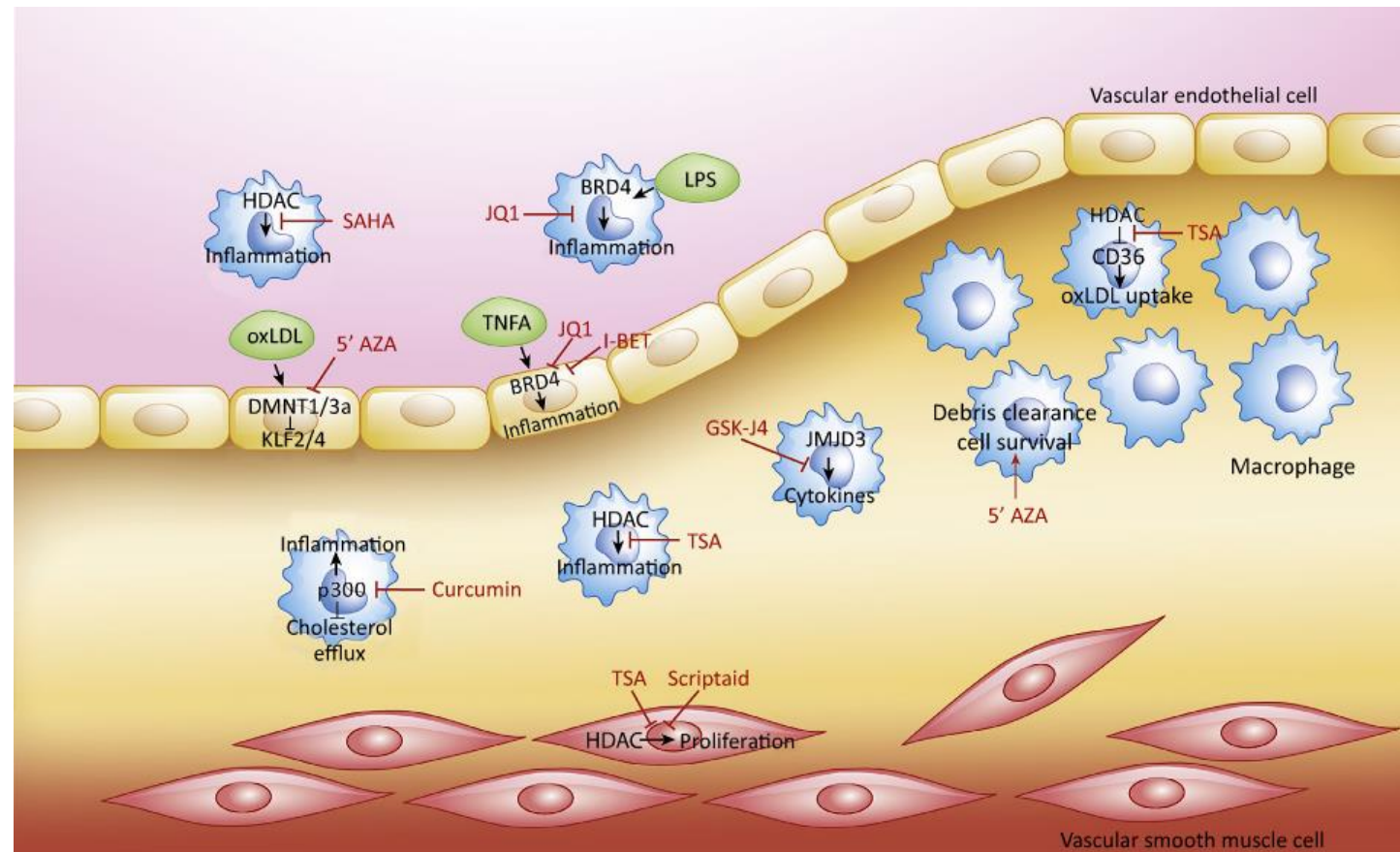


(Data from SNPedia)

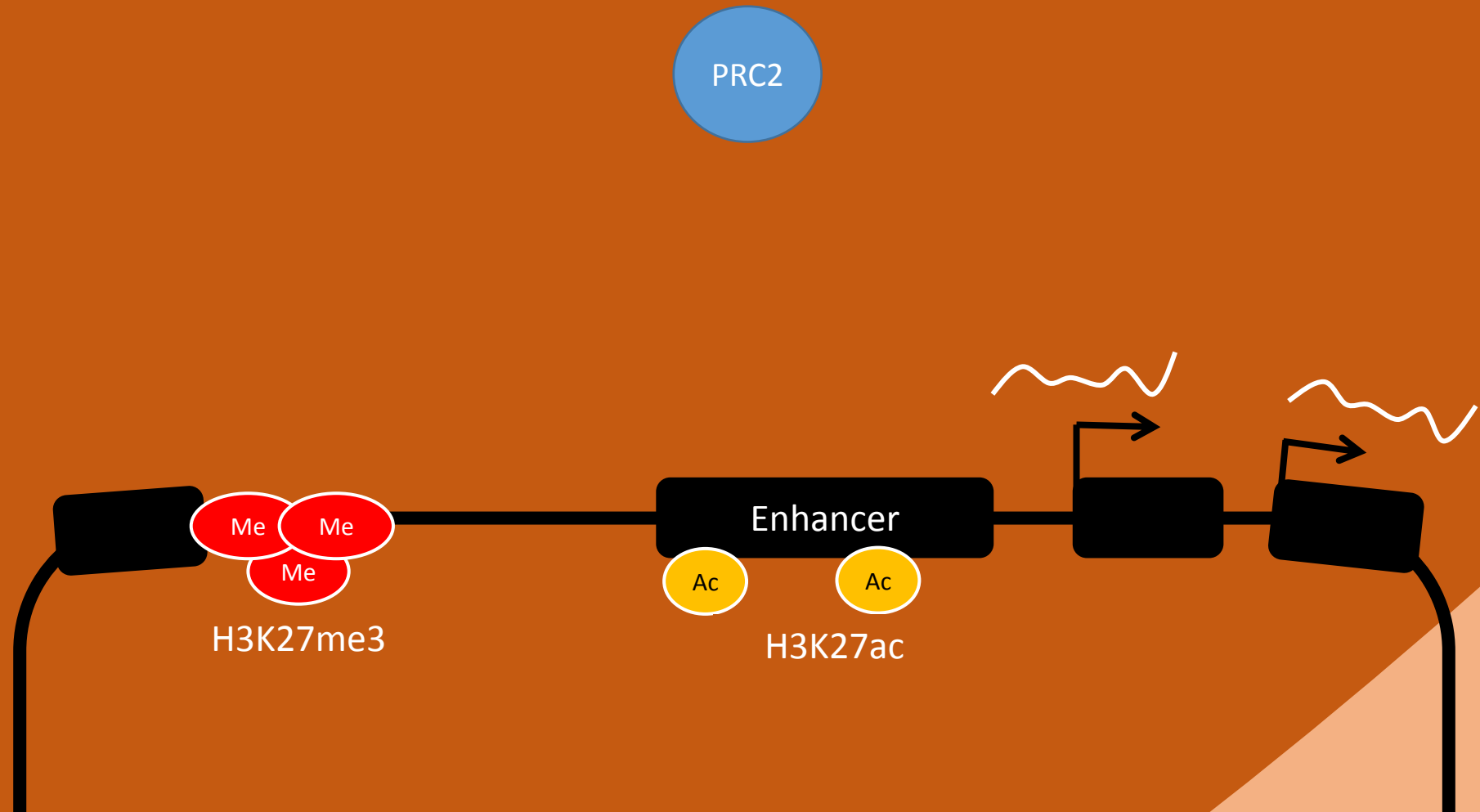




Emerging role of epigenetics in atherosclerosis



Davidovich, *Nature Structure & Molecular Biology*, 2013
Kaneko, *Nature Structural & Molecular Biology*, 2013
Cifuentes-Rojas, *Molecular Cell*, 2014
Beltran, *Genome Research*, 2016



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Kaneko, *Nature Structural & Molecular Biology*, 2013
Cifuentes-Rojas, *Molecular Cell*, 2014
Beltran, *Genome Research*, 2016
Bose, *Cell*, 2017

