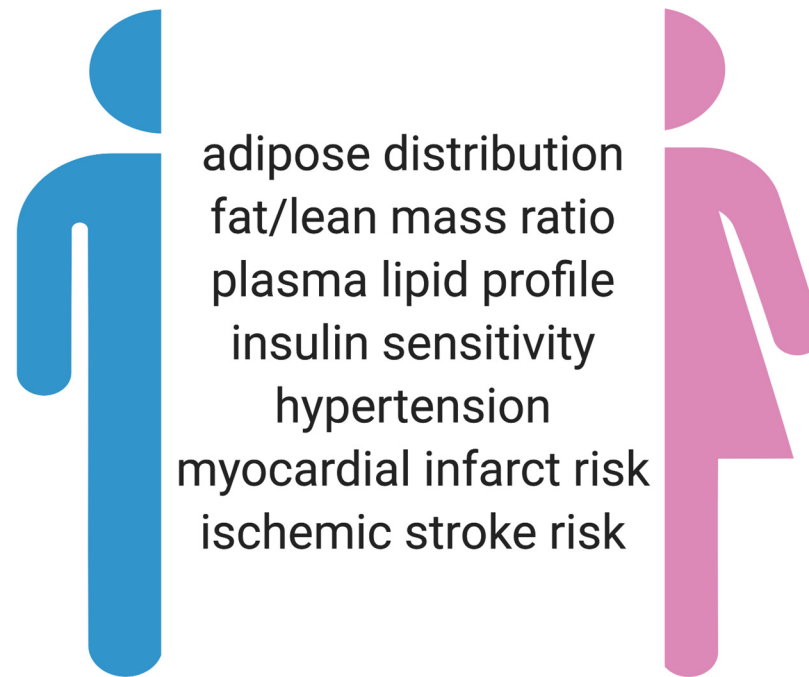


Kdm5c Gene Dosage Determines Sex Differences in Adiposity

Carrie Wiese, PhD
Human Genetics, Reue Laboratory

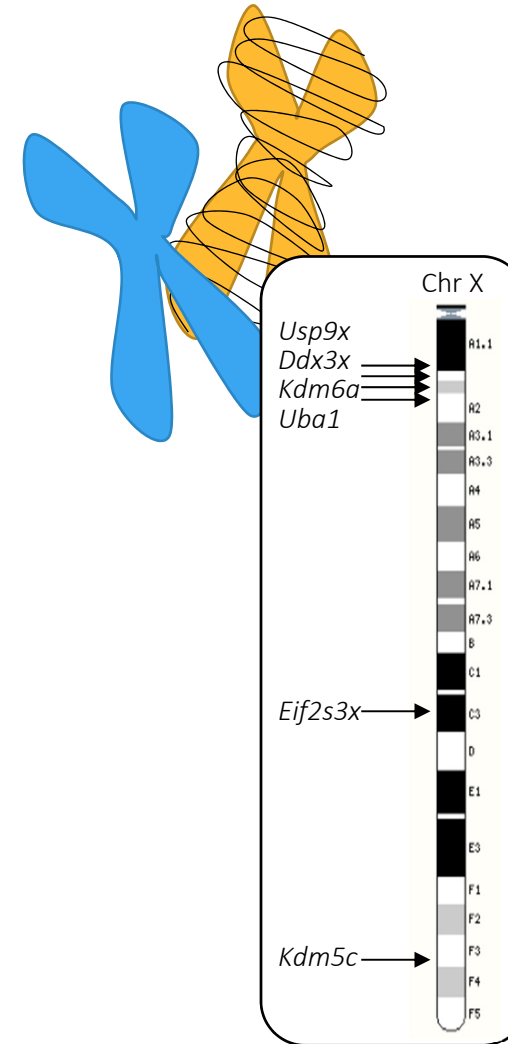
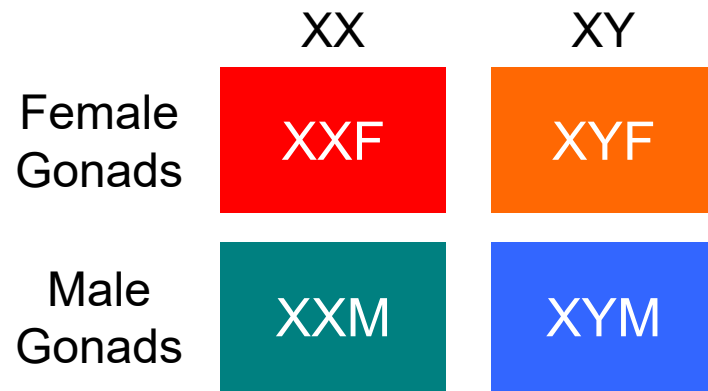


Gonadal hormones
Sex chromosome complement

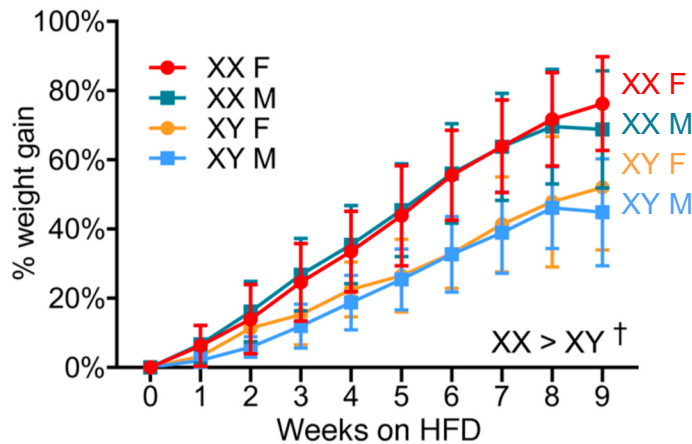
Sex Chromosomes Impact Body Weight and Adiposity

Some X Chromosome Genes Escape Inactivation

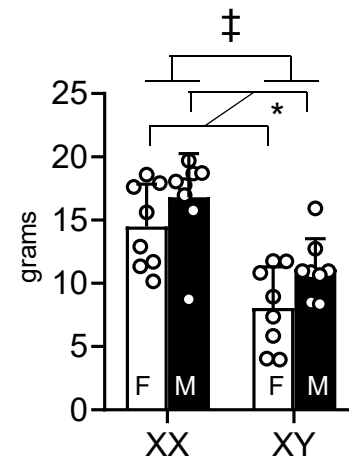
Four Core Genotype



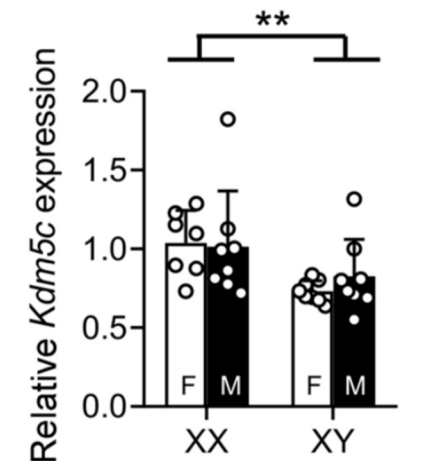
Percent Weight Gain



Fat Mass

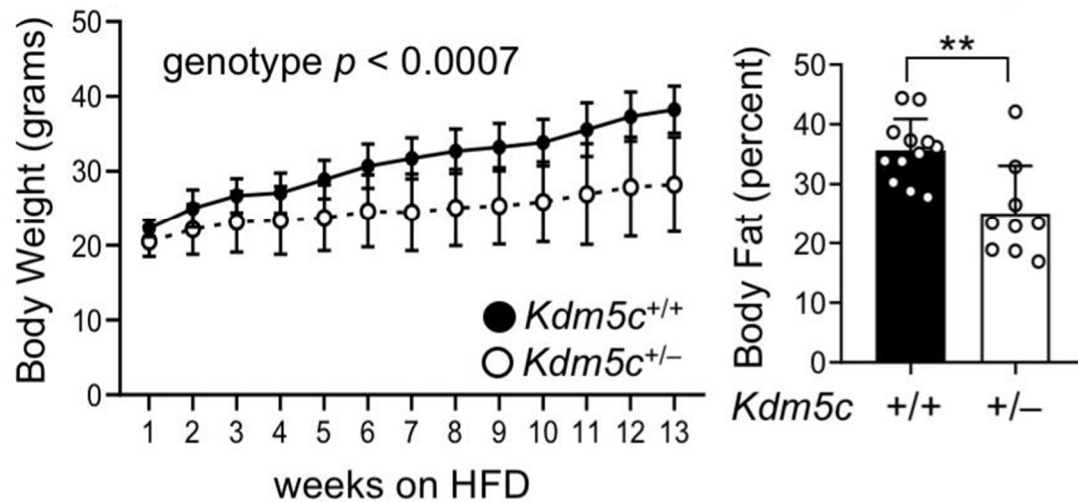


Adipose *Kdm5c* Expression



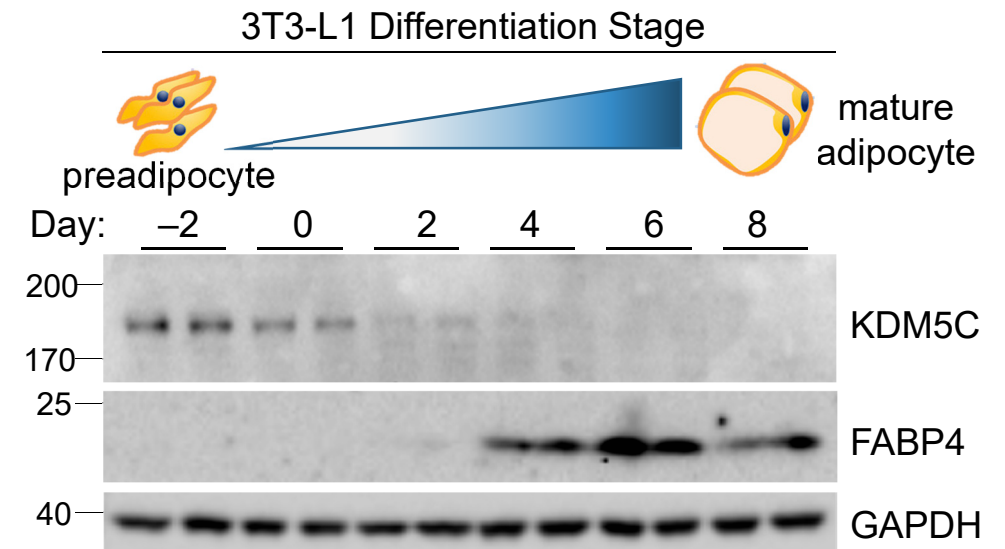
KDM5C: histone 3, lysine 4 demethylase

Kdm5c Dosage Recapitulates XX/XY Adiposity Phenotype

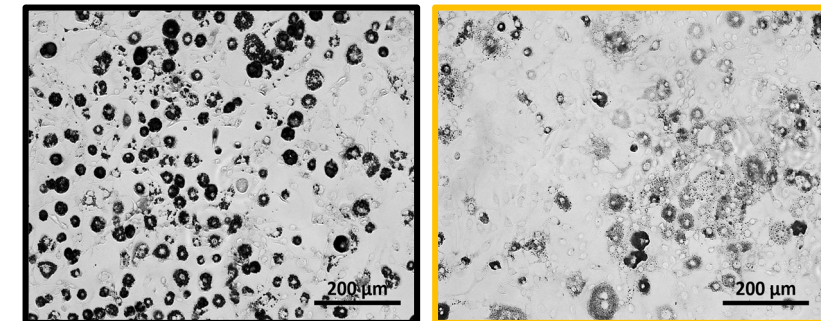
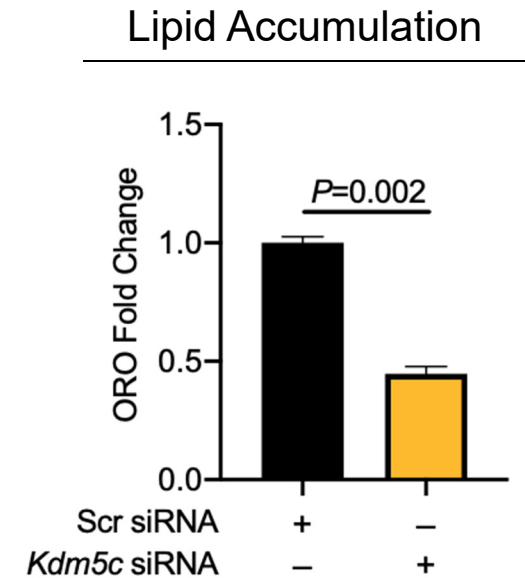
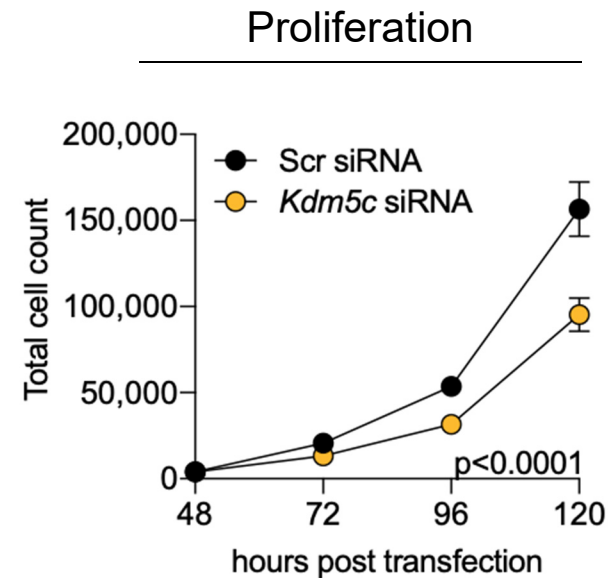
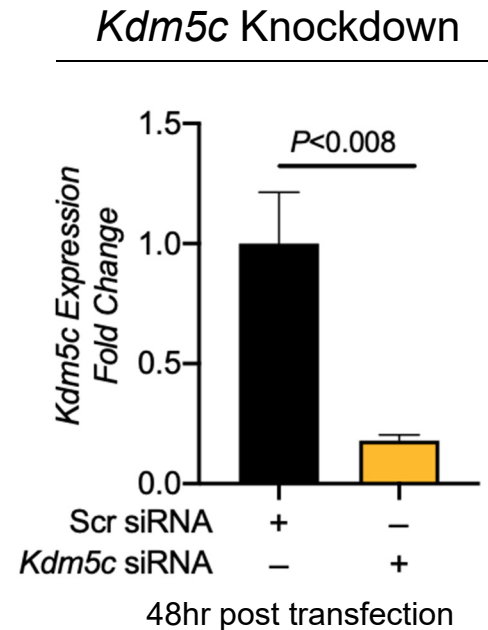
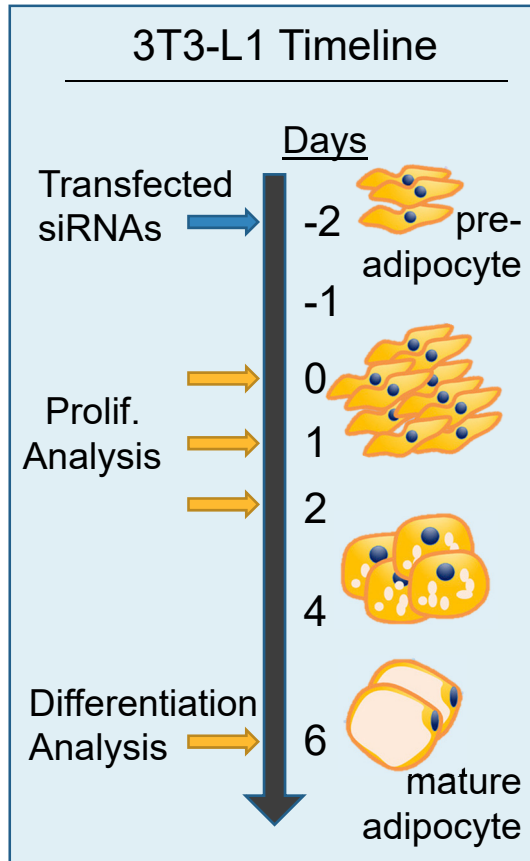


KDM5C: histone 3, lysine 4 demethylase

KDM5C Protein is Highest in Preadipocytes

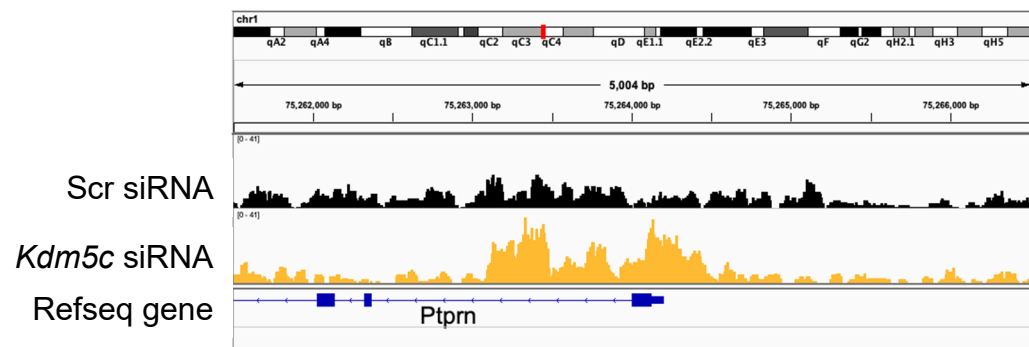


Kdm5c Knockdown Reduces Preadipocyte Proliferation and Lipid Accumulation



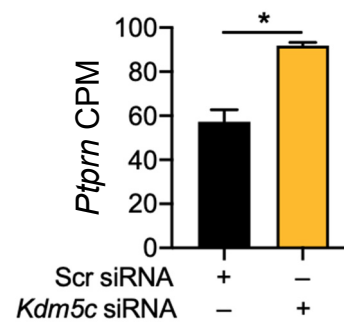
Kdm5c Dosage Alters Chromatin Structure and Gene Expression

Chromatin Accessibility (ATAC-seq)

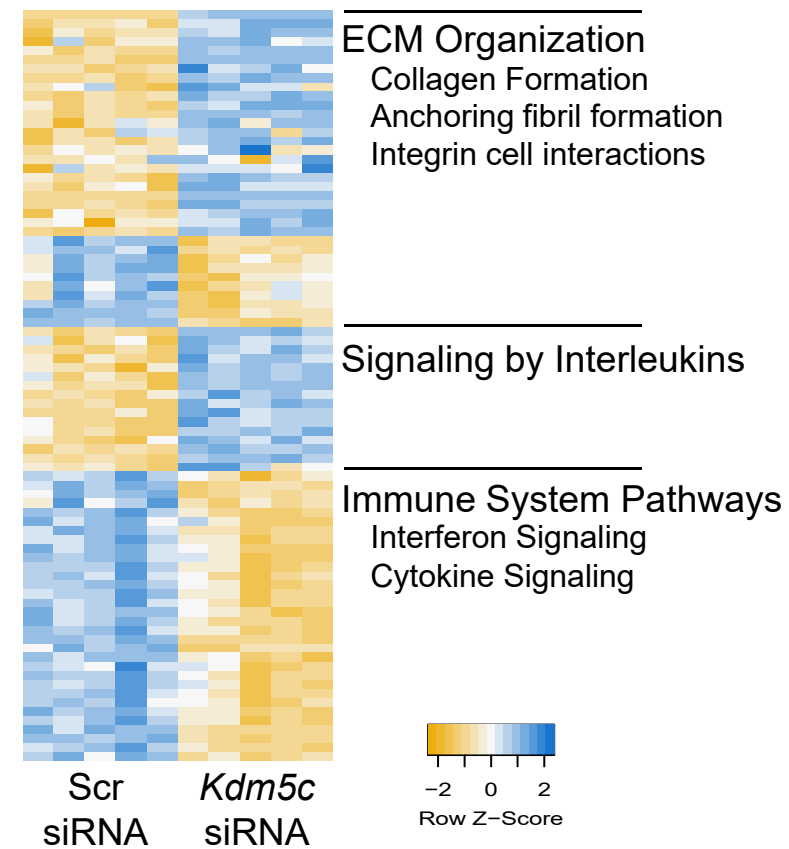


Ptpn: protein tyrosine phosphatase receptor N

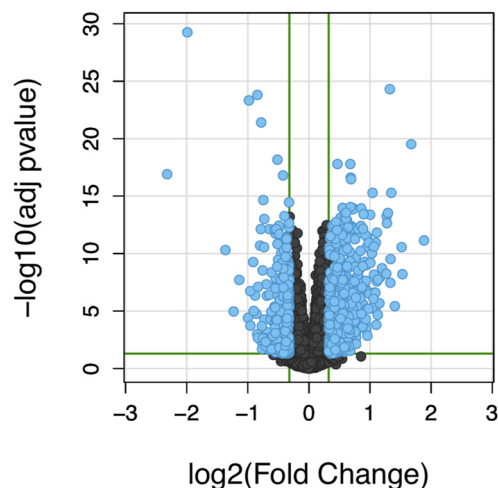
Gene Expression (RNA-seq)



Pathway Analysis



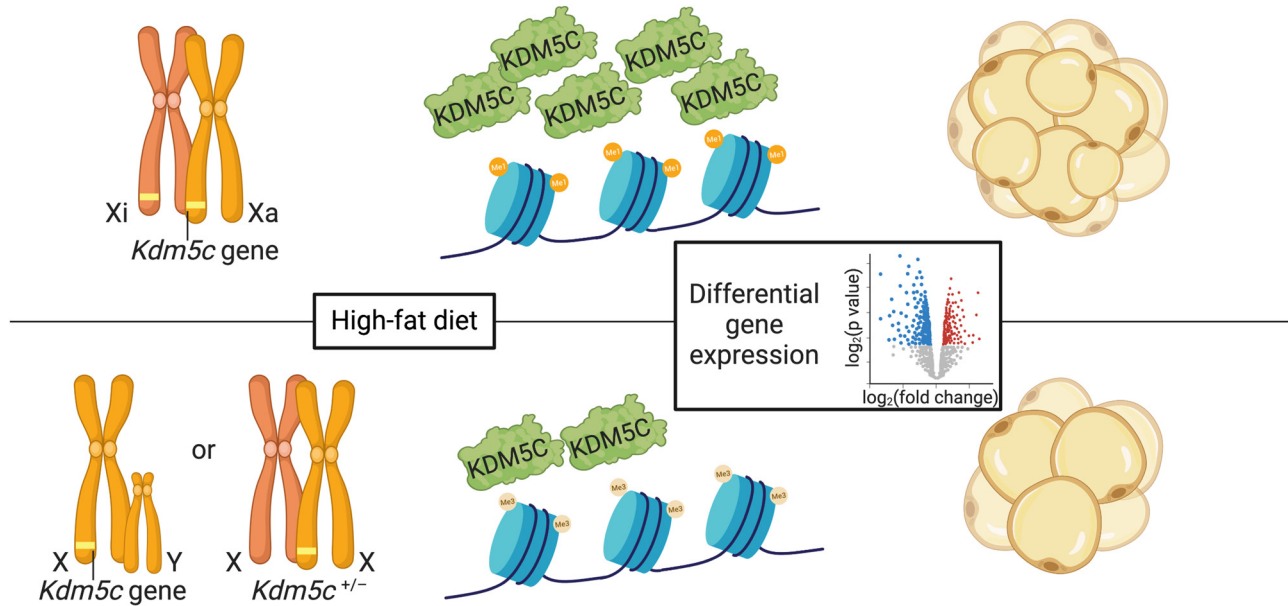
Comparison of DEGs and Promoter Accessibility



With *Kdm5c* knockdown,
675 genes are differentially expressed.

48% of these DEGs have differentially
accessible regions (ATAC-seq) in their
proximal promoter region.

Kdm5c Gene Dosage Determines Sex Differences in Adiposity



- *Kdm5c* gene dosage is a determinant of adipose sex differences.
- Modulating preadipocyte *Kdm5c* expression levels reduces proliferation and differentiation capacity by altering chromatin structure and gene expression.

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Karen Reue Lab, Art Arnold Lab, Matteo Pellegrini Lab, Kerrin Small Lab, Twins UK Cohort

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