

# Fine-mapping a trans-eQTL hotspot

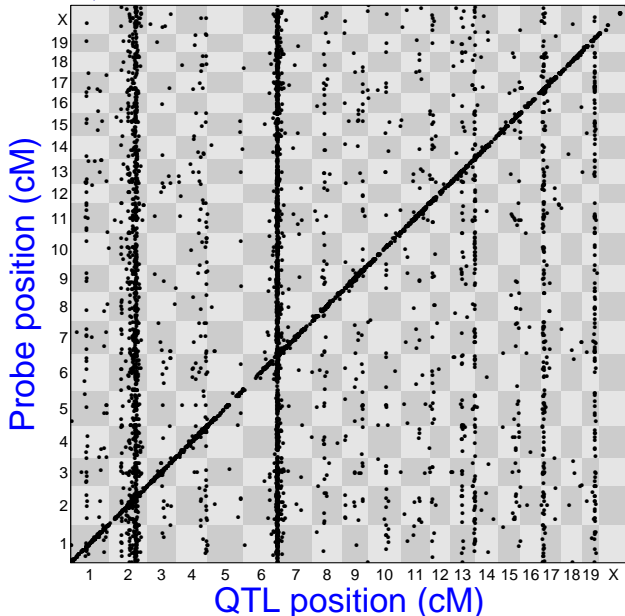
Jianan Tian

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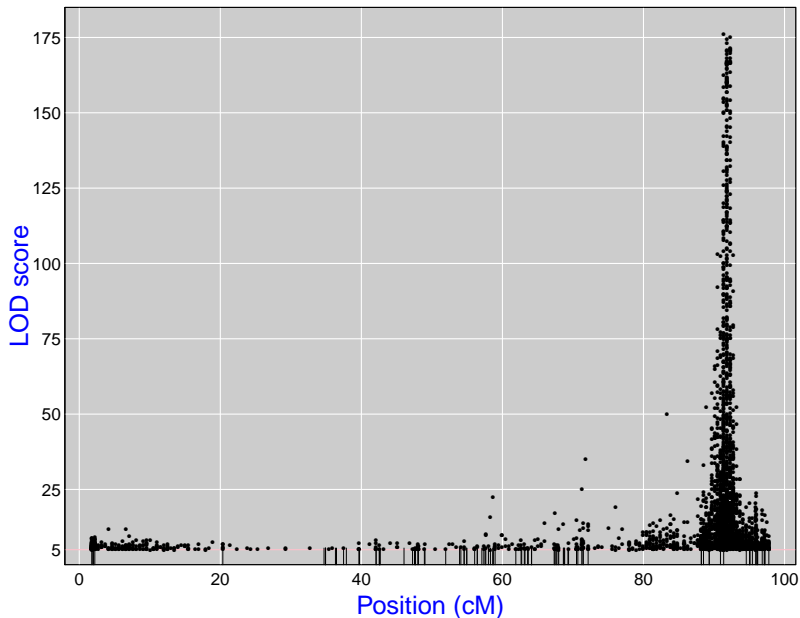
## C57BL/6J (B6) x BTBR intercross

- ▶ Collaboration with Alan Attie
- ▶ ~ 500 mice, all leptin knockouts
- ▶ Genotypes at ~ 2000 markers
- ▶ Gene expression microarray on 6 tissues
  - islet, adipose, gastrocnemius, hypothalamus, kidney, liver
- ▶ Numerous clinical phenotypes

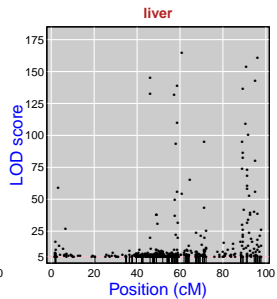
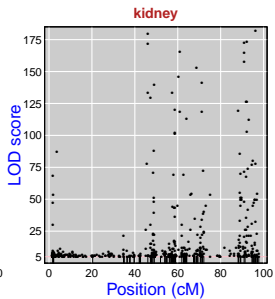
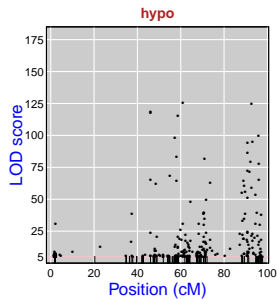
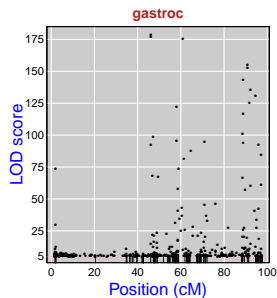
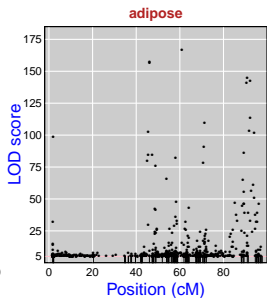
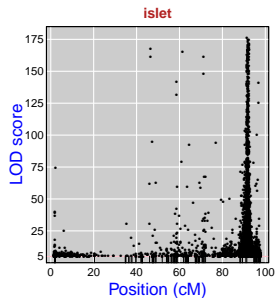
# Islet eQTL: cis/trans plot



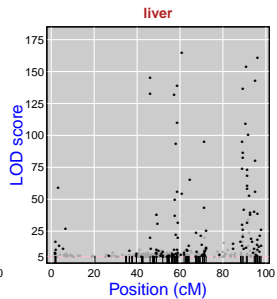
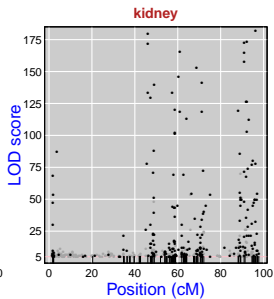
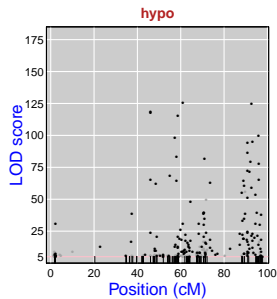
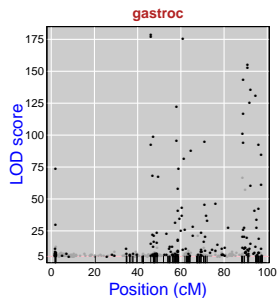
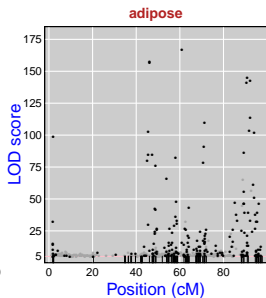
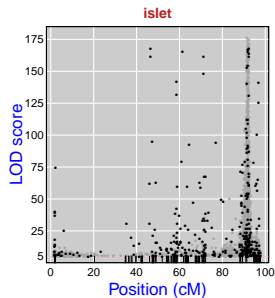
## Islet eQTL, chr 6



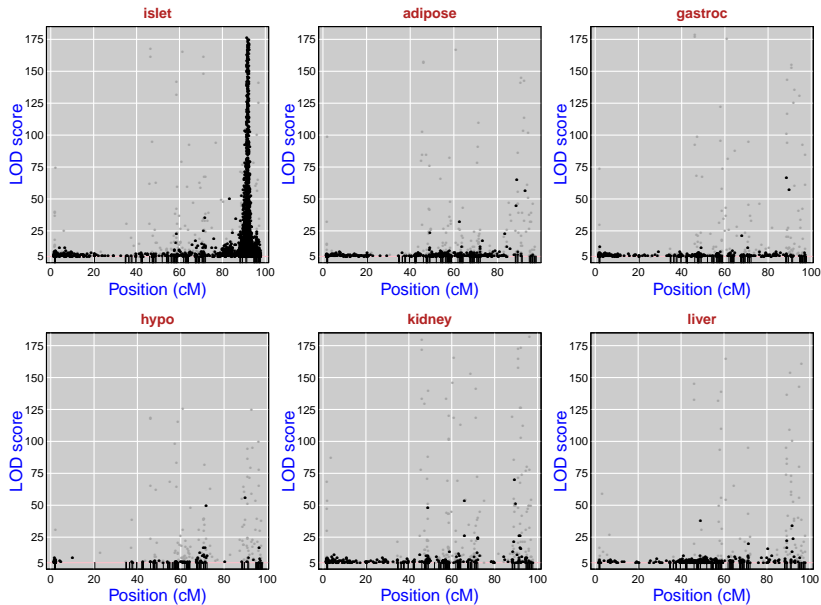
# All six tissues, chr 6



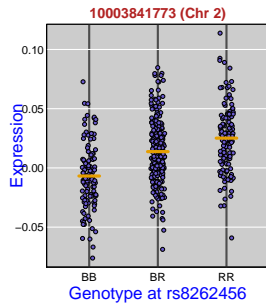
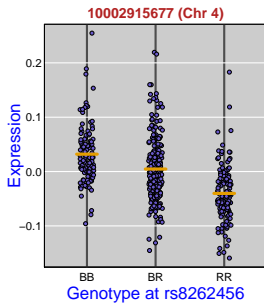
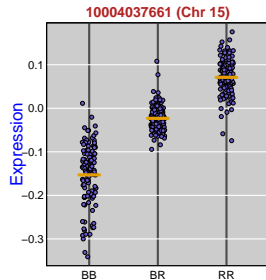
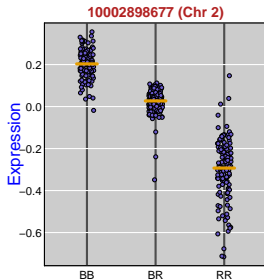
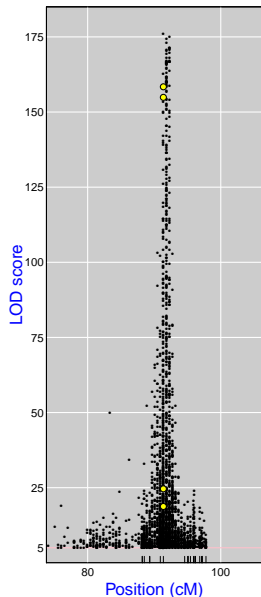
# All six tissues, chr 6: cis-eQTL



# All six tissues, chr 6: trans-eQTL

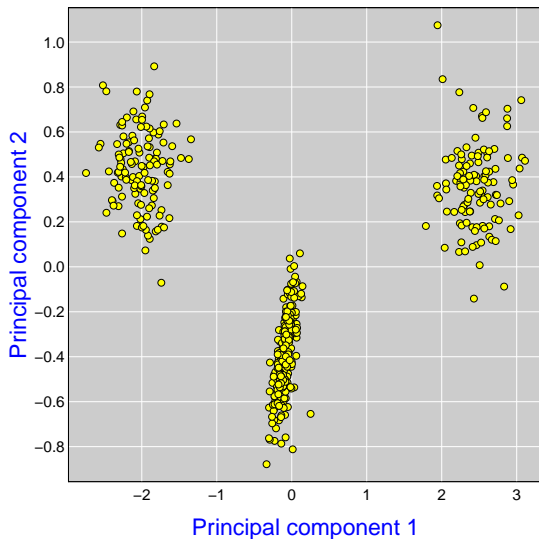


# Islet eQTL, chr 6

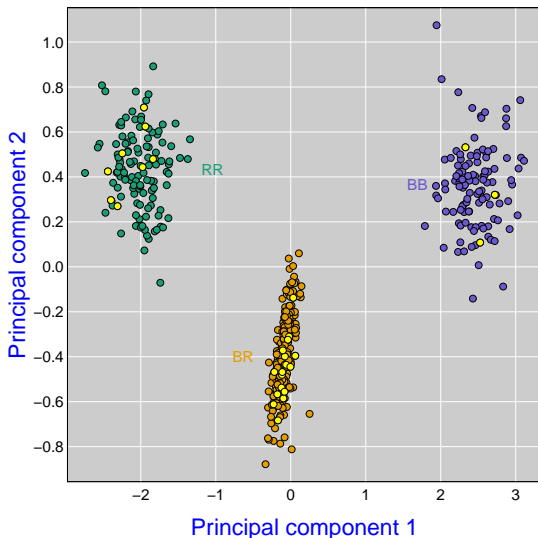




## From expression pattern to QTL genotype

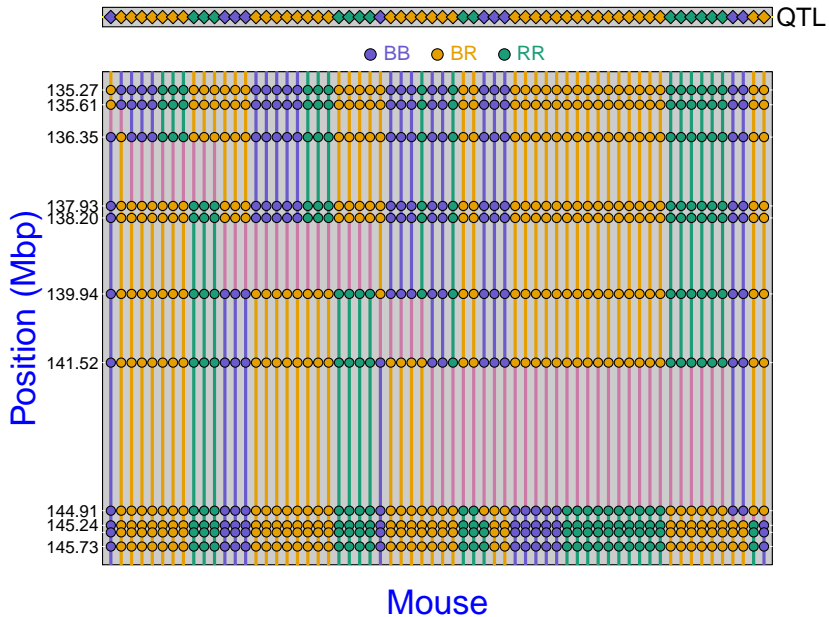


# From expression pattern to QTL genotype

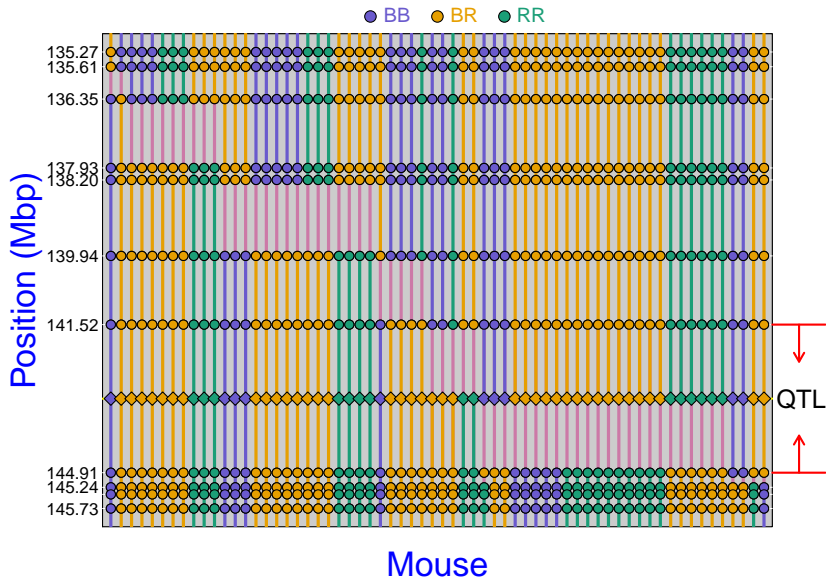


Non-recombinant: mice with the same genotype in the region  
yellow = recombinant mice in the region

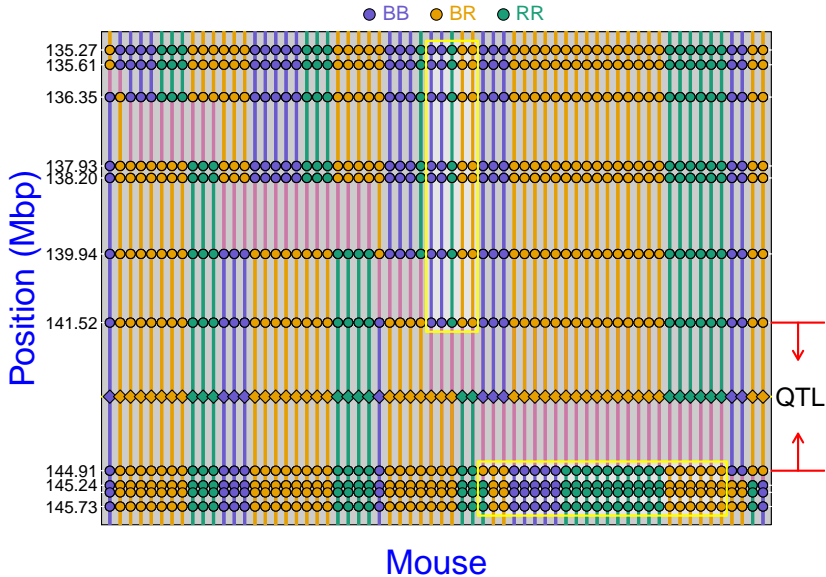
# Recombinant mice



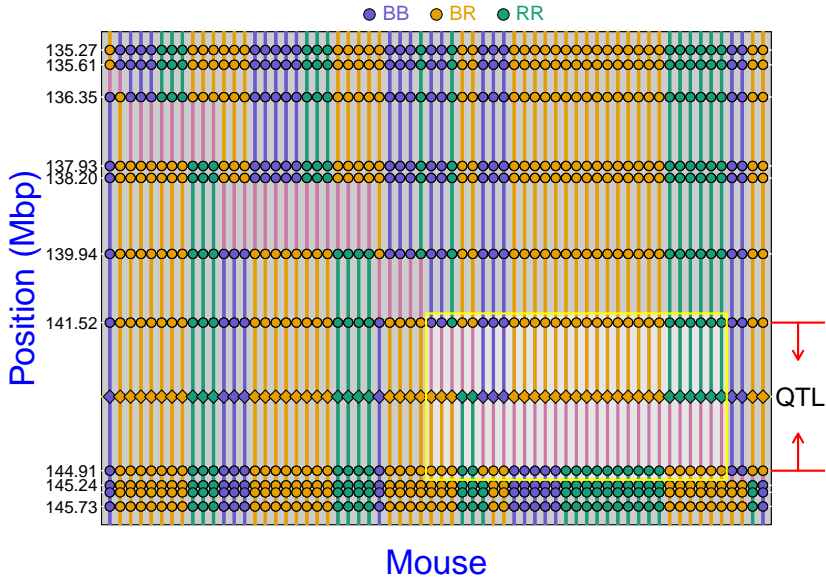
# Recombinant mice (3.39 Mbp)



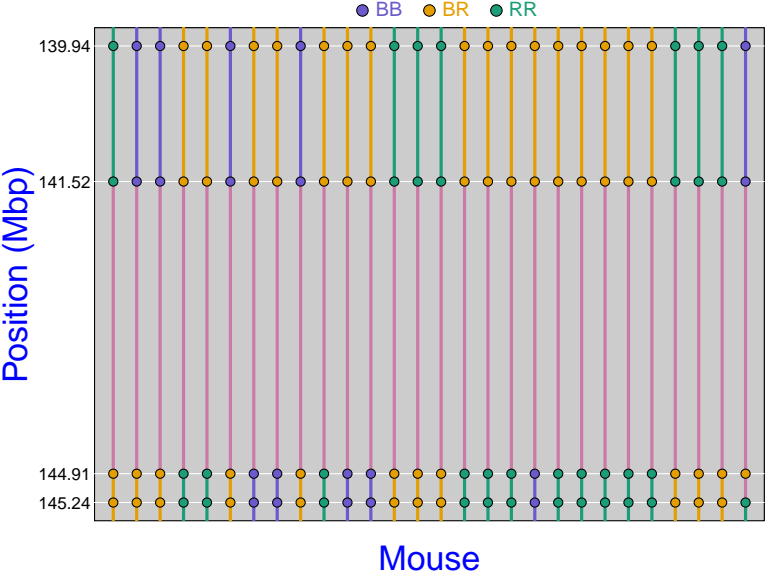
# Recombinant mice (3.39 Mbp)



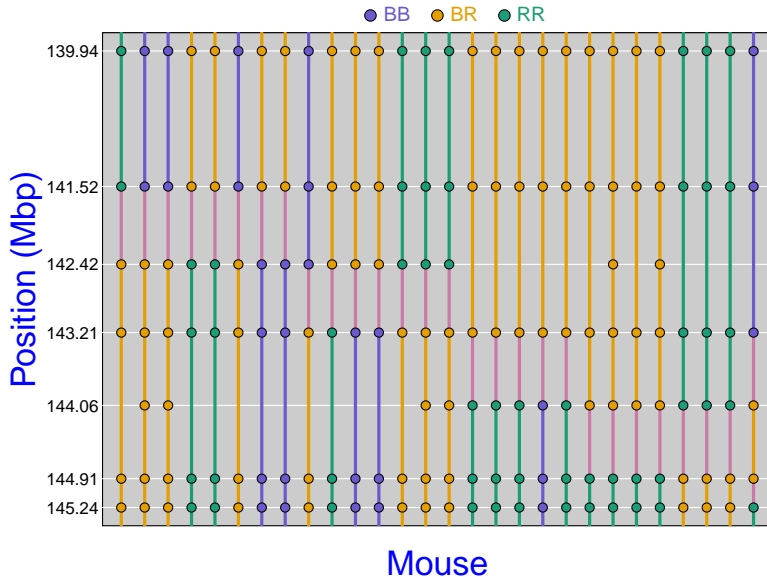
# Recombinant mice (3.39 Mbp)



# Close up



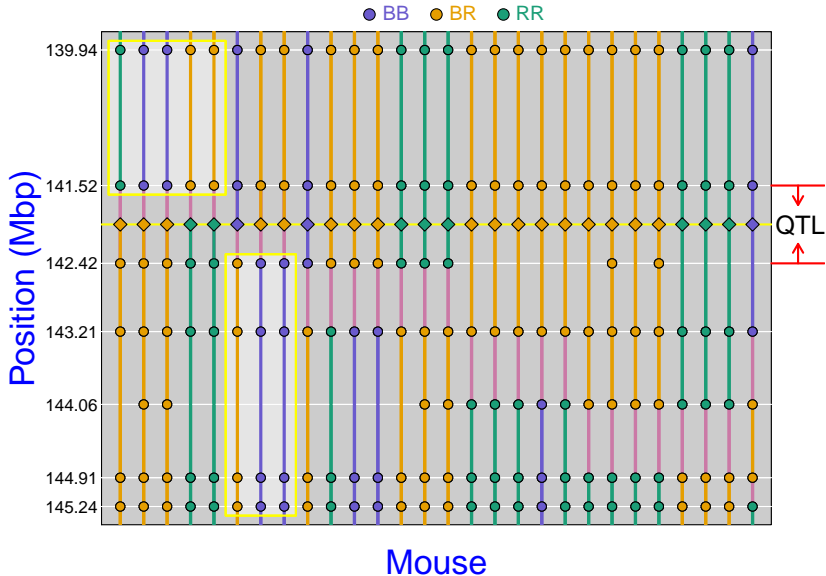
# New genotypes: 3 more markers



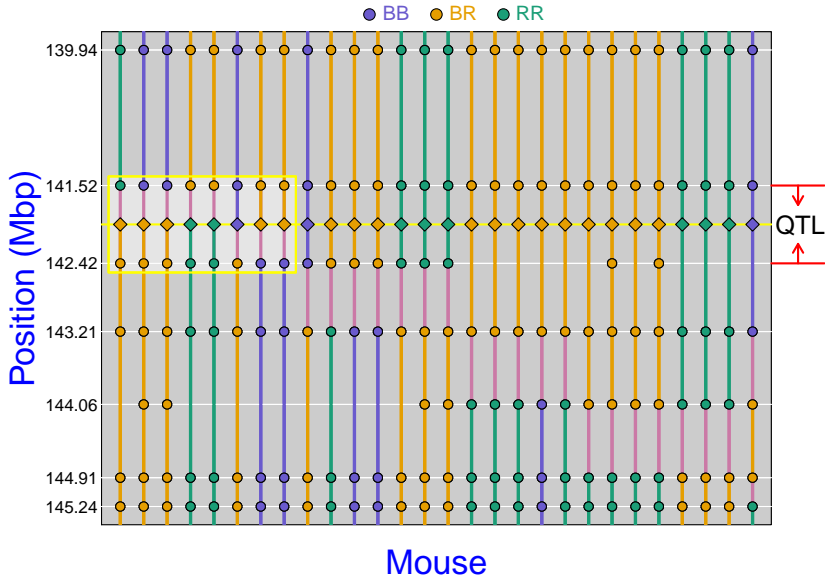




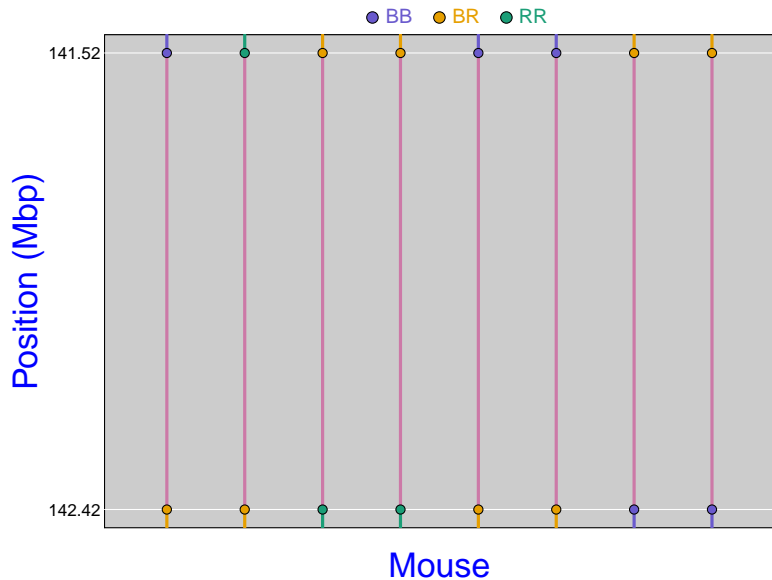
# New genotypes: 3 more markers (0.90 Mbp)



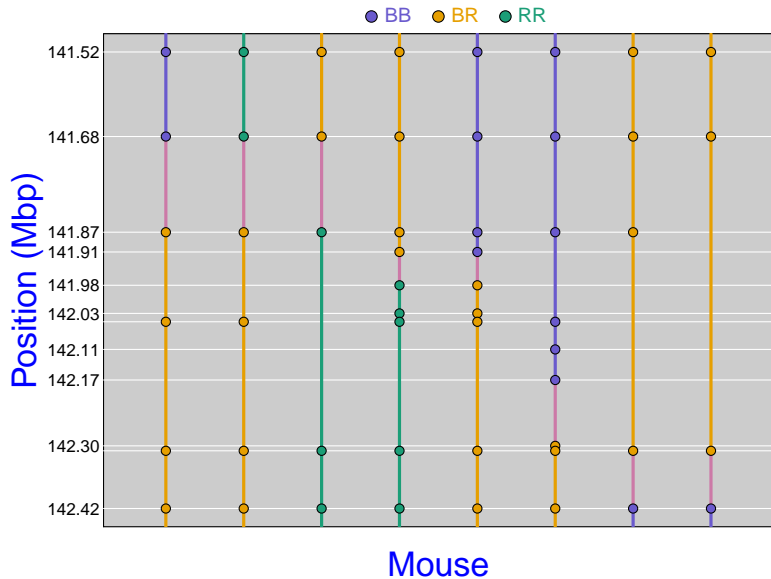
# New genotypes: 3 more markers (0.90 Mbp)



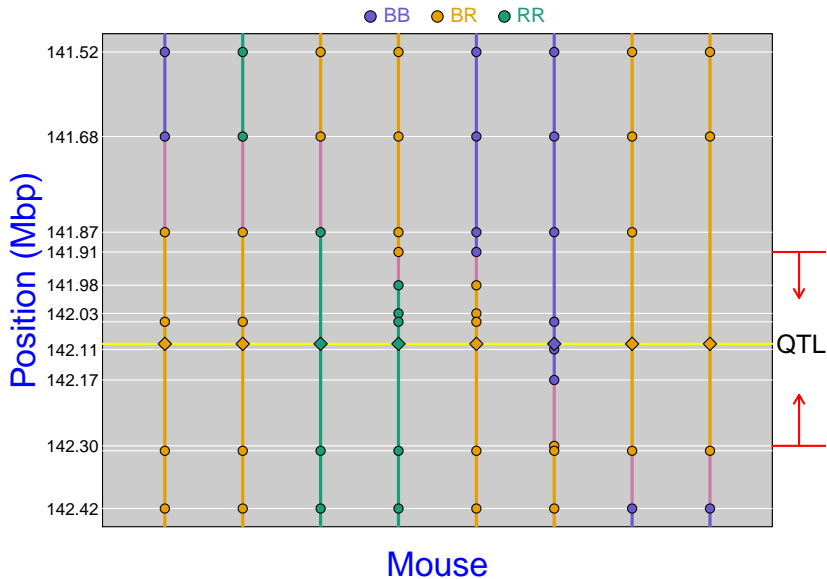
# Closer up



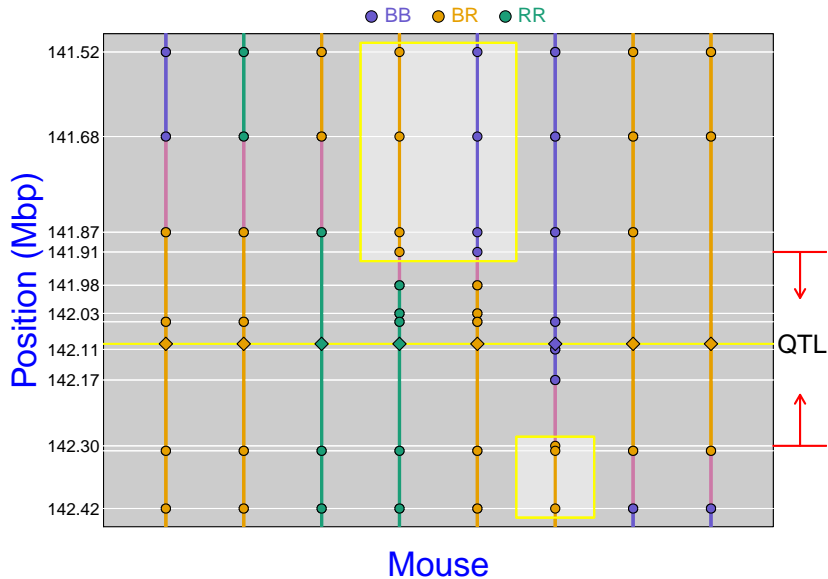
## New genotypes: 10 more markers



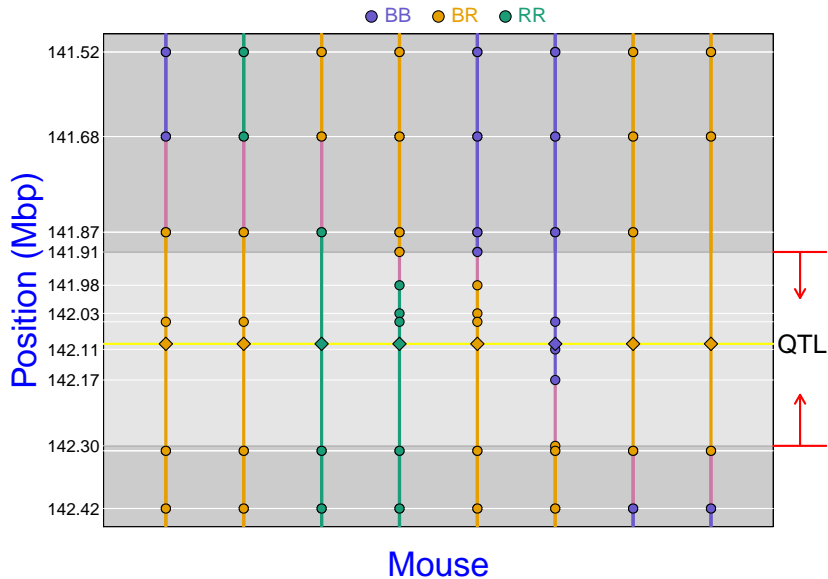
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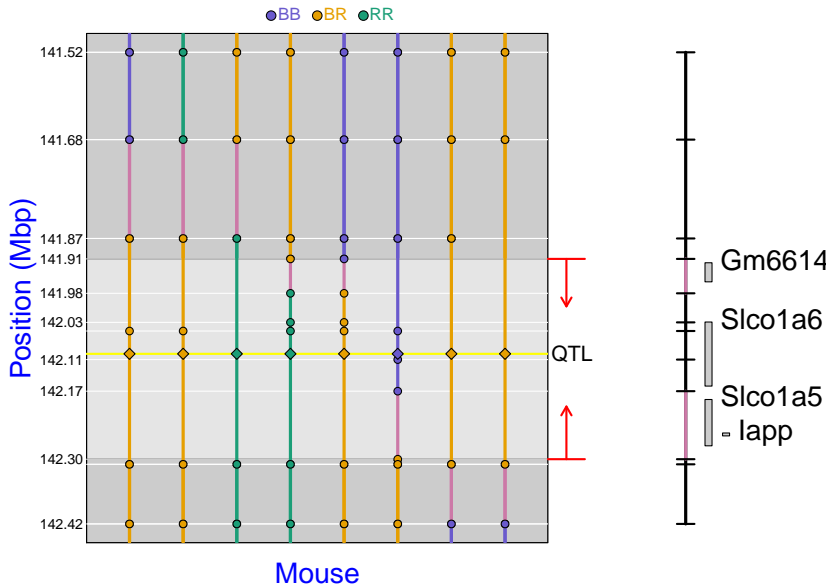


# New genotypes: 10 more markers (0.39 Mbp)





# Genes in the interval (0.39Mbp)



# Summary

- ▶ Islet-specific trans-eQTL band affecting  $\sim 2500$  transcripts
- ▶ Expression pattern of non-recombinant mice  $\rightarrow$  QTL genotypes of recombinant mice
- ▶ Adding markers targeting the crossovers reduced the QTL interval
  - ▶ Interval: 13Mpb  $\rightarrow$  3.39Mbp  $\rightarrow$  0.39Mbp
  - ▶ Protein Coding Gene: 87  $\rightarrow$  23  $\rightarrow$  4

# Acknowledgements

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