

Course BIOS data QTL lookup & analysis

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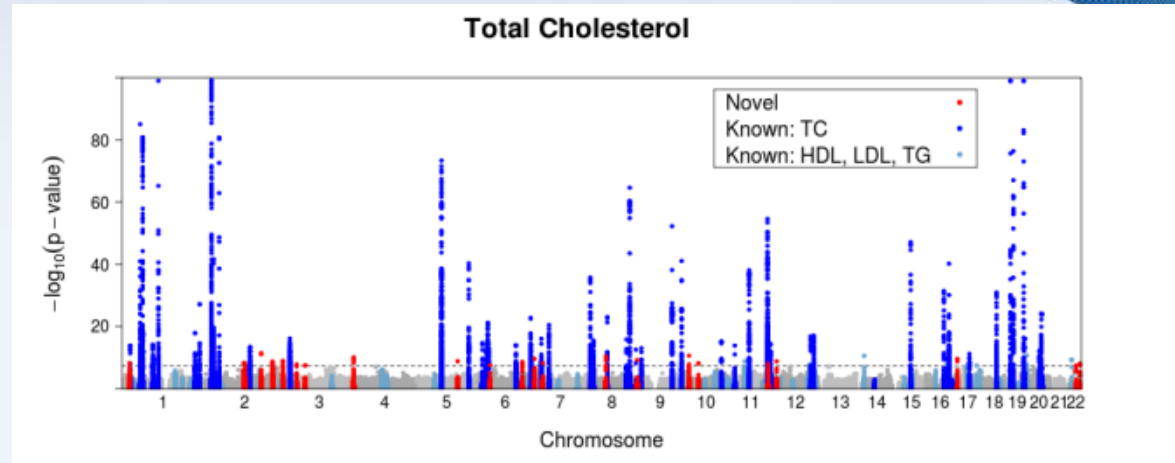
31-03-2017

Contents

- GWAS results
- Integrative genomics
 - What are eQTLs and meQTLs
- QTL lookups
- Available datasets
- QTL analysis in the BIOS datasets
- Practical

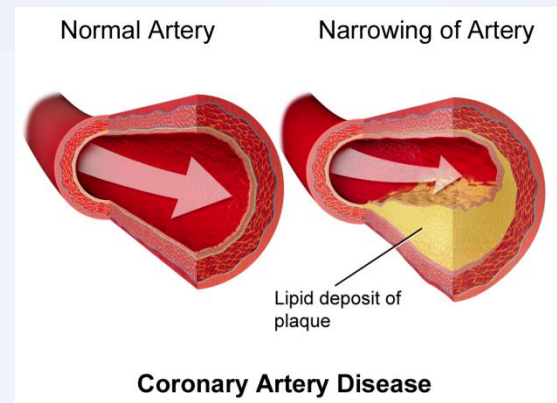
GWAS results

- How does this:



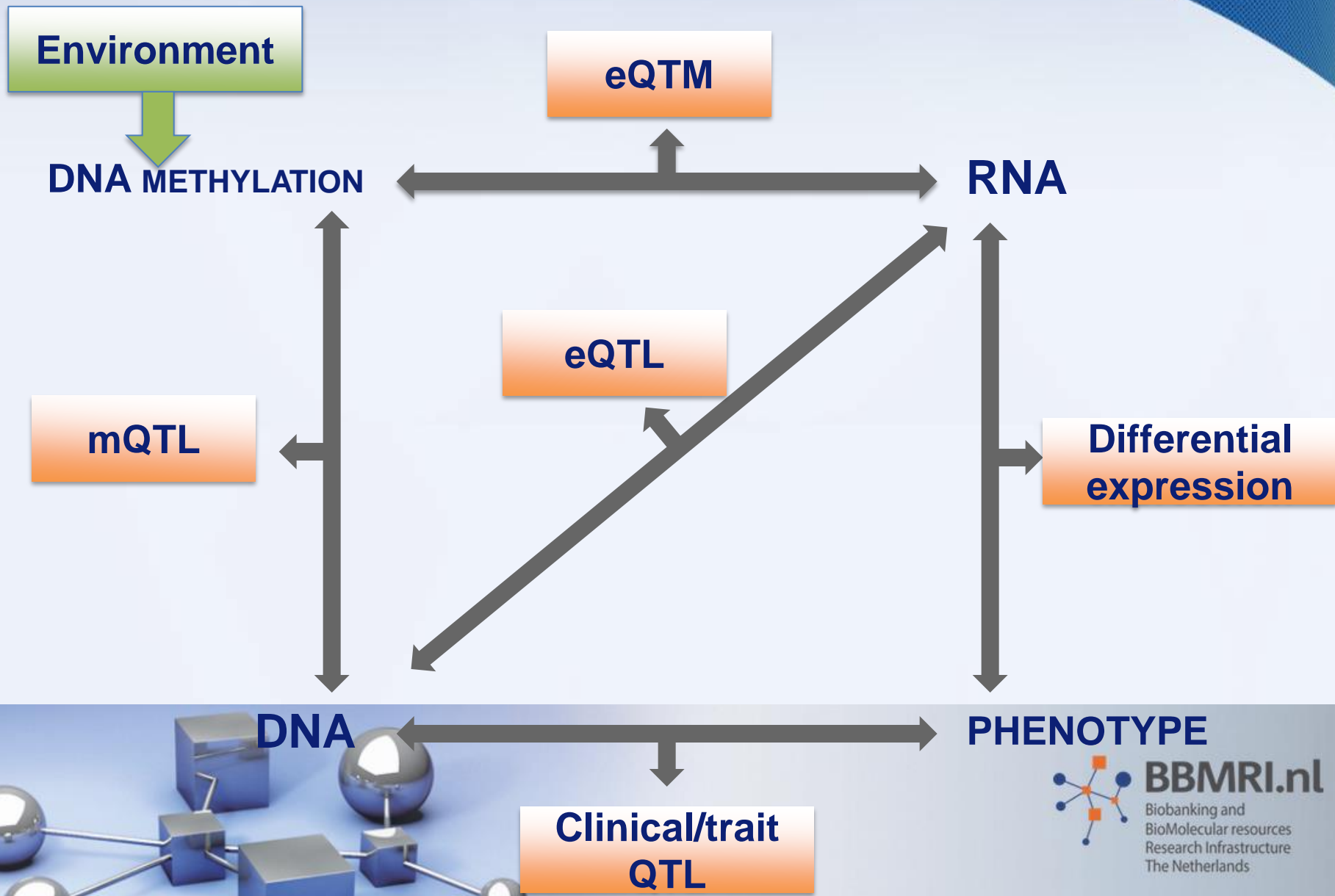
- Result in this:

- Many GWAS hits located in intronic or intergenic regions (Maurano *et al.*, Science 2012)



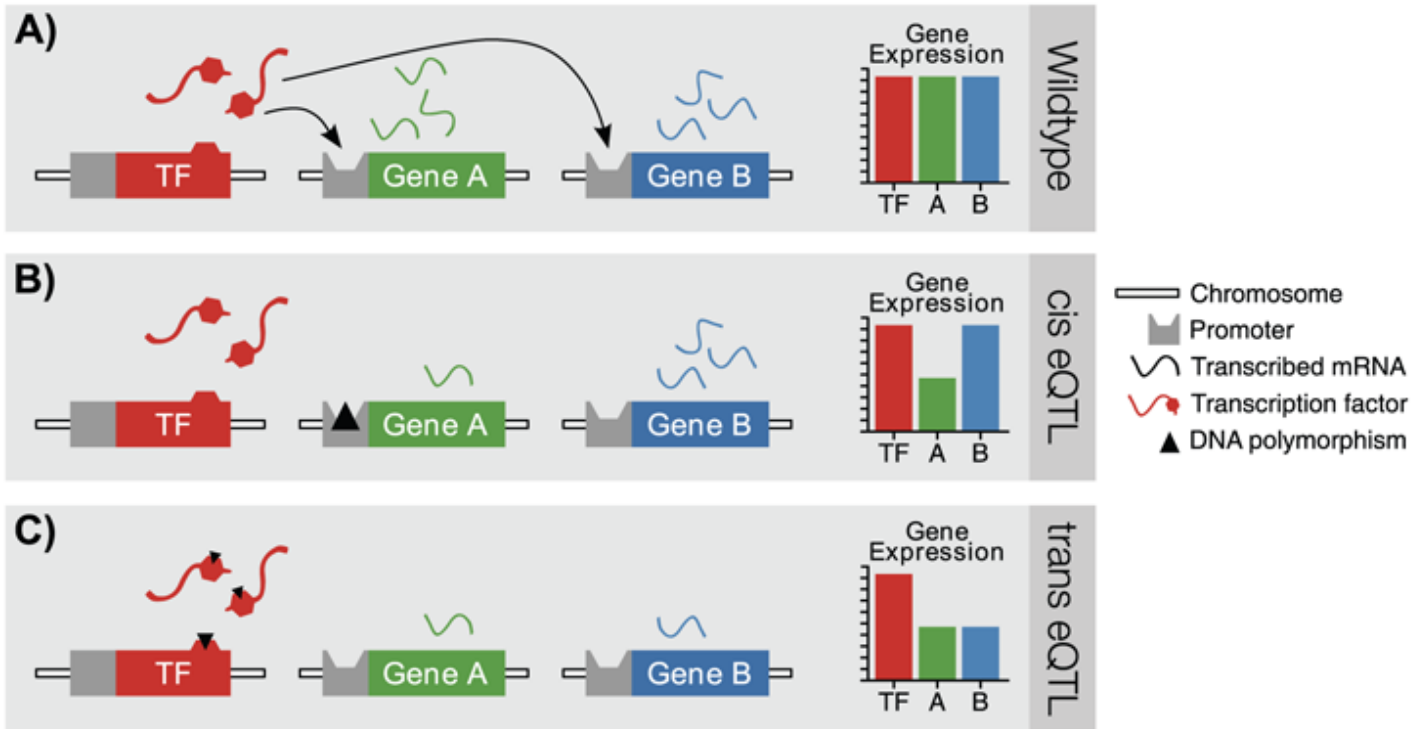
Source GWAS: Global Lipids Consortium, Nat. Gen. 2013

Integrative genomics:



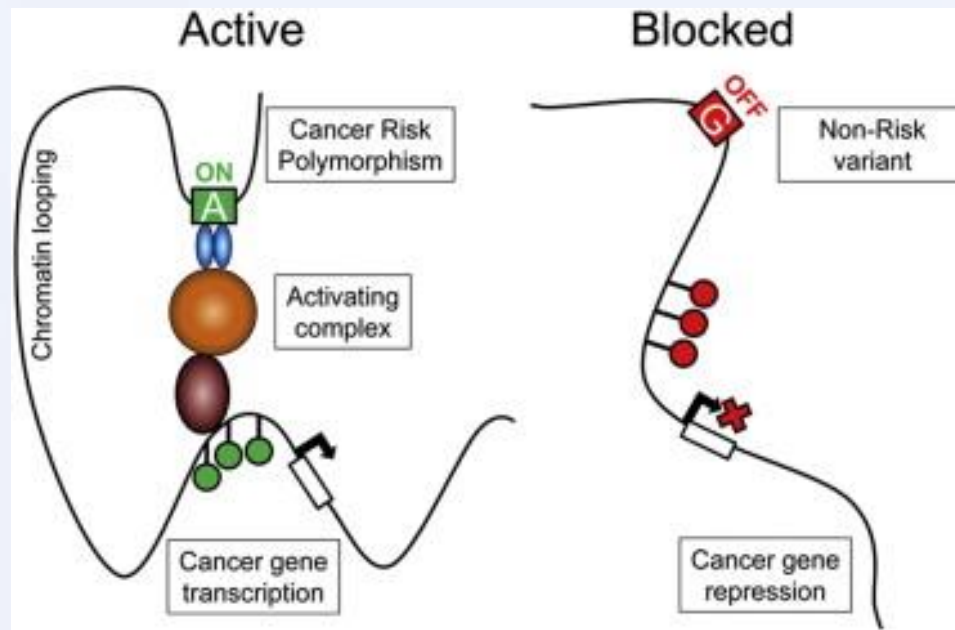
What are eQTLs and meQTLs

- expression Quantitative Trait Locus



What are eQTLs and meQTLs

- methylation Quantitative Trait Locus



QTL lookups

- QTLs categorized within BIOS datasets
- Lookup QTLs using BIOS QTL browser genenetwork.nl/biosqtlbrowser/

Pros	Cons
Easy to use	Only significant QTLs
No analysis time needed	On SNP at a time

QTL lookups

- Example lookup:

Locus	SNP
PHC1-A2ML1	rs4883201
ASAP3	rs1077514
ABCB11	rs2287623

- Looking up these SNPs in the qtl browser reveals:

Locus	SNP	Cis meQTL	Trans meQTL	Cis eQTL
PHC1-A2ML1	rs4883201	✗	✗	✓
ASAP3	rs1077514	✓	✗	✗
ABCB11	rs2287623	✗	✗	✗

Source GWAS: Global Lipids Consortium, Nat. Gen. 2013

Available datasets

- Within BIOS several datasets are available to look further into GWAS hits
 - Genotype/imputations
 - RNA-Seq expression levels
 - Methylation array
 - Metabolomics
- Datasets come pre-prepared for usage
- Correlate SNPs with complete datasets

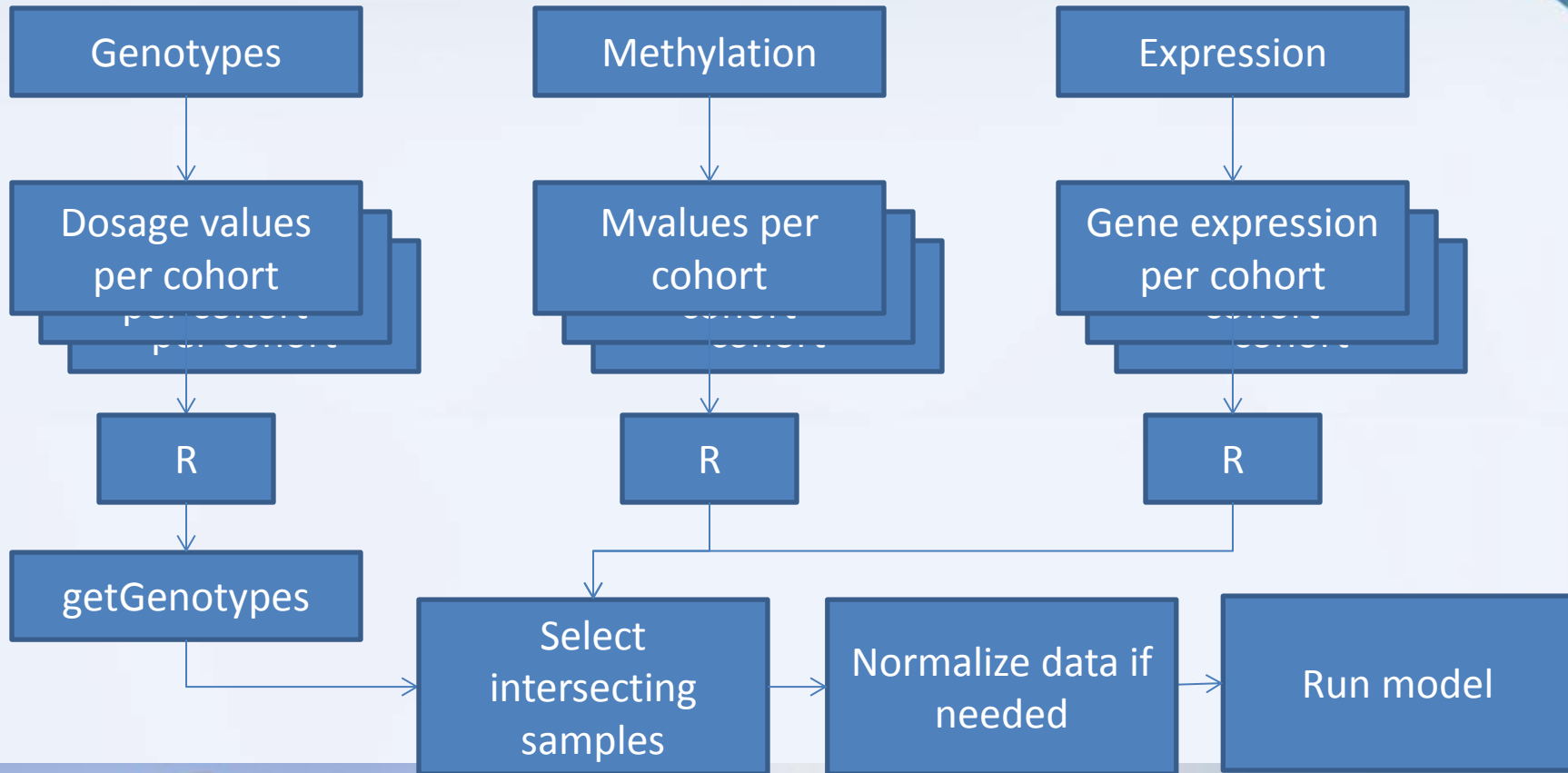


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QTL analysis with BIOS datasets



Practical

- Two parts:
 - eQTL analysis
 - meQTL analysis
- Main tools:
 - R
 - BBMRIomics
 - edgeR
 - MatrixEQTL



Practical

- Data preprocessing
 - BBMRIomics package (previous practical)
 - Correction
 - Covariates or Principal components
 - Normalization
 - Expression, TMM+CPM or FPKM
 - Methylation, Betas or Mvalues
 - Meta-analyze or run all at once



Practical

- MatrixEQTL
 - http://www.bios.unc.edu/research/genomic_software/Matrix_eQTL/
- Commonly used tool for eQTL analyses
 - For example: GTEx
- Several models can be used
 - Linear
 - ANOVA
- Big advantage: Speed
 - Minutes instead of hours/days
 - Optimized for R and Matlab



Practical

- Start practical
- 20-30 min eQTL
- 20-30 min meQTL
- If you're fast, feel free to try your own code/models or the bonus questions

