Pathways and Genes under positive selection in metabolic diseases

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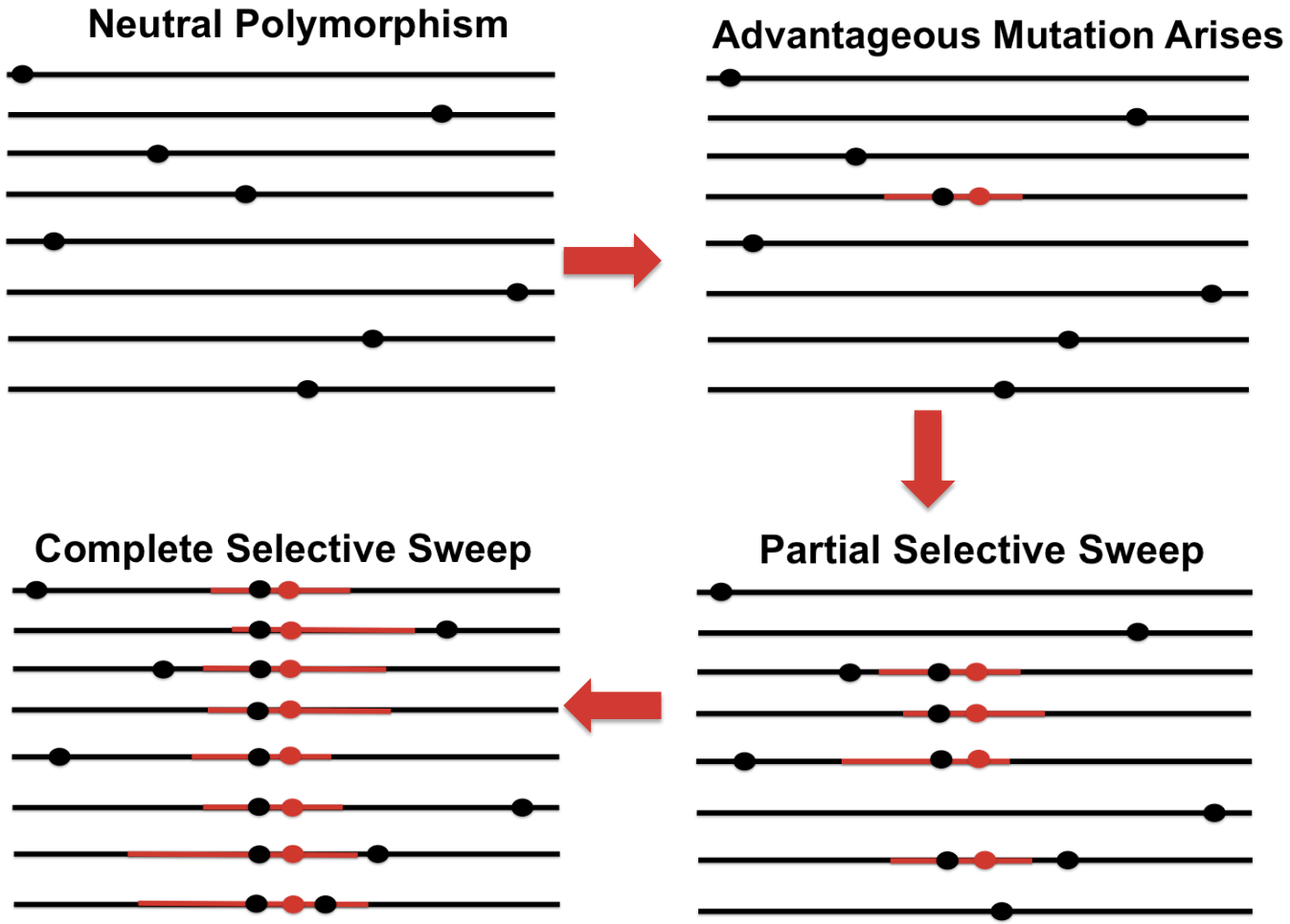
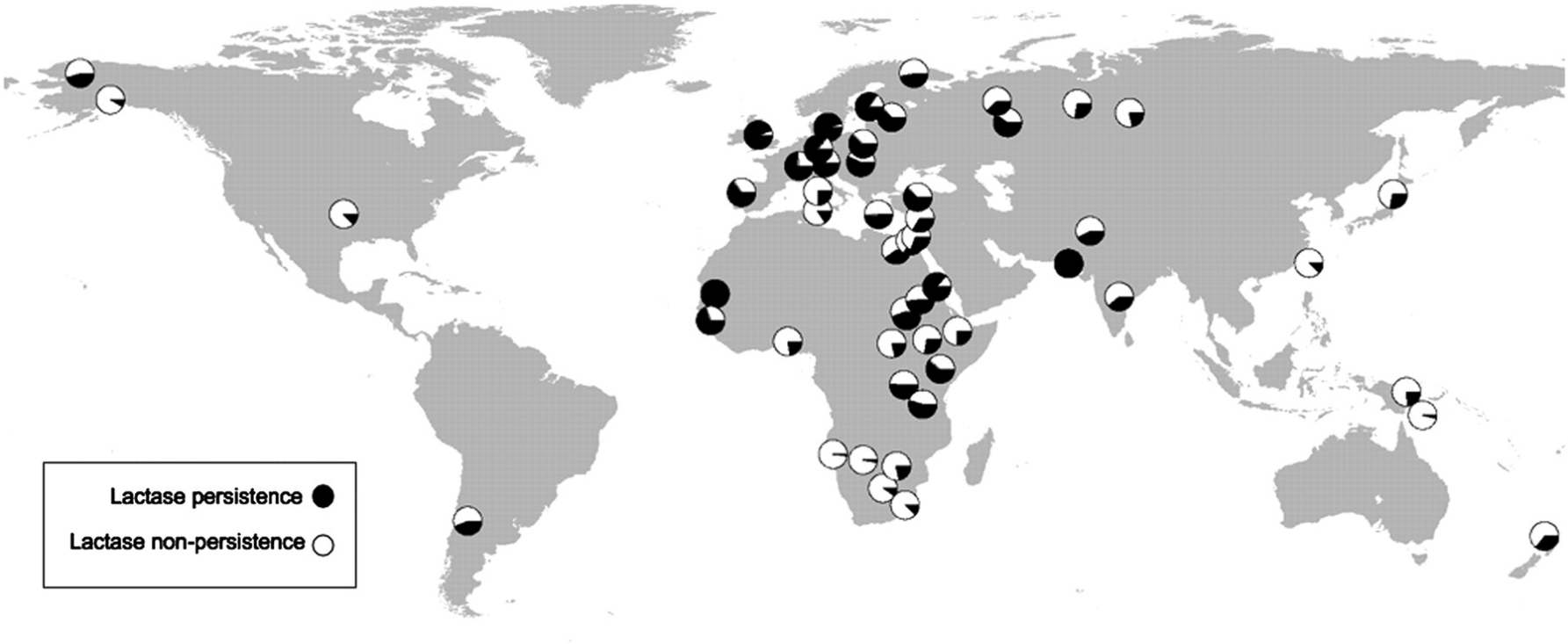
Positive Selection



Why do we study positive selection?



Ingram et al. 2009

Gene Set Enrichment Analysis (GSEA)

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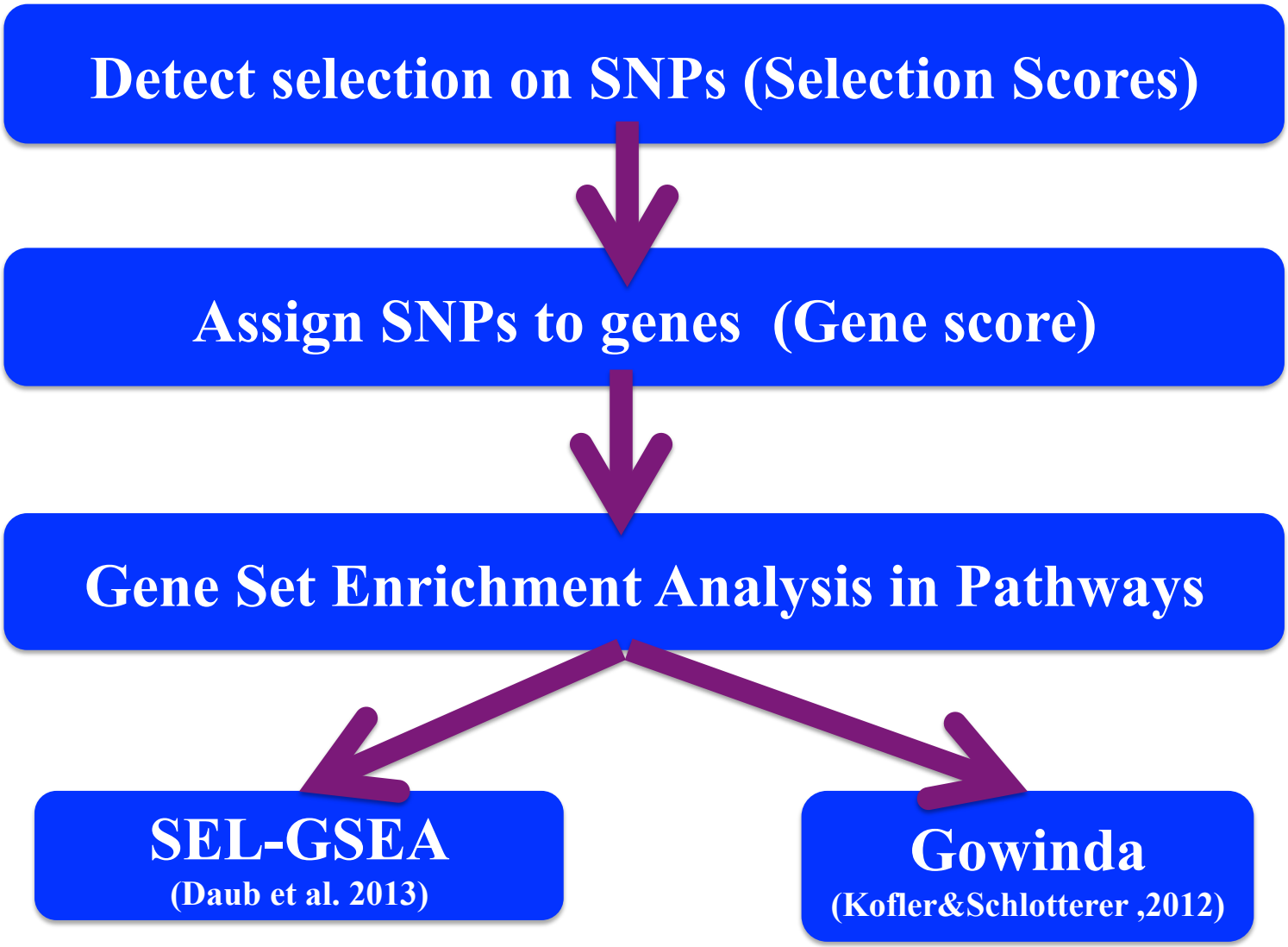
Data

1. SNP data: Hapmap phase II (3 populations (CEU, YRI, CHB+JTP)
2. Gene data: Entrez NCBI database on the 5/2014 (Number of genes: 27081)
3. Gene Sets: Biosystems database on the 5/2014. (Number of pathways: 2362)

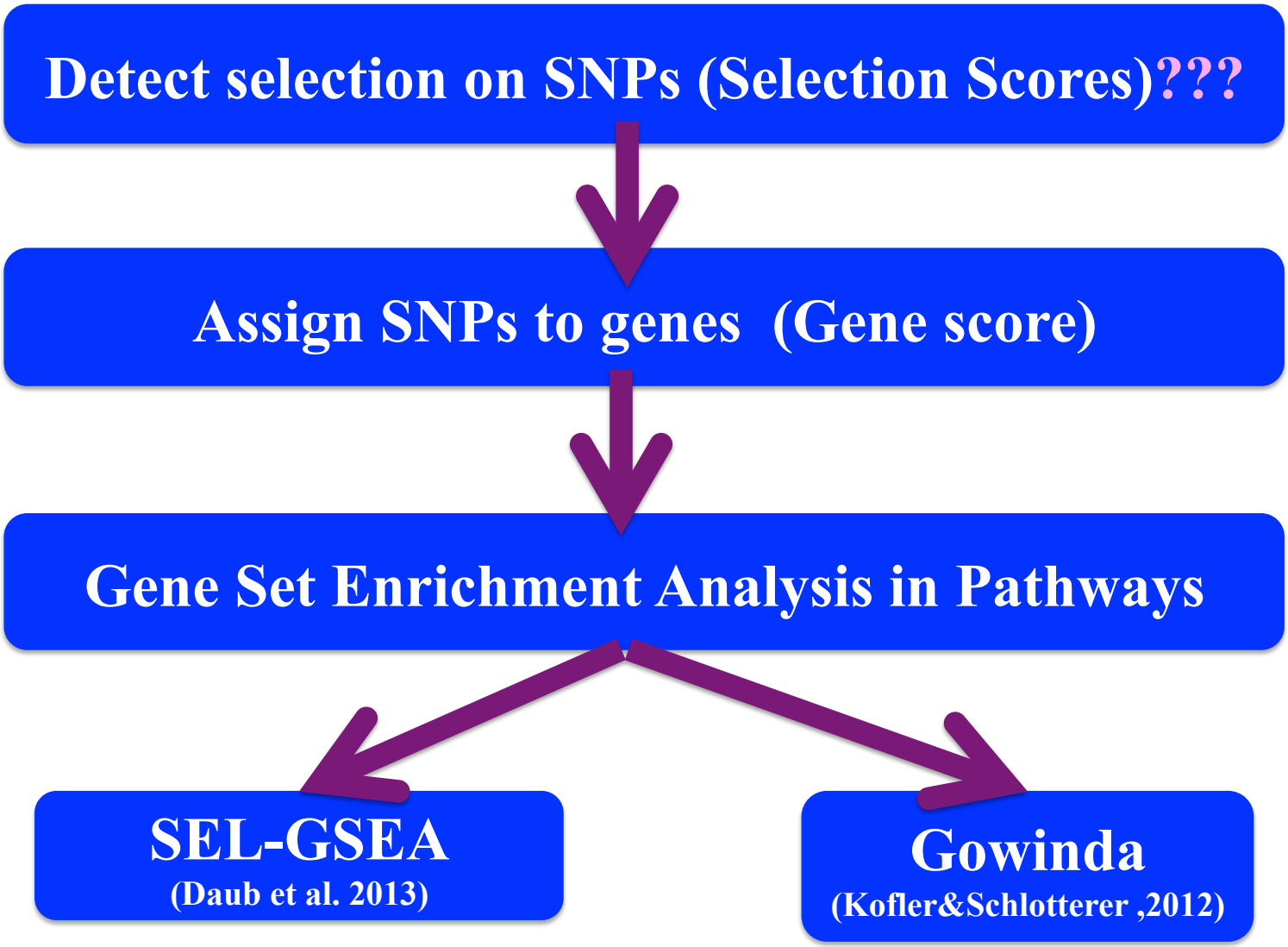
How to detect positive selection on pathways?



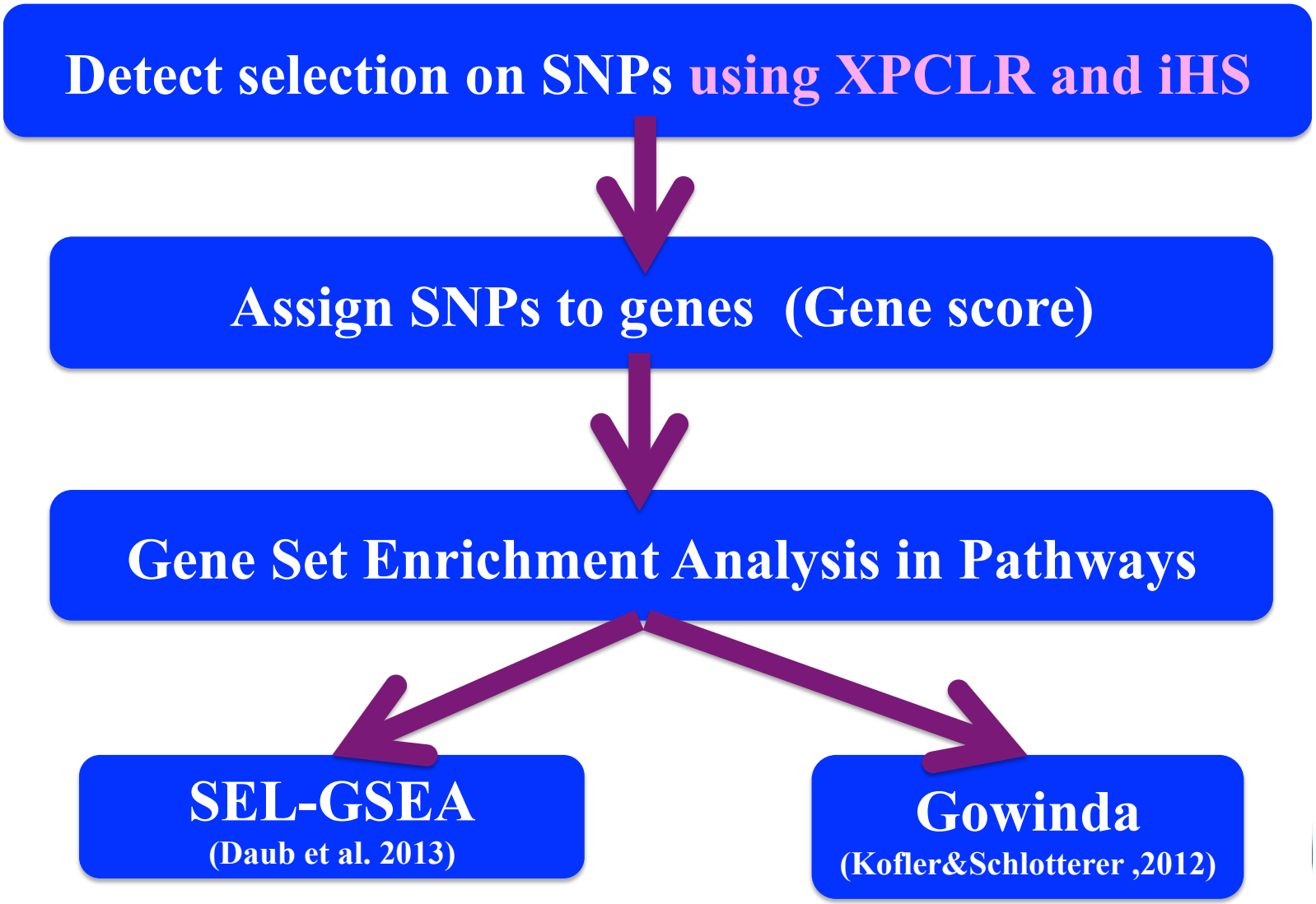
SEL-GSEA

1. Python tool for Gene and Gene Set Enrichment Analysis following Daub et al. (2013) methodology
2. Using SNP data and a gene-set list
3. User-friendly and flexible
4. Freely available:
   `https://github.com/INTERCROSSING/SEL_GSEA`

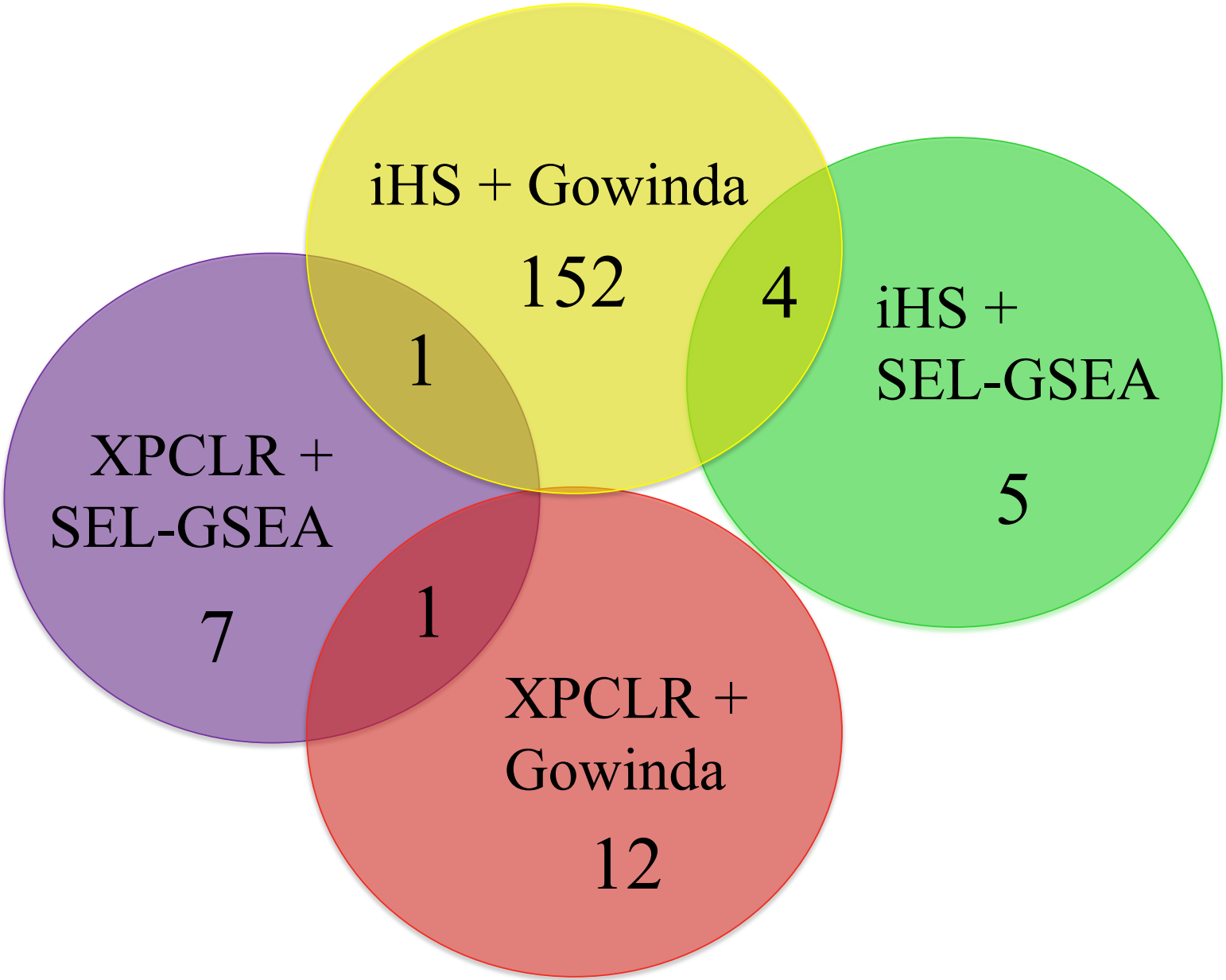
Which method to use to detect selection on SNPs?



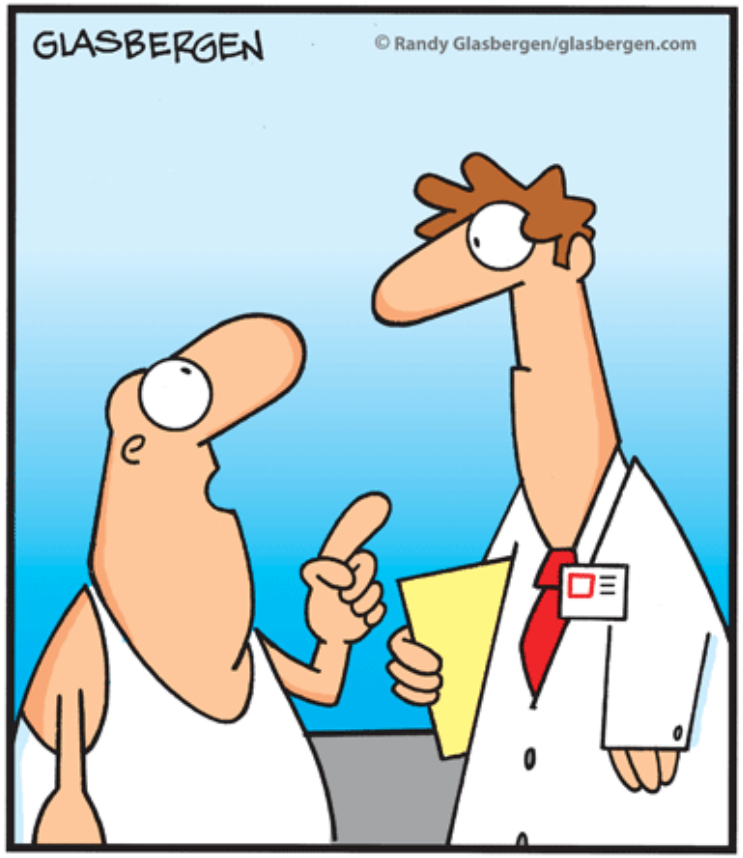
Which method to use to detect selection?



Results of GSEA

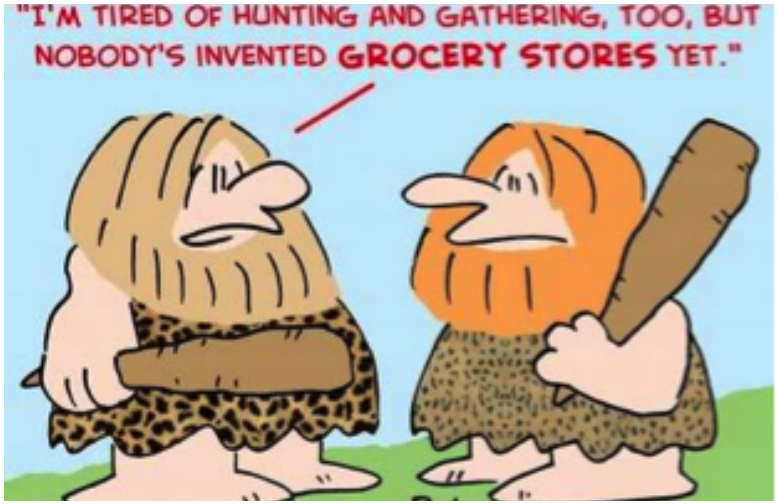


What about metabolic diseases?

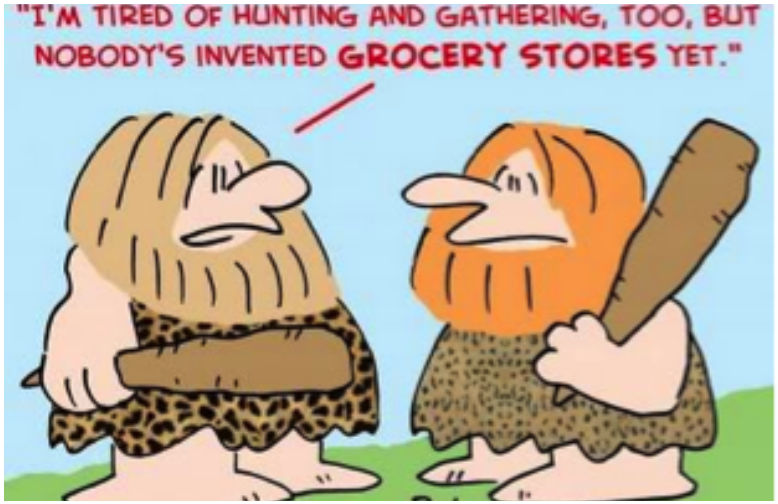


"Diabetes has increased dramatically over the past 20 years. That proves that diabetes is caused by global warming!"

From hunting ... to ... burgers



From hunting ... to ... burgers



1. Glycolysis and gluconeogenesis (4.2e-05)
2. Signal attenuation (0.0003)
3. Glucose transport (0.003)

Gene Analysis

683 genes directly or indirectly associated with:

1. obesity or
2. metabolic syndrome or
3. diabetes

Positively selected genes in metabolic diseases

1. 25 candidate genes for positive selection
2. 12 of them play a risk role
3. 7 of them play a protective role
4. 10 of them were detected to be under positive selection before
5. 15 new candidates for metabolic diseases

Take Home Message

1. multifactorial diseases
2. study the whole system

Acknowledgements

Eric Bazin (LECA, Grenoble), Oscar Gaggiotti (LECA, Grenoble /St Andrews, UK)

Thank you for your attention.

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Any Questions?