Pathways and Genes under positive selection in metabolic diseases

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Positive Selection

Neutral Polymorphism

Advantageous Mutation Arises

Complete Selective Sweep

Partial Selective Sweep

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Why do we study positive selection?

Ingram et al. 2009

Pathways and Genes under positive selection in metabolic diseases
Gene Set Enrichment Analysis (GSEA)

Data

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

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Data

1. SNP data: Hapmap phase II (3 populations (CEU, YRI, CHB+JTP))
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How to detect positive selection on pathways?

Detect selection on SNPs (Selection Scores)

Assign SNPs to genes (Gene score)

Gene Set Enrichment Analysis in Pathways

SEL-GSEA (Daub et al. 2013)

Gowinda (Kofler & Schlotterer, 2012)
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?

Detect selection on SNPs (Selection Scores)???

Assign SNPs to genes  (Gene score)

Gene Set Enrichment Analysis in Pathways

SEL-GSEA  
(Daub et al. 2013)

Gowinda  
(Kofler&Schlotterer ,2012)

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Which method to use to detect selection?

- Detect selection on SNPs using XPCLR and iHS
- Assign SNPs to genes (Gene score)
- Gene Set Enrichment Analysis in Pathways
  - SEL-GSEA (Daub et al. 2013)
  - Gowinda (Kofler & Schlotterer, 2012)
Results of GSEA

- XPCLR + SEL-GSEA
- iHS + Gowinda
- XPCLR + Gowinda
- iHS + SEL-GSEA

<table>
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<th>Venn Diagram Details</th>
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<tr>
<td>XPCLR + SEL-GSEA</td>
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<td>iHS + SEL-GSEA</td>
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“Diabetes has increased dramatically over the past 20 years. That proves that diabetes is caused by global warming!”
From hunting ... to ... burgers

"I'M TIRED OF HUNTING AND GATHERING, TOO, BUT NOBODY'S INVENTED GROCERY STORES YET."

Pathways and Genes under positive selection in metabolic diseases
From hunting ... to ... burgers

1. Glycolysis and gluconeogenesis (4.2e-05)
2. Signal attenuation (0.0003)
3. Glucose transport (0.003)
683 genes directly or indirectly associated with:
1. obesity or
2. metabolic syndrome or
3. diabetes
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

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Thank you for your attention.
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Any Questions?