**Transcriptome and genome sequencing uncovers functional variation in human populations**

Geuvadis main paper outline. Oct 17, 2012 TL

1. **Data production and quality**

* Distributed RNAseq works well, and we have a great dataset

1. **Transcriptome variation in human populations**

\* Extensive population variation in various transcriptome features can be seen only by sequencing populations

* Discovery of additional transcriptome features, especially rare events that are underrepresented in annotations
* Quantification of qualitative and quantitative mRNA variation between individuals and populations: almost equal amounts of expression level and splicing variation
* Quantifying individual variation in a wide spectrum of transcriptome features: splicing, repeat expression, RNA editing, fusion genes, n-TARs
* miRNA variation contributes to mRNA variation in human populations

1. **Regulatory variation in the human genome**

\* Genome + RNA sequencing data gives us an unprecedented view to both rare and common regulatory variation and its functional mechanisms

* Over 7000 of classical eQTLs but going beyond: hundreds of asQTLs (at least), and QTLs to the other transcriptome features that we measure.
  + Causal variant discovery
  + Functional annotation of the QTLs
  + Interactions between variants
* Rare regulatory effects on both expression and splicing
  + Underlie the vast majority of allelic variation between individuals
  + Variants can be mapped: likely to be an extremely important class of functional variants.

**4. Improved interpretation of loss-of-function variation**

* Validation of functional effects of LoF variants
* Improved models of functional effects
* Ubiquitous compensatory mechanisms

**5. Data sharing and visualization**

\* This is the one of the most important transcriptome variation reference datasets, and the data is there for everyone to access

* Annotations: the best functional annotation of 1000g Phase 1 variants
* Data file sharing at EBI ENA/arrayexpress
* Visualization in Ensembl browser