

Using the manual: From genotype to phenotype

You are already familiar with the fundamental mechanisms that interpret genetic information; transcription and translation are part of the 'central dogma' of molecular biology, that information flows from DNA to RNA to protein. These processes are part of the core material.

But the story becomes more complex. The devil, as usual, is in the details. Only about 2% of your genome codes for proteins. An even smaller fraction codes for identified functional RNAs. On the other hand, almost half your genome is a huge number of copies of bits and pieces of DNA spliced in by transposons - parasites of the genome. If you randomly pick a sequence in the genome, how do you decide if it is functional or not? What are the possible mappings between a piece of DNA (a bit of genotype) and its effect on the animal (phenotype)? How can you identify the mappings? Are these mappings the same for all of us? If a sequence is not functional is it therefore not part of a gene? And just what is a 'gene'?

Reading:

MBoC(6th) Ch8: ANALYSING PROTEINS, pgs. 452-455, *STUDYING GENE EXPRESSION AND FUNCTION*, pgs. 502-506. **Ch9: 535-540.**

Rinn et al (2007) **Functional Demarcation of Active and Silent Chromatin Domains in Human HOX Loci by Noncoding RNAs**

Arboleda-Velasque (2019) **Resistance to autosomal dominant Alzheimer's disease in an APOE3 Christchurch homozygote: a case report**

Zalocusky (2019) **An Alzheimer's-disease-protective APOE mutation** (commentary on Arboleda-Velasque et al (2019))

The ENCODE Project Consortium (2012) **An integrated encyclopedia of DNA elements in the human genome**

Graur (2013) **On the Immortality of Television Sets: "Function" in the Human Genome According to the Evolution-Free Gospel of ENCODE** (commentary on the Encode Consortium (2012))

Stoeger et al (2018) **Large-scale investigation of the reasons why potentially important genes are ignored**

Chabris et al 2012 **Most Reported Genetic Associations With General Intelligence Are Probably False Positives**

Sniekers et al (2017) **Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence**

Need to think about

What is a gene?

Need to know and understand

Monogenic vs Polygenic traits

Qualitative vs quantitative traits

Epistasis, modifier loci and alleles

Functional RNAs