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Comparing polygenic signals across species

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Whereas there are well established methods for translating findings about single genes from humans to non-humans, there is an urgent need for methods to translate the polygenic signals obtained from GWAS across species. This is difficult because GWAS produces information about SNPs rather than genes, however SNPs are inherently species specific. My lab is helping to develop two complementary methods to address this problem. Both methods depend on translation of GWAS signals from SNPs to genes. In one method, this is done by choosing the gene that is nearest to an implicated SNP. The list of orthologous genes from two or more species are then projected into a previously defined gene network and a random walk is used to defuse the signal to neighboring genes. The overlap between the network defined by each species is then assessed for significance relative to permuted gene sets. In the second method, SNPs are used to predict gene expression and these predictions are used to estimate the effect of each gene's expression on phenotype, creating what we term a polygenetic transcriptomic risk score (PTRS). A PTRS can then be used in conjunction with orthologous genes such that a PTRS defined in one species can be used to estimate an analogous trait in individuals from another species. In preliminary work we found that both methods identify highly statistically significant overlap in the signals associated with both BMI and body length. We are extending these methods to behavioral traits, including those relevant for substance use disorders.