Cross-species comparisons generally require careful adjustment for any bias due to species-specific idiocyncracies in preprocessing. We take a conservative approach when comparing the effects of social status on human versus macaque immune cell gene expression. Because humans and rhesus macaques diverged >20 million years ago and are only ~94% genetically similar, there are many genetic polymorphisms differentiating us. This poses a problem when mapping RNA-sequencing data to the genome. If we were to map both species’ reads to one common genome, then we might observe apparent immune differences between species that actually reflect artifacts of mapping (at least one species) to the wrong genome. To overcome this obstacle, we will map RNA-seq data to their species-specific genomes (human: GRCh38; macaque: Mmul\_10) using kallisto. All downstream analyses will be conducted only on genes that are present in both the human and macaque genomes (i.e., orthologs). This will allow us to minimize any potential bias in our conclusions that are a result of a gene being present in one species but absent in another. Note that the human genome is higher quality than the macaque genome. For comparison purposes, will also conduct all analyses on RNA-seq from both species mapped to the human genome. We expect similar results from both the species-specific mapping and human-specific mapping approaches.

To compare the effects of social status on gene expression between the two species, we will model each gene’s normalized expression as a function of social status using a linear model approach implemented in the R package *limma*. From these models, we will focus on the effect size estimates (βstatus) of social status on the expression of each gene. As a first step, we will quantify the similarity of status effects in either (i) direction and/or (ii) magnitude. We will use Fisher’s exact tests to quantify extent of directional similarity in status effects (up versus down regulation), while we will use Spearman’s rank correlations to quantify similarity in relative magnitude of social status effects across different genes. Such an analysis will allow us to coarsely quantify any global similarities between status effects in both humans and rhesus macaques.

Next, we will take a conservative (compared to local FDR) Bayesian approach, multivariate adaptive shrinkage (<https://www.nature.com/articles/s41588-018-0268-8>), to identify if a given gene shows status effects in humans, macaques, or both. The benefit of this approach is that it it avoids between-species comparisons “significance” when identifying which genes are status sensitive in monkeys, humans, or both. For instance, instead of saying that *gene A* is significantly (FDR < 0.05) associated with status in humans, but not in macaques (even if it is just above the FDR threshold; e.g., FDR = 0.06), this approach will use evidence from models of *gene A* in macaques and humans to calculate the likelihood of a status effect in one or both of the species. At the end of this analysis, we will have a list of genes that are associated with social status in monkeys, humans, or both. We will then conduct a categorical enrichment analysis (e.g., gene ontology) on each set of genes to identify which physiological processes (e.g., pro-inflammation), are associated with status in one or both species.