Heart Failure (HF):
- Affects ~6.2 million Americans (2013-2016), with projected 46% prevalence increase 2012-2030\(^1,2\)
- Significant cause of death
- High financial cost to HC system\(^3,4\)

Impetus for Study:
- Currently HF treatment uses a “common pathway” assumption
- Want personalized gene approach\(^3,4\)

Context:
- Sweet et al. (2018) analyzed RNA expression profiles for non-failing (NF) v. Ischemic Cardiomyopathy (ICM) v. Dilated Cardiomyopathy (DCM) tissue samples from human hearts
- Searching for Differentially Expressed Genes (DEG’s) \(\rightarrow\) pathway analysis

Results from Sweet et al. (2018):

My Contribution:
- Matlab script that can be easily adjusted to alter DEG selection criteria
- RNA-seq from 13 ICM, 37 DCM, and 14 NF human LV samples; 57974 genes

My Adjustable Algorithm:
- Rid data of missing/nonsensical entries
- Can require \(\geq \frac{1}{2}\) of entries to exceed 0 for each group (NF/DCM/ICM)
- Flexibly set row mean cutoffs, requiring at least one (or both) of two row means to exceed the cutoff
- Sift for genes with change in mean expression in one of two ways:
  - \(\Delta\) mean > threshold (i.e. > 5)
  - |Fold change (FC)| b/w row means > threshold (i.e. 1.5)
- T-test on log\(_2\)(RPKM+cutoff)
- Benjamini-Hochberg procedure to sift out false positives
- Work in progress to account for covariates of age & sex
- Pathway analysis in IPA

Effort to first replicate 2018 DCM results:
- Some dissimilarity b/w sets; working to incorporate covariate adjustment
- 543 DEG’s compared to 561; many genes are same, some different

Discussion and Next Steps:
- Flexible algorithm to adjust parameters
- Repeat 2018 work, expand w/ new DEG sets, and verify results w/ larger HF set