1. **Preparation of files before running HINT**

\*note: any file highlighted in ***bold*** is provided

1. Create BED file for *APPV717I* vs. NDC comparison to input into HINT using all possible peaks
   1. R code located in **ATAC-seq\_DiffBind\_chipenrich\_Pipeline\_final.R** file

#53,598 all possible total peaks here

>ATACSeq.report.V717I\_full

#Convert to a data frame

>ATACSeq.report.V717I.out\_full\_df <- as.data.frame(ATACSeq.report.V717I.out\_full)

#Select columns 1-3 (chr or seqnames, start, end)

>ATACSeq.report.V717I.out\_full\_df <- ATACSeq.report.V717I.out\_full[, c(1:3)]

#Export as a BED file, e.g. 210511.dATACpeaks\_full.V717I.bed (to use for HINT!)

>rtracklayer::export.bed(ATACSeq.report.V717I.out\_full\_df, con = "210511.dATACpeaks\_full.V717I.bed", format = "bed")

1. Create BED file for *PSEN1A79V* vs. NDC comparison to input into HINT using all possible peaks
   1. R code located in **ATAC-seq\_DiffBind\_chipenrich\_Pipeline\_final.R** file

#53,345 all possible peaks here

>ATACSeq.report.A79V\_full

#Convert to a data frame

>ATACSeq.report.A79V.out\_full\_df <- as.data.frame(ATACSeq.report.A79V\_full)

#Select columns 1-3 (chr or seqnames, start, end)

>ATACSeq.report.A79V.out\_full\_df <- ATACSeq.report.A79V.out\_full\_df[, c(1:3)]

#Export as a BED file, e.g. 210511.dATACpeaks\_full.A79V.bed (to use for HINT)

>rtracklayer::export.bed(ATACSeq.report.A79V.out\_full\_df, con = "210511.dATACpeaks\_full.A79V.bed", format = "bed")

1. Create BED file for *PSEN2N141I* vs. NDC comparison to input into HINT using all possible peaks
   1. R code located in **ATAC-seq\_DiffBind\_chipenrich\_Pipeline\_final.R** file

#53,345 possible peaks found

>ATACSeq.report.N141I\_full

#Convert to a data frame

>ATACSeq.report.N141I.out\_full\_df <- as.data.frame(ATACSeq.report.N141I\_full)

#Select columns 1-3 (chr or seqnames, start, end)

>ATACSeq.report.N141I.out\_full\_df <- ATACSeq.report.N141I.out\_full\_df[, c(1:3)]

#Export as a BED file, e.g. 210511.dATACpeaks\_full.N141I.bed

>rtracklayer::export.bed(ATACSeq.report.N141I.out\_full\_df, con = "210511.dATACpeaks\_full.N141I.bed", format = "bed")

1. Merge three replicate .bam files for NDC into one combined .bam file using the **merge\_NDC.sh** script
2. Merge three replicate .bam files for *APPV717I* mutation into one combined .bam file using the **merge\_V717I.sh** script
3. Merge three replicate .bam files for *PSEN1A79V* mutation into one combined .bam file using the **merge\_A79V.sh** script
4. Merge three replicate .bam files for *PSEN2N141I* mutation into one combined .bam file using the **merge\_N141I.sh** script
5. Gather the motifs from the CISBP database under the MEME suite (???)
6. Add the collection of CIS-BP motifs under cisbp\_hint.tar.gz to the following path: /home/prvaldes/rgtdata/motifs/
   1. (base) [prvaldes@tscc-login12 motifs]$ tar -zxvf cisbp\_hint.tar.gz
7. Create motif logos from CIS-BP database
   1. Run **setupLogoData.py** to generate logos for all available repositories
      1. (base) [prvaldes@tscc-3-21 rgtdata]$ python setupLogoData.py –all from the /home/prvaldes/rgtdata/ folder
      2. >>> CREATING logos for ['cisbp\_hint', 'uniprobe\_secondary', 'jaspar\_plants', 'hocomoco', 'swissregulon', 'uniprobe\_primary', 'jaspar\_vertebrates']

>>> cisbp\_hint

1. **Running the HINT program**
2. Run TF footprinting for *APPV717I*vs. NDC comparison using the **RGT-HINT-ATAC-AD\_V717I\_NDC\_footprinting.sh** file
   1. (base) [prvaldes@tscc-2-14 HINT]$ bash RGT-HINT-ATAC-AD\_V717I\_NDC\_footprinting.sh
3. Run TF footprinting for *PSEN1A79V*vs. NDC comparison using the **RGT-HINT-ATAC-AD\_A79V\_NDC\_footprinting.sh** file
   1. (base) [prvaldes@tscc-2-14 HINT]$ bash RGT-HINT-ATAC-AD\_A79V\_NDC\_footprinting.sh
4. Run TF footprinting for *PSEN2N141I* vs. NDC comparison using the **RGT-HINT-ATAC-AD\_N141I\_NDC\_footprinting.sh** file
   1. (base) [prvaldes@tscc-2-14 HINT]$ bash RGT-HINT-ATAC-AD\_A79V\_NDC\_footprinting.sh
5. Perform motif matching for *APPV717I* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_V717I\_NDC\_motif\_matching\_cisbp\_full.sh** file
   1. (base) Phoebes-MacBook-Pro:Shell\_Scripts phoebevaldes$ bash RGT-HINT-ATAC-AD\_V717I\_NDC\_motif\_matching\_cisbp\_full.sh
6. Perform motif matching for *PSEN1A79V* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_A79V\_NDC\_motif\_matching\_cisbp\_full.sh** file
   1. (base) Phoebes-MacBook-Pro:Shell\_Scripts phoebevaldes$ bash RGT-HINT-ATAC-AD\_A79V\_NDC\_motif\_matching\_cisbp\_full.sh
7. Perform motif matching for *PSEN2N141I* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_N141I\_NDC\_motif\_matching\_cisbp\_full.sh** file
   * 1. (base) Phoebes-MacBook-Pro:Shell\_Scripts phoebevaldes$ bash RGT-HINT-ATAC-AD\_N141I\_NDC\_motif\_matching\_cisbp\_full.sh
8. Perform differential analysis for *APPV717I* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_V717I\_NDC\_differential\_cisbp\_full.sh** file
   * 1. (base) [prvaldes@tscc-3-0 Scripts\_2021]$ bash RGT-HINT-ATAC-AD\_V717I\_NDC\_differential\_cisbp\_full.sh
9. Perform differential analysis for *PSEN1A79V* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_A79V\_NDC\_differential\_cisbp\_full.sh** file
   * 1. (base) [prvaldes@tscc-3-3 Scripts\_2021]$ bash RGT-HINT-ATAC-AD\_A79V\_NDC\_differential\_cisbp\_full.sh
10. Perform differential analysis for *PSEN2N141I* vs. NDC with the CISBP motif database using the **RGT-HINT-ATAC-AD\_N141I\_NDC\_differential\_cisbp\_full.sh** file
    * 1. (base) [prvaldes@tscc-3-3 Scripts\_2021]$ bash RGT-HINT-ATAC-AD\_N141I\_NDC\_differential\_cisbp\_full.sh