Using BMI Data Warehouse and High Performance Cluster for Genomics Analysis

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http://www.altanalyze.org
Why we need the HPC?

- Process thousands of RNA-Seq samples processed per year (single-cell and bulk).
- Complex software setup and administered.
- Significant computational requirements for deeper analyses.
- Reduce analysis time from months to days.
- Human data must be secure and compliant.
- Data must be backed up and stored remotely.
Tools we frequently use on the HPC:

- RSEM
- AltAnalyze
- TopHat
- Cufflinks
- Homer
- GATK
- BEDTools
- Trinity
- samtools
- FASTQC
- R
- km
- Jellyfish
- vcf tools
- Picard tools
- kallisto
- sailfish
- Miso
- DEXSeq
- rMATS
Example Project: Human AML

- **Goal**: Discover mutations in AML that impact splicing, tumorigenic and survival.
- Hundred of deeply sequenced RNA blood samples (n>800), microRNA-Seq (n>150), methylation arrays (n>150) from public repositories (GEO, CGHub, TARGET).
- Most samples have no mutational profile provided.
HPC is REQUIRED for Analysis!!

- Only sequence provided for most samples. TCGA missing novel isoforms and poor alignment.
- 800 RNA-Seq samples = ~400 days of compute time on a single high-end machine (16GB RAM). Possible in 10 days on the HPC (40 parallel jobs).
- Requires ~25 TB of hard disk space, fast access with back-up. Data must be secure (genotypes).
- Combined analyses require 128 GB of RAM and a dozen CPUs (1 machine).
- Complex software required.
Novel Integrative Research Opportunities

- Integrative models of gene expression, splicing, microRNA, mutations, methylation and prognosis.

**Mutational Profiles**

**TCGA - Gene Expression**

**TCGA – Alternative Splicing**

**TCGA - Methylation**

**Cross-Omic Molecular Correlations**

**Survival Profiles**
Novel Integrative Research Opportunities

- Associate *splicing* signatures from TCGA to TARGET and uncharacterized AMLs (Leucegene) to find mutations.

**TCGA Splicing Signatures:**
- U2AF1 Mutant Patients

**U2AF1 Predicted**
- Leucegene Matching Splice Signature

**Machine Learning Supervised Classification of Mutational Profiles**

**Visualization and Validation of Predicted Patient Mutations**

**200GB Data Visualized**
Novel Integrative Research Opportunities

- Find de novo splicing signatures and associate with prognosis.
Genomic Analysis and High Performance Computing

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Agenda

• Introduction to HPC
• HPC Infrastructure overview
• Applications and customers
• Genomics using HPC
• Workflow tools
• Q & A
HPC and Linux Team

Kevin

Carmen

Jason

Mark
Introduction to HPC

• Why use it?
• How to get access?
Why use the HPC?

Local machines generally have limited resources

- Processors
- Memory
- Storage
- Time
Why use the HPC?

Focus on what you need to accomplish

- No need to compile software and dependencies
- Approximately 400 software packages / versions currently available
Why use the HPC?

Scale out

• With MPI, jobs can run on multiple nodes simultaneously
• With job dependencies, independent steps can be run simultaneously
How to use the HPC?

• Email help@bmi.cchmc.org to have your account setup
• Access can be via:
  NoMachine (NX)
  Citrix (in progress)
  SSH
• Data volumes can be mounted to your Windows or Mac computer for easy access
HPC Infrastructure at CCHMC

• We have 3 different HPC environments
  – Clinical Exome
    • Restricted access
  – Research production and development HPC
    • Available to
      – all CCHMC personnel
      – UC and other external collaborators
HPC Infrastructure at CCHMC

• Clinical Exome
  – 96 cores
  – 10G ethernet
  – Inside CCHMC network
  – Strictly for clinical purposes
  – CLIA/CAP compliant
**HPC Infrastructure at CCHMC**

- Production research HPC
  - Currently at ~700 cores
  - Mostly HP blades
  - Cores range from 4 – 16 per node
  - RAM ranges from 8G – 256G per node
  - 2 - Tesla (K10) compute nodes for GPU computing
  - 10G ethernet
  - Direct connection to Isilon high performance storage cluster
HPC Infrastructure at CCHMC

- Development research HPC
  - Currently at ~600 cores
  - Older HP blades
  - 4 or 8 cores per node
  - 1G ethernet
HPC Infrastructure at CCHMC

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<th>2014</th>
<th>2015</th>
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<td>Total jobs</td>
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<td>Total job hours</td>
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<tr>
<td>Jobs / hour</td>
<td>104</td>
<td>183</td>
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<tr>
<td>Average job time</td>
<td>~47 minutes</td>
<td>~44 minutes</td>
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- Users: > 50
- Applications: > 300
Some of the Research Areas

- Genomics
- Metagenomics
- Protein docking, folding and structure prediction
- Natural language processing
- Functional neuroimaging
- Molecular dynamics
- Pharmacodynamics
- Large scale rendering
Genomic Applications using HPC
Genomic Applications using HPC

• Output data from the sequencers are stored in the Isilon storage cluster.
• Offline Base Caller – Base calling and QSEQ formatted output.
Genomic Applications under HPC

• Demultiplexing and “bcl to fastq” conversion is done using home-grown scripts.
• Further downstream analysis conducted by individual researchers per their needs.
• FASTQ files are available for users to download to run through their own analysis process.
Common Genomics Software Used

• BWA, Bowtie – Sequence alignment
• Affy Power Tools – To analyze and work with Affymetrix GeneChip® arrays
• bamtools – Tools to work with BAM and SAM files
• bedtools, plink – Genomic analysis tools
• R/Bioconductor
Common Genomics Software Used

- Kallisto, RSEM, sailfish, Trinity - RNA-Seq
- Mothur, QIIME, LEfSe, MetaPhlAn, PhyloPhlAn – Metagenomics
- MACS – ChIP-Seq
- miRanda, miRDeep2 – miRNA experiments
- vcf tools
Workflow Tools

• Workflow tools let you create a pipeline.
• Connects to a cluster in the backend.
• Determines and manages job dependencies automatically.
• Either a thick client or web-based.
Workflow Tools

• LONI – Java-based thick client.
• Galaxy – Web-based workflow software. We have a local instance.
• GenePattern – Broad institute – Broad user community.
• AltAnalyze – Command-line and GUI available.
Other Research Tools

- Linux/HPC Team also manages the following tools.
  - Strand NGS
  - SAS
  - Genome Browser (https://gb.research.cchmc.org)
  - Mascot (https://research.cchmc.org/mascot/)