Supporting Single Cell RNA-seq Analysis: A Core's Perspective

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Common applications of scRNA-seq

• Explore which cell types are present in a tissue
• Identify unknown/rare cell types or states
• Elucidate the changes in gene expression during differentiation processes or across time or states
• Identify genes that are differentially expressed in particular cell types between conditions (e.g. treatment or disease)
• Explore changes in expression among a cell type while incorporating spatial, regulatory, and/or protein information
Growing demand for scRNA-seq support
A Community Approach

Klein Lab
- encapsulation expertise
- analysis expertise
- methods development

Single Cell Core
- encapsulation
- scaling
- experiment design
- standardization
- training

Bioinfo Core
- analysis
- scaling
- experiment design
- standardization
- training

Sequencing Core
- library prep
- sequencing

Researcher
- experimental question
- experimental materials
- experiment design

Harvard Medical School
- funding
Standardizing using reproducible, scalable, validated best practice workflows

Sequencing Samples

Configuration

bcbio-nextgen
Tool Integration
Scaling and resiliency

RNA-seq
Alignment
Quantitation

Analysis
Annotation
Query
Visualization

Quality
Alignment
Coverage

bcbio-nextgen
Python toolkit to automate best practice NGS pipelines
Challenges and Opportunities

- Complex designs - replicates, batches, technologies
- Close collaborations to allow for rapid, iterative analyses
- Rapidly emerging methods and evolving tools
  - Which ones to use?
  - Keeping versions consistent/synchronized (esp. among computing environments)
  - Different results from different methods
  - Lots of open questions
Call this a hot take if you must, but I'm going on record and saying it: differential expression on single-cell RNA-seq is a mess. 10 different methods = 10 wildly different answers with minimal overlap. Hard to believe it's 2019 and we're likely resorting to "called DE by >= 2"
Challenges and Opportunities

- Projects take longer to complete
- Practical approach to training
  - Internal training through retreats, development of materials, group discussions
  - Community training through our Bioinformatics Training Program
Funding

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Harvard Medical School
Harvard Stem Cell Institute
Harvard Catalyst
National Institute of Environmental Health Sciences (NIEHS)
Harvard University Center for AIDS Research (CFAR)
AstraZeneca
Boehringer Ingelheim