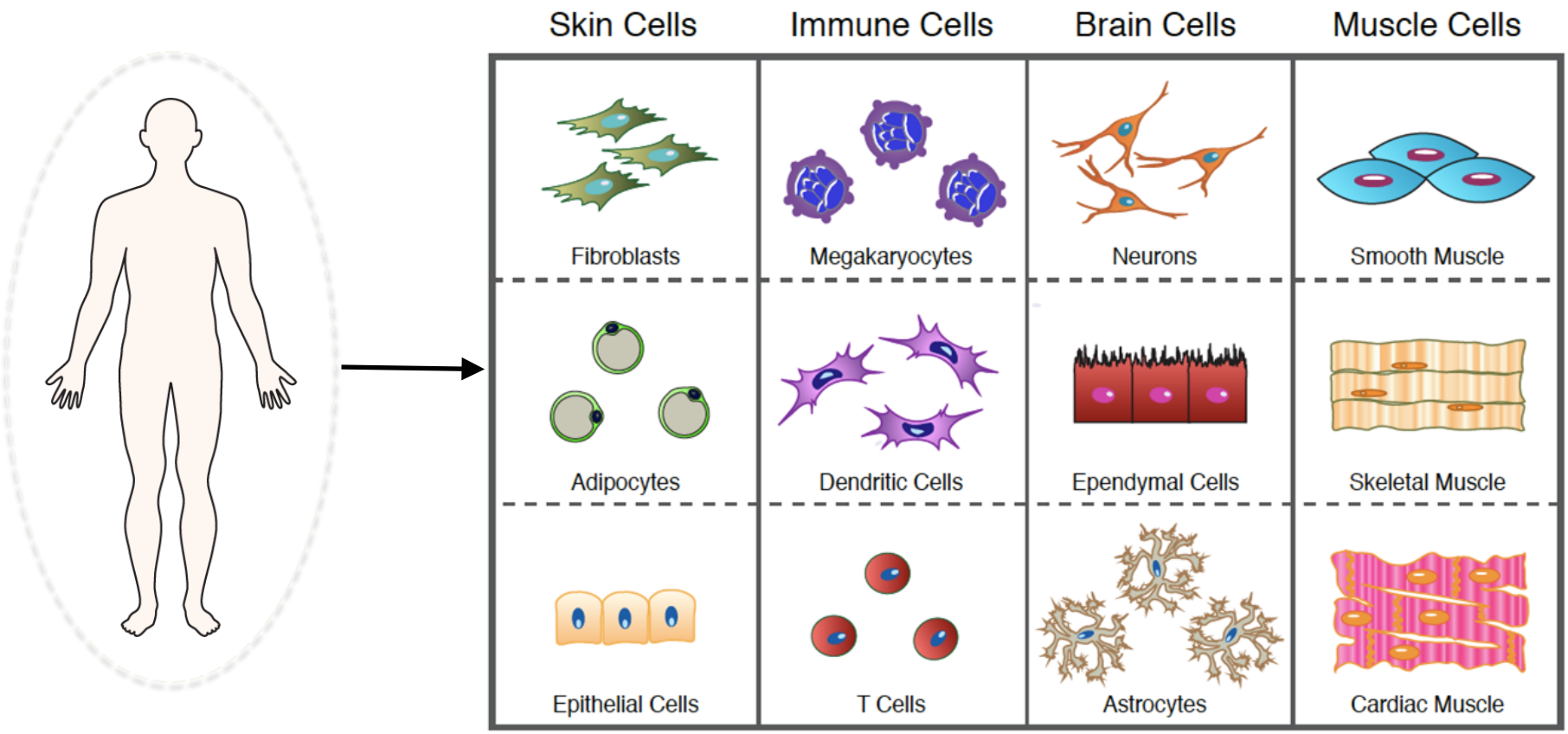
# The Human Cell Atlas

**Aviv Regev**

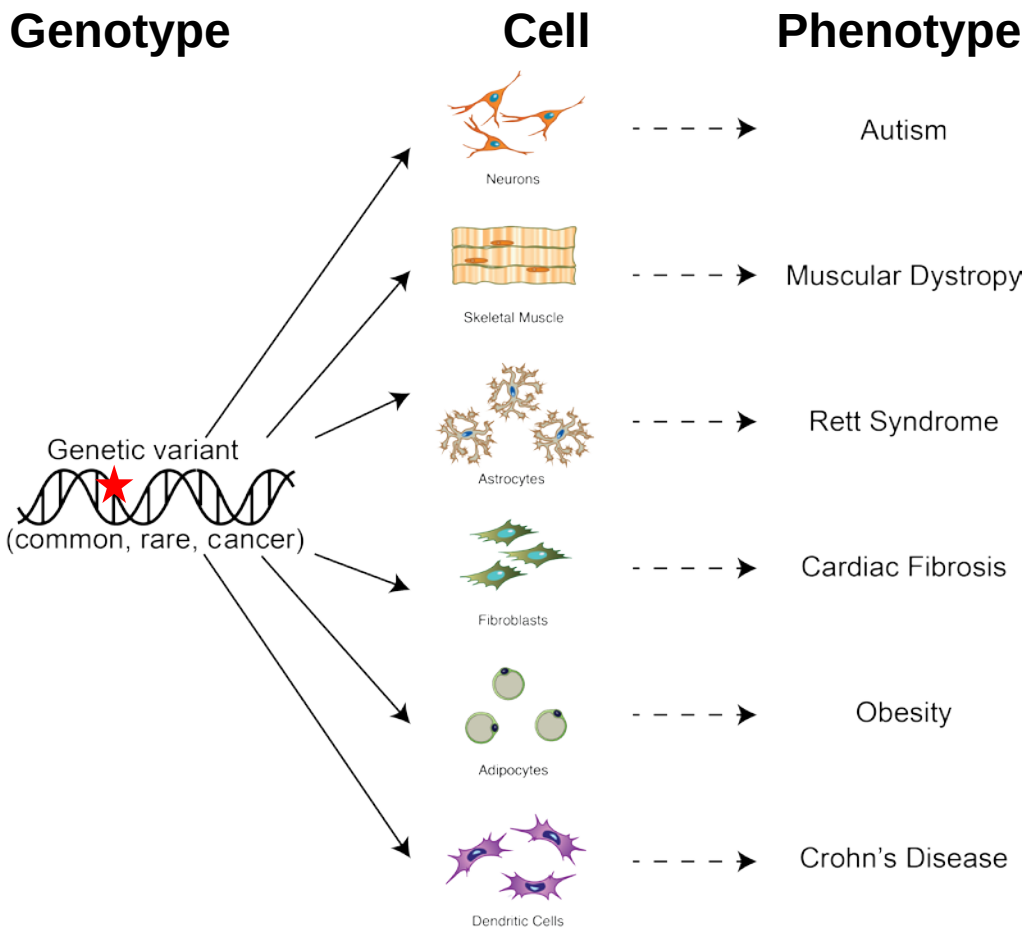
Department of Biology, MIT
Broad Institute
Howard Hughes Medical Institute

# Cells are our core constituents



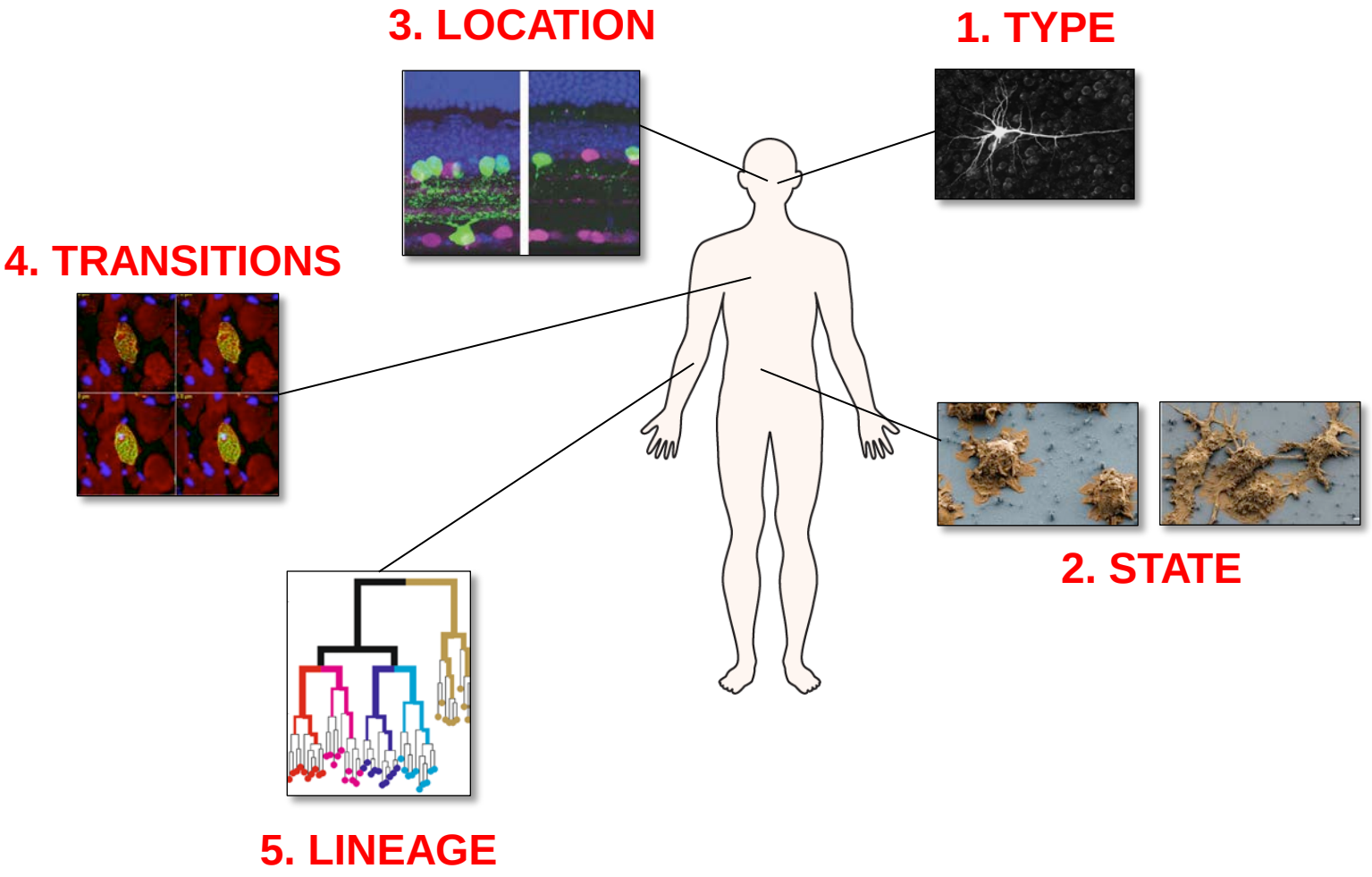

**Cells are classified by characteristic molecules, structures, and functions**

# Cells: a key intermediate from genotype to phenotype



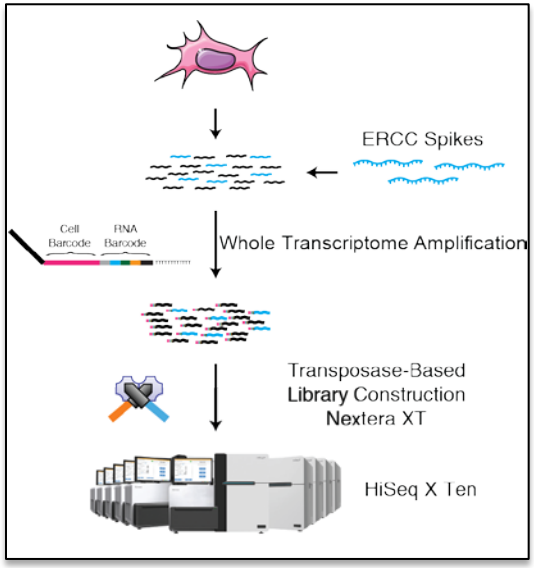

**Knowing our cells is essential for functional dissection of genetic variants**

# What is a cell atlas?

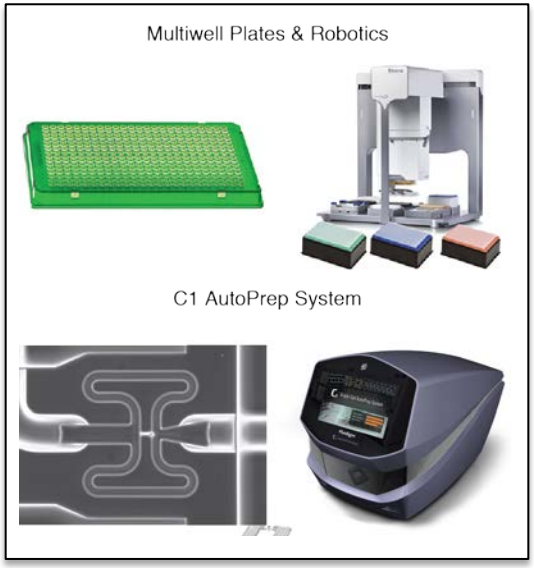



**Current knowledge partial, decades and centuries old**

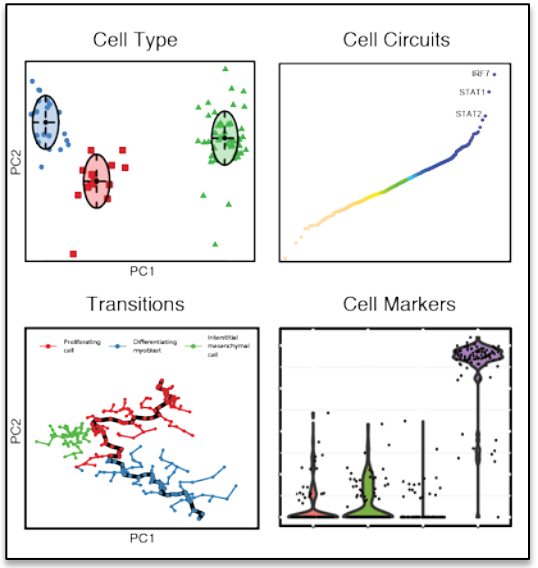
# Single cell genomics makes this possible




✓ **Core technology**



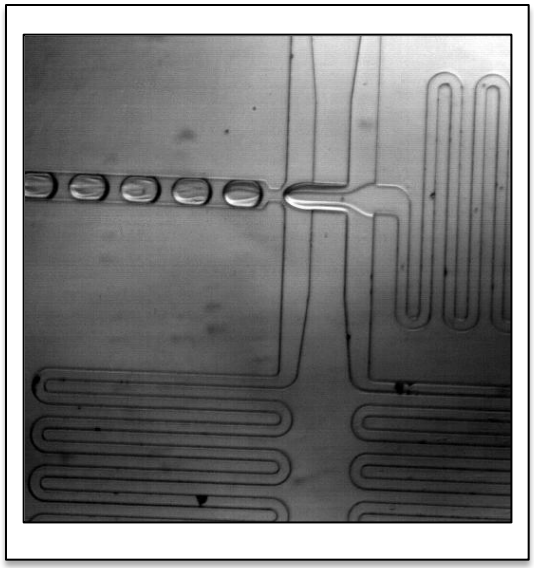

✓ **Sample prep**



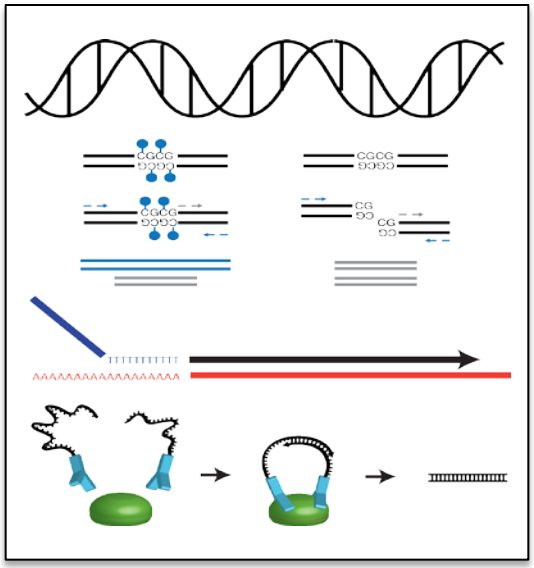

✓ **Computation**

**May 2012: 18 cells** → **July 2014: ~100,000 cells**

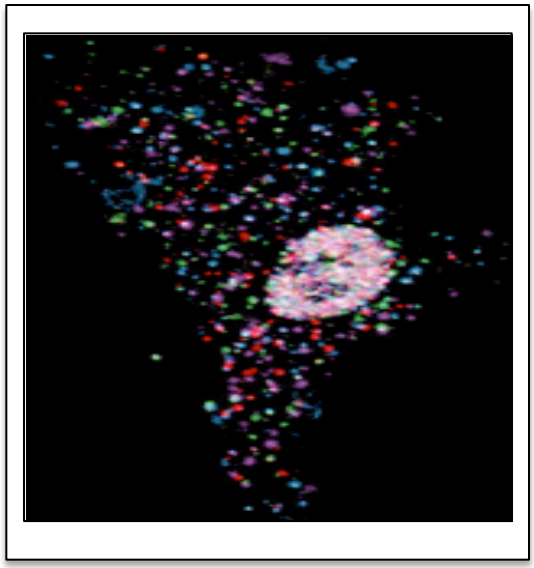
# Emerging capabilities bring scale and resolution



**Scale**
5,000 cells/sec;
¢2.8/cell prep



**Measurement**
DNA, RNA,
epigenome, protein

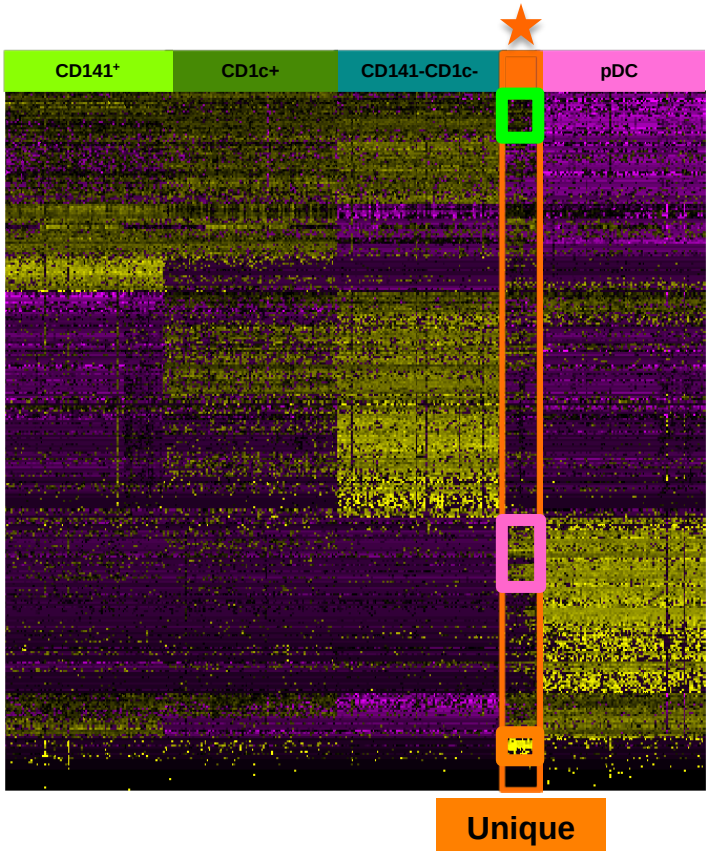


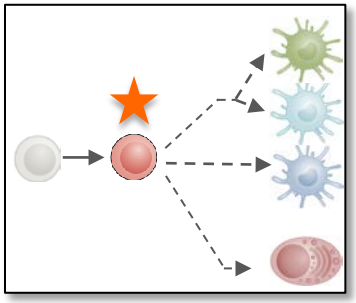
**Location**
Registry to 2D, 3D

# Already rapidly leading to new insights

myeloid

Asian-American
24 yr old
**768** blood DCs



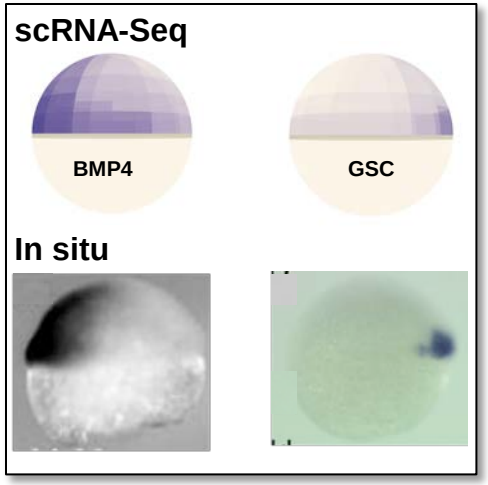



pDC

- ✓ **New population: 1.9-3.2% of DCs; 0.04-0.064% of PBMCs**
- ✓ **Validated in 10/10 independent individuals**
- ✓ **Placed in lineage: a blood progenitor?**

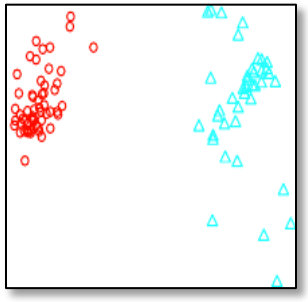
# Already rapidly leading to new insights

## LOCATION

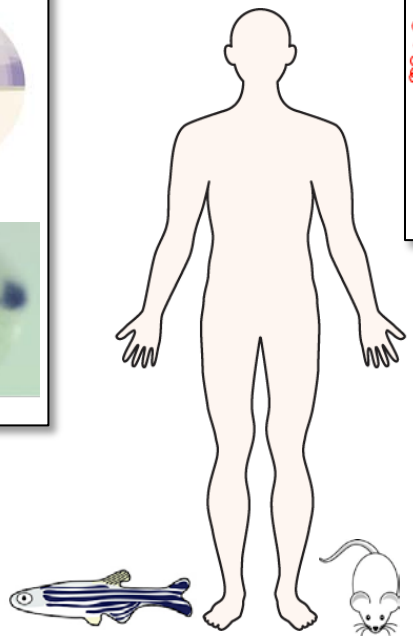



Fish embryo

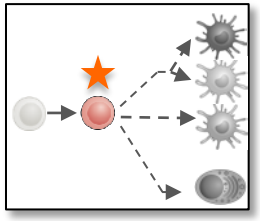
## TYPE



Retina neurons



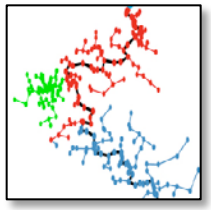
## LINEAGE



New human immune blood progenitor

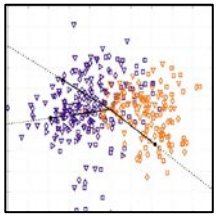
## TRANSITIONS

‘Early responder’ immune cells

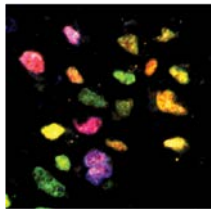


Muscle cell differentiation

## STATE

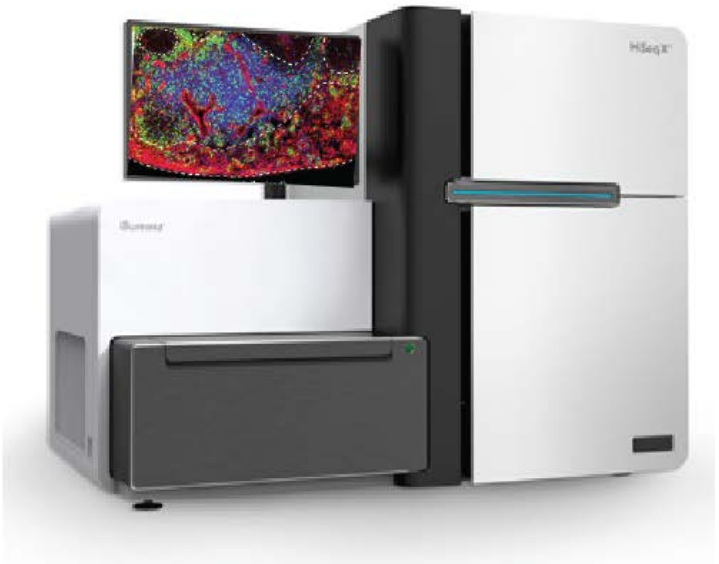


Pathogenic T cells in MS model



CSC spectrum in glioma

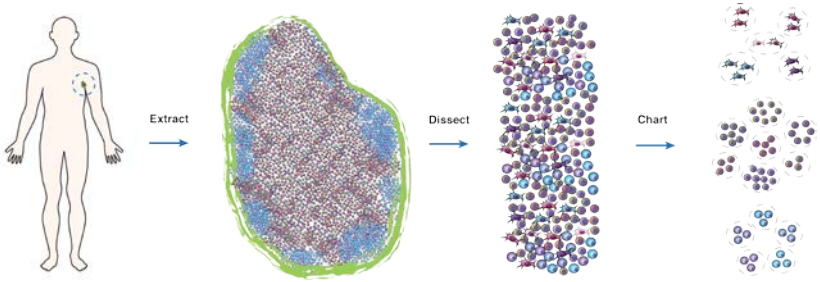
# The sequencer: a microscope for the 21st century



# The Human Cell Atlas Project

## What? A census of all cells

- Types
- States
- Transitions
- Location




## Why? A reference map for function

- Foundational, fundamental knowledge
- Function of genetic variants
- Heterogeneity in disease
- Eventually characterize in individual patients

# The Human Cell Atlas Project

**How? A unified project**

- **Pilot project in complementary systems (e.g., blood, gut, liver)**
- **Consortium with expert communities**
- **Standard, controlled process**
- **Shared analytical tools**
- **Drive costs to ~$0.15/cell***

**Why? Standardized and impactful**

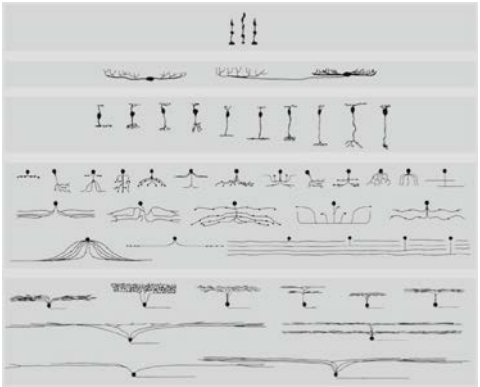
- **Managed: Only standard process ensures we are not deceived by noise**
- **Scale: Drive cost down**
- **Technology advancing: Novel sample prep, cell isolation, analytical tools**
- **Resources for entire community**
- **Commensurate with clinic**

* with drops, $10^5$ reads/cell, @ $0.4-0.6/cell with HiSeq X10 yields

# The Human Cell Atlas Project

## Large

- **Adult human: ~2X10$^{13}$ cells (excluding red blood cells)**
- **300 ‘major’ cell types**
- **….but, ~100 sub-sub-types just of retinal neurons**

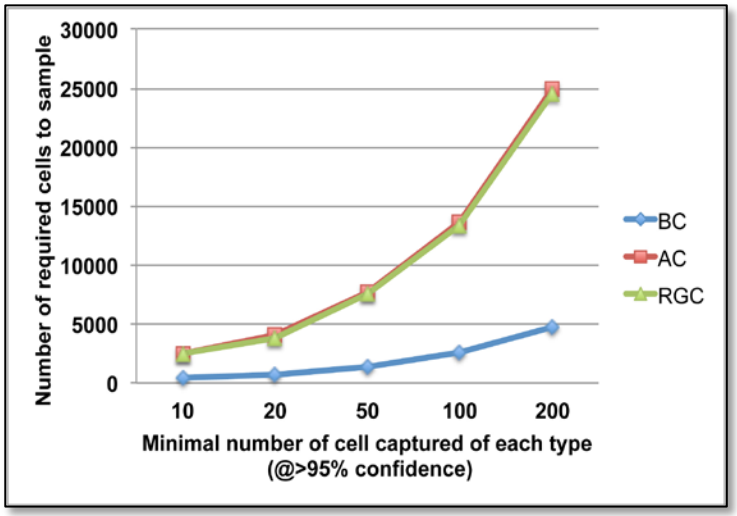


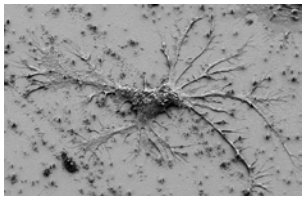
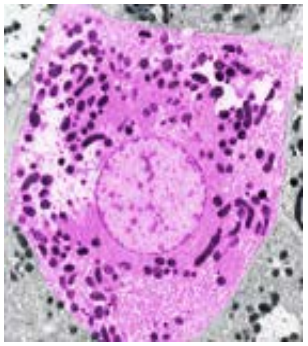
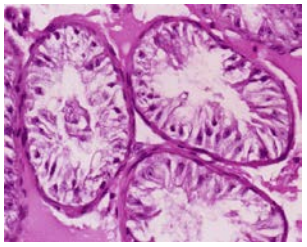
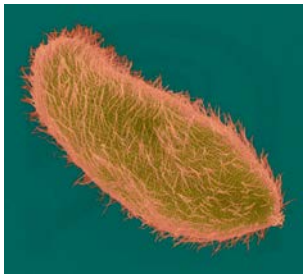
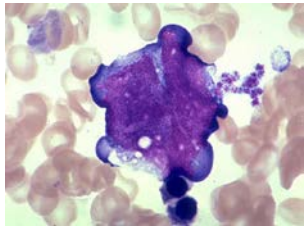
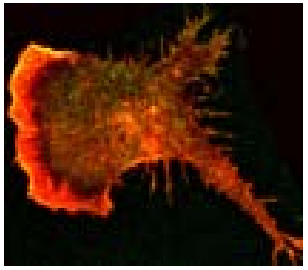
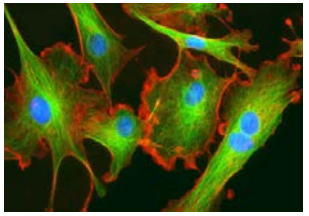
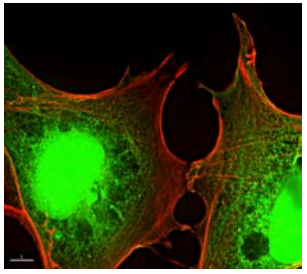
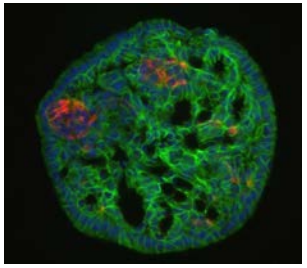
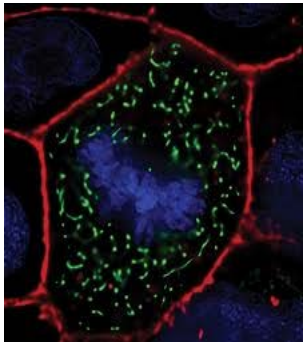
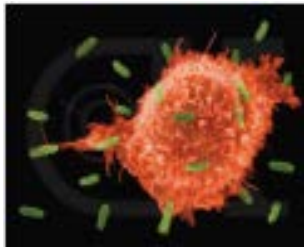
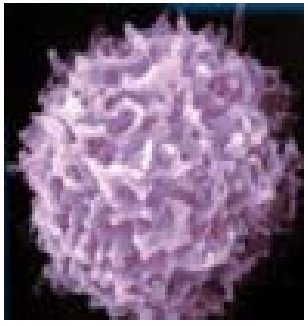
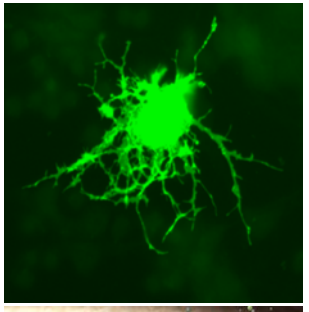
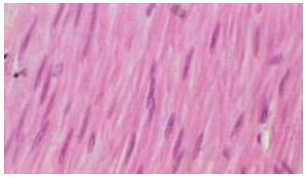
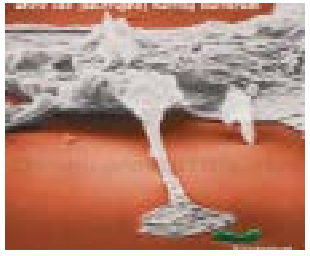
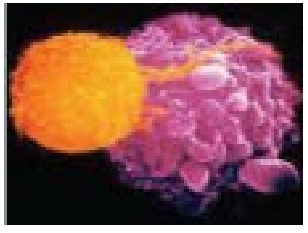
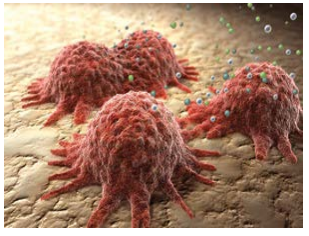
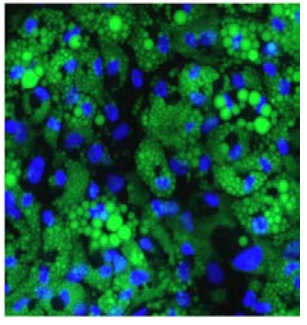
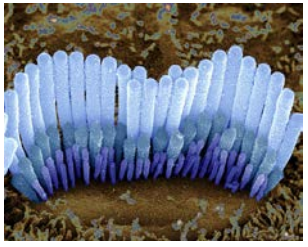
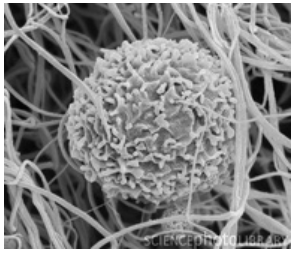
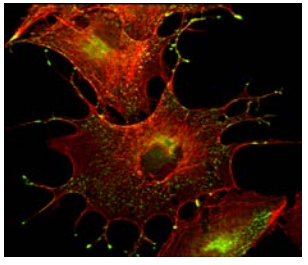
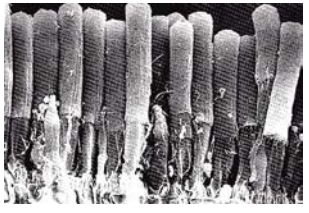
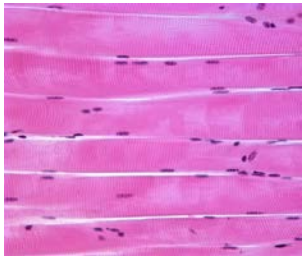
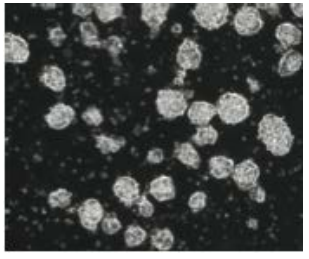
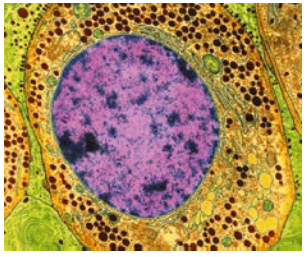
**Photoreceptors (3)**
**Horizontal cells (1)**
**Bipolar cells (12)**

**Amacrine cells (50)**

**RGCs (30)**

## … but finite




**150M neurons in retina,**
**~40K required for survey**

Retinal bipolar cell (BC): 12 sub types, rarest @5%
Retinal amacrine cell (AC): 50 subtypes, rarest @1%
Retinal Ganglial cell (RGC): 30 subtypes, rarest @1%