Human Cell Atlas - Asia Meeting
Nov 30 - Dec 1, 2017
Okinawa, Japan

Mission

Human Cell Atlas (HCA) is an international consortium aiming to create comprehensive reference maps of all human cells - the fundamental units of life - as a basis for both understanding human health and diagnosing, monitoring, and treating disease. To embody the global nature of this project, the HCA aims for a greater representation of human diversity - defined by gender, genetics, geography, environment and age. To enable a greater representation, the first HCA Asia meeting in Okinawa aimed to bring together leading scientists in the field of single cell genomics to discuss and identify scientific and logistical issues in the context of the high human diversity in Asia, and to establish a coordinated framework to represent Asia in the global HCA.

Executive summary

A group of 51 scientists from Japan, South Korea, Singapore, and India along with national and international funders convened to share, discuss, and devise strategies to establish a regional framework of HCA. The scientists were represented from 23 universities and research institutes. The two day meeting was divided into six thematic sessions ranging from imaging, technology platforms, stem cells, cancer and coordination. Each session followed ample time for discussions (avg. over 50 minutes) around sample sourcing, diseases, ethics, genomic platforms, data sharing, and pilot projects. The participating members recognize the importance of synergizing our efforts to the global HCA while maintaining visible representation and leadership in the region. The members also expressed a **common interest in building a reference dataset from the Asian population** with the **emphasis on targeting prevalent diseases in the region** such as liver, colon, gastric, oral, cervical cancers and proposed the **creation of an interim organizing committee** to devise concrete pilot projects to jumpstart collaboration and to explore local ethics regulation and funding opportunities. A subset of the data to be generated by HCA-Asia collaborators (such as, single cell RNA_seq data derived from normal tissues adjacent to tumors) was identified to be in harmony with the data proposed to be generated in the global HCA that does not consider a disease contexture. Thus, HCA-Asia will strengthen the efforts undertaken by the global HCA.

Discussion Summary (abridged from meeting notes)

Scope

What is the primary focus of HCA?

1. “Skydive” approach to obtain a broad understanding of cellular diversity. What is a cell type?
2. Stratify cells for deeper exploration into molecular makeup and gene regulation.

Creating “general catalogue” of healthy cells is the mission.

It was recognized that it is necessary to have a scientific coordinator in each country and in the region.

To complete the "Human" component of HCA, it is necessary to engage scientists from Asia and other regions like Africa and South America.

56% of world's population is from the Asian region.
We need to incorporate other nations in the region for the collective Asian effort (e.g. sequencing, sampling) including China, HK, Taiwan, Vietnam, Thailand, Malaysia, Indonesia, etc.

Rather than having one group focusing on one organ, multiple (international) labs working on the same organ is ideal to generate the most informative reference, especially in the context of large documented human genomic diversity in Asia.

> Diseases
Gastric, colon, liver cancers are most prevalent in the Asian region.
Tumor biopsies allow extraction of healthy tissues.
But how can we define "healthy?" or what is "normal" -> therefore, we need to build the human cell reference - with an appropriate genetic background.

Technology
Standardizing technology platforms are essential.
While the use of a commonly agreed platform may be efficient, this practice can create a 'monopoly' effect and inhibit competition. Therefore, it is necessary to hold discussions on use of competing technologies and data generation modalities.

At current rate, more cells lead to less detectable genes. This hampers our understanding of molecular composition and its regulation. This approach may be ideal to define cell types, but may be less efficient to build a gene network.

Intrinsic noise from scRNA-seq may hamper interpretation of cell type/transition but DNA methylation (and/or ATAC seq) may be more straightforward.

Centralized database will be more valuable (stronger reference) and benefits small labs. DCP is free, storable, scalable, engineered by CZI.

Unique technologies/samples

- Japan: RIKEN has been leading in the ncRNA field and FANTOM projects. Technologies such as Nx-seq (nano-wells), RamDA-seq (single cell full-length total RNA seq), C1 CAGE (5'-end) are accessible. CiRA in Kyoto is leading in the iPS cell technology will be essential for regenerative medicine.
- Singapore: A*Star leads in the MER-FISH (spatial) technology along with wider access to clinical samples. Multiethic country access to wide range of genetic background.
- Korea: Samples from brain-dead patients can be obtained; many cancer samples have already been profiled using single cell technologies. Multiomics technologies (e.g. SIDR) for simultaneous DNA and RNA seq is also accessible.

Ethics
What are the data sharing policies in each country?

1. Japan: the IRB regulation in Japan is changing. Treatment of RNA and DNA is different. FANTOM has received samples from outside and shared data under ethics.
2. Korea: As long as seq data have patients' consent it can be public. Population study data is easier than individual data.
3. Singapore: Data can be shared as long as one agrees not to use it for commercial use (only for academic purposes). The committee is still maturing.
4. India: samples cannot be shared outside, but data can be shared as long as it is anonymized.

Funding situation

1. India: No funding plan for HCA at the moment. The government expects that there be contextures of phenotypes. Making a case for healthy reference is challenging but regional support will be helpful. With limited available funding, some single-cell data will be generated on single cells derived from normal tissue that serve as "controls" for cells derived from tumor tissue.
2. Japan: MEXT (ministry in Japan) is aware of HCA activities. New phase of single cell program in RIKEN from April 2018 will support this effort but need greater promotion to acquire national funding.
3. Korea: National Research Foundation (NRF) on behalf of ministry is already funding projects and reasonably confident that funding will increase - to several million dollars per year from 2019-2020. Making healthy reference and ethical regulation need to be carefully reviewed. We need compelling arguments to persuade NRF and ministry to support HCA Asia.
4. Singapore: Could not invite funders due to short notice. Single cell research is A*Star's priority focusing on disease and applied research (e.g. diagnostics). But there is interest in healthy atlas but may need to tackle simultaneously with disease such as cancer, cardiovascular, immunity and technology development in the view to turn it into diagnostics.
5. CZI: Confident to commit to HCA - especially for data coordinate platform (DCP). Aiming to support by central facilities (e.g. storage, help desk) with partnership with other funders. Provide funding to set up centralized ethic and also support executive offices. Support international efforts through multiple rounds of RFAs.

Organization

Establish an interim (preparatory) organization committee consisting of key leaders (1-2) from each country. The committee members are the first point of contact related to global HCA and regional HCA. They are also responsible for communicating and promoting HCA activities to local research community and funders.

Keywords from the meeting

1. Biology:
    a. immunity (in aging, tumor, geographic/environment diversity, tissue-specific)
    b. stem cells (ES/iPSC, tissue stem cells, organoids, cancer stem cells)
    c. cancer (liver, colon, gastric, oral, cervical) - most prominent in Asian countries
    d. Strong relevance and funding opportunity around liver, colon, gastric cancer in Asia; possible to extract both healthy and disease samples

2. Technology:
    a. 10x genomics, C1 CAGE, Nx1-seq (nano-wells), RamDA-seq
    b. MER-FISH, super-resolution microscopy
    c. Epigenome: scMethyl-seq, ATAC-seq
    d. Multiomics (SIDR seq)
    e. Laser Capture Microdissection (LCM)

f. 10x is commonly supported but should stay flexible (e.g. Nadia, iCell8). Make efforts to benchmark across platforms and utilize cell spike in controls when possible

3. Computational
    a. Local data centers
    b. HCA/CZI Data Coordinated Platform
    c. Follow the common standards for sample and data preparation.
    d. Promote Open Data Policy in own country
    e. ShoGin Database from Kyoto University
    f. Start with local data centers but integrate to the global DCP for a stronger reference

Conclusion and action items

The members recognize that strong outreach efforts to local funders is needed. In general, funders are seeking disease phenotypes (and/or economical returns such as diagnostics). At the same time, we as a HCA community emphasize the importance and relevance of building a human reference - especially from the Asian population - to enrich our understanding of diseases, its intervention and regenerative medicine.

The members recognize there are universal challenges such as sampling techniques, data normalization, platform comparisons. It is sensible to engage with the global HCA community to solve these issues together, while addressing regional challenges.

It became apparent that each country has their own terms and conditions around ethics (e.g. data and sample sharing). It will be imperative for each country's representatives to engage with the local ethics committee and promote open sample/data policies to "accelerate science".

In order to execute concrete plans going forward, the members discussed and agreed to establish an interim (preparatory) organizing committee to define targets, draft documents for funders, and initiate pilot studies.

Acknowledgements

Local representatives
Japan: Dr. Piero Carninci (RIKEN), Dr. Jay W. Shin (RIKEN)
Korea: Dr. Young Joon Kim (Yonsei University), Dr. Jong Hoon Park (Sookmyung Women's University)
Singapore: Dr. Shyam Prabhakar (A*Star, Genomic Institute of Singapore)
India: Dr. Partha P. Majumder (National Institute of Biomedical Genomics)

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10x Genomics

Coordination staffs
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Emi Ito (RIKEN)
Masaaki Furuno (RIKEN)
Akira Furukuawa (RIKEN)
Toshiaki Higo (RIKEN)

Appendix I: Program

Day 1: Thursday, November 30, 2017

13:00-14:00 Registration

14:00-14:45 Session I: Commencement
Session chair: Jong Hoon Park

Welcome	Piero Carninci
Human Cell Atlas	Jay Shin
Chan Zuckerberg Initiative	Kevin Moses

14:45-16:00 Session II: Imaging technologies
Session chair: Shyam Prabhakar

Imaging Technologies for single cell analysis
Yasushi Okada /RIKEN
Super-resolution microscopy
Sang-Hee Shim/Korea University
MER-FISH
Kok Hao Chen/Genome Institute of Singapore A*Star
Single cell seq based on histological locations
Kyeung Min Joo/SungKyunKwan University School of Medicine

16:00-16:30 Coffee break

16:30-17:45 Session III: Single cell genomics technologies
Session chair: Partha Majumder

Single cell analytical platform
Yutaka Suzuki/University of Tokyo
Simultaneous gDNA and total RNA
Woong-Yang Park/Samsung Medical Center
Tumor microenvironment by Nx1-seq
Shinichi Hashimoto/Kanazawa University
10x Genomics (sponsor talk)
Tarjei Mikkelsen/10x

Discussion item: Common Coordinated platform

17:45-18:15 Transport to Rizzan Sea Park Hotel

18:30-20:00 Dinner reception @ RIZZAN

Day 2: Friday, December 1, 2017

9:00 Session start
9:00-10:30 Session IV: Cancer biology
Session chair: Woong Yang Park

Detecting somatic mutations in single cells
Young Seok Ju/KAIST
Drug resistance and Intra-tumor heterogeneity
Ramanuj DasGupta/Genome Institute of Singapore, A*Star
Drug-induced cellular response
Erik Arner/RIKEN

Discussion items: Asia Tumor Cell Atlas

10:30-11:00 Coffee break

11:00-12:30 Session V: Stem cells/ageing
Session chair: Akira Watanabe

Hair follicle stem cells
Hironobu Fujiwara/RIKEN
Ageing
Aki Minoda/RIKEN
SHOGoiN database
Wataru Fujibuchi/Kyoto University

Discussion items: Stem Cell Atlas, Immune Cell Atlas
(Photo time after the session)

12:40-14:00 Lunch @ OIST cafeteria

14:00-15:30 Session VI: Establishing HCA Asia Network - Part I
Session chairs: Roger Foo, Yutaka Suzuki
Topic 1: Tissues, disease, sampling
Topic 2: Profiling platforms

15:30-16:00 Coffee break

16:00-17:15 Session VI: Establishing HCA Asia Network - Part II
Session chairs: Seon-Young Kim, Jay Shin
Topic 3: Funding
Topic 4: Coordination

17:15-17:30 Closing remarks Young Joon Kim

Appendix II HCA materials

To join the global HCA
https://www.humancellatlas.org/joinHCA

HCA SLACK channels
https://humancellatlas.slack.com

White paper
https://www.humancellatlas.org/files/HCA_WhitePaper_18Oct2017.pdf

Publications
http://www.nature.com/news/the-human-cell-atlas-from-vision-to-reality-1.22854
https://elifesciences.org/articles/27041

News articles (press releases)
https://www.humancellatlas.org/news