Breakout Session Topic: Disease - Designing Flagship Projects

Date/Time: Monday, 9 June, 5:10 - 6:10 SGT

Breakout Leaders: Musa Mhlanga and Vinicus Maracaja-Coutinho

Scribes: TBC

Onsite Room: Auditorium

Zoom Room: https://events.humancellatlas.org/2025GM/v/s-2862102

Breakout Description

This session will focus on shaping flagship disease projects within the Human Cell Atlas (HCA), with an emphasis on diseases that impose the highest burden of disease as measured by DALYs. Drawing from community input across Africa and Latin America, survey responses identify a core group of diseases already under active study—including malaria, Dengue, HIV, colorectal cancer, CNS tuberculosis, and autoimmune hepatitis—which align strongly with global and regional DALY metrics.

While the flagship strategy will prioritize high-DALY diseases to maximize global health impact, it will also incorporate community-identified priorities where feasible. These include:

- Maternal and fetal health conditions, such as pre-eclampsia and preterm birth
- Metabolic syndromes (e.g., diabetes, obesity)
- Regionally prevalent cancers, such as breast, gallbladder and pancreatic cancer
- Systemic and autoimmune diseases, with multi-organ manifestations

Concerns raised in the survey highlight the need to avoid overlooking rare and neglected diseases entirely and to ensure equitable participation:

> “Representation from various population groups across all continents is essential.”
> “Equitable representation of global genetic diversity across bio-networks is still lacking within HCA.”
> “It would be good to have workshops on library prep and data analysis techniques.”

This session will aim to define 2–3 flagship projects that are technically feasible, high-impact, and collaboratively executable—anchored in DALY data and guided by the strengths and priorities of the African and Latin American HCA community.

Key Questions to discuss and explore

1. Which diseases combine research momentum, biological insight, and practical feasibility for HCA to pursue as flagship projects?

2. How can we overcome technical and infrastructural barriers (e.g., IRB approval, sequencing access) to support multi-site flagship collaboration?

3. What strategies can ensure inclusion of rare, systemic, and neglected diseases alongside high-prevalence global diseases?

Scribe notes and takeaways

Actions:

- Discussion raised some interesting ideas about diseases that could be targeted in a flagship project
- More documentation and share all the challenges from established projects. Next goal or step, linked what's shared the day.

Summary:

The session focused on generating ideas for flagship HCA disease projects that combine research momentum, biological insight, and practical feasibility. Participants were asked to consider scale, impact and resource limitations in different regions. The following diseases were discussed.

- Diseases associated with the liver (Hepatitis B, auto-immune hepatitis, Cirrhosis, Cancer, fatty liver disease) are globally distributed and high in lower middle income countries and are likely to increase in the future. Biobanks in India and established cohorts in Brazil and Columbia.
- HIV, TB (existing cohorts across Africa and Latin America)
- Lower respiratory infection cohorts are being set up in Malawi and South Africa, Vietnam and Kenya, but they will be collecting naval cells as a proxy and not primary tissues associated with the diseases.

- Diseases associated with aging, a large cohort in Brazil and other cohorts around the world.
- Burden of cancer survivors and the effect cancer has on cells causing disease and abnormalities later in time (noted that this may be too broad/diverse for one project).

Key takeaways/recommendations

- Capacity strengthening is important. Research on samples should be carried out locally, and there should be an incentive for local researchers to generate data e.g. private portals or data sharing embargoes.
- UNESCO partnership could be leveraged to strengthen capacity and to explore environmental impact on disease.
- Knowledge sharing can help HCA members learn from previous projects like AIDA about the practicalities of multi-site collaborations e.g. data sharing across borders and dealing with vendors. It was noted that the HCA Executive Office could support this.
- The disease survey is still open for members who want to express their thoughts on diseases that should be prioritized by HCA.

Notes:

1. Which diseases combine research momentum, biological insight, and practical feasibility for HCA to pursue as flagship projects?

Musa Mhlanga: Idea of HCA transitioning from healthy atlas to atlas that's more disease focussed - translationally focussed, emerged in Milan 2024, HCA see as essential to impactful use of amazing atlases that have been built over the last 5 years. Looking for a way to translate where atlas would be most effective. Using DALI indicator, so hope is to directly impact largest number of lives from the use of the atlas. Related: Survey sent to Africa and Latin America - contextualise answer, which diseases combine research momentum, biological insight and practical feasibility. Keep in mind looking for scale/impact and resource-limited environments, difficult to get access to complex tissues, so PBMC would be an advantage. Final goal - 2-3 flagship projects

Chloe Villani: Outcome Musa and others pushing - is now part of HCA strategy, never planned to disease initially (studying disease a bit of a pandora's box) but they need to start somewhere. HCA is in a place to target disease to leverage a broad network, disease surveys help identify what the community cares about. HCA Keen on figuring out which flagship project should be prioritized. Funding opportunities. Other opportunities to help empower different parts of the world (many people around the world can't get involved of HCA if there isn't a disease focus)

Hideki Ueno, Kyoto University: Proposing Chronic hepatitis B - Cirrhosis causes cancer, they can get samples from countries, we can show HPV chronic infections in Cirrhosis, we can use data sets to learn about liver cancer and chronic hepatitis.

Chloe Villani: Important that we are pragmatic, good to know if you have a cohort, do you know others who have a cohort (e.g. liver, blood etc.)? That can help.

Hideki Ueno: Colleagues in India, they have lots of samples but issue, they don't ship them outside the country.

Musa Mhlanga: Hep B is a very good one, globally distributed, especially high in LMICs, indirectly featured in Cancers caused by them.

Chris Moxon, University of Glasgow/Malawi Queen Elizabeth Central Hospital: Existing malaria, HIV, TB atlases, is that a coordinated approach?

Musa: I think more uncoordinated

Chris: Obvious ones for a more coordinated approach, HIV and TB, there are centres across Africa that have HIV and TB cohorts (and Asia and Latin America) lower respiratory infection, biggest killers, they are putting together cohorts in Malawi and South Africa, Vietnam and Kenya.

Musa: In the top 5 Dalis, respiratory infection, separation between infection and disease, important thing to know, are these cohorts collecting primary tissues associated with the disease? challenge collecting tissues.

Chris: limited autopsies in those sites, they are creating naval cells, (proxy). On the disease concept, the key thing is, if you want local researchers involved, collecting healthy cells is too abstract a concept.

Ankita Chatterjea, John C Martin Centre India: We are trying to focus on some diseases that have huge public health relevance, prioritizing common diseases. Collection of autopsies without ethical hindrance If we focus on the blood and tissue of interest, obese individuals more likely to show systemic information, metabolic syndrome could be an interesting area of focus. Fatty liver disease - 32% on average, 1 in 3 people now suffering fatty liver disease, associated with lifestyle disorder.

To understand the disease, paired biopsy samples are needed. They have a biobank that stores samples. Auto-immune hepatitis increased in the last 10 years. Major impact of auto-immune liver disease, acute chronic liver failure. If we focus on immune cells, that could also be an interesting point to study.

Vincius: Established cohorts in Brazil, Columbia and Chile.

Ricardo Khouri, FIOCRUZ: Research in viral infections, overlap of viral infections in Brazil, complications in Brazil associated with diabetes, hypertension, would be welcome if we could look at relation between infections, the burden e.g. outbreak of …. And the Zika virus 10 years ago) Chikungunya infection is systemic, attacks many different organs.

Vincius: important to obtain samples across multiple countries, e.g. HIV

Patricia Savarino, Brazil: Speak on behalf of research in Sao Paulo, starting a project on aging, a cohort of 10,000 people that they will study over the next 10 years, so all sorts of diseases related to aging, cardiovascular and neuro diseases. Cohort is based on workers at the university, so they have access to them. Ageing is an important topic which everyone can contribute to, interesting to compare similar ancestry.

Alfredo Roddriguez, University of Mexico: Increasing burden of cancer survivors - every year more people survive cancer, therapies causing something in the cell, so could look at something that is happening causing disease and abnormalities later in time. Samples: access to patients that can be followed over time and adults via hospital networks in Mexico.

Musa: Strong interaction of a few things, Hepatic space, fatty liver disease and metabolic disease are significant and (some intersection). Cross-talk - respiratory infection and chronic respiratory diseases, easily top 5 DALIs around the world. Some focus areas e.g. Liver (focused cohort) respiratory (lung) ageing (important because we live an ageing society) Stratify across different ages where possible, cancer survivors, cancer difficult a bit diverse but age stratification important for translational understanding

Chloe: Not to forget that we have a tier 2 metadata Genetic Diversity task force to capture a broad demographic, not dismissing metadata as we move into disease, we care about age, ancestry.

Musa: clarifying - cohorts should be distributed across age

Chloe: regional opportunities with cancers that common in a region, helpful to know what people are interested, regional funding opportunities

2. <u>How can we overcome technical and infrastructural barriers (e.g., IRB approval, sequencing access) to support multi-site flagship collaboration?</u>

Vincius; how can we deliver results across different sites, e.g. library generation etc.

Chloe: tied to this is capacity building, e.g. people shouldn't have to ship their samples, data sharing, legal entities, but some institutions prevent you from doing it. Ways of doing it in private portal settings. Share data: we can share the codes to reproduce the data.

Vinicius: Launching in Africa and South America

Audience member: Advocate for AIDA across 5 nations over the past ~2 years, logistical hindrances, taken care of by the coordinating team: India strict rule for non-transfer of samples, the coordinating sample got CZI to distribute finding to different area, submit data, protocol was open to everyone in the project, and data could be submitted in a single place and can be accessed, the multisite projects are possible.

Chloe: The way CZI manages data through AWS.

Musa: Things we should think about globally, how we overcome and instituted technical barriers.

Patricia: Suggestion for Chloe - gathering experience from ancestry problems, a lot to share, same with AIDA (come up with some kind of knowledge management tool - not only about sharing samples and data analysis we have a lot of experience to share)

Vinicius: finances

Chris: Obviously, capacity building isn't just about providing access, through the potential disease networks that can use hub and spoke models, region in africa and asian region, in an environment that's quite different. Data sharing, in the Genomics revolution in Africa, recognised there's a conflict. The cost of sharing is high, everybody does the sequencing and shares the data immediately, so sometimes what happens is data is analysed by others, disincentivizing for people going to efforts, because they are producing the data which others use first. it stops capacity developing. need some way of protecting people doing the sequencing. link them to the analysis people. Examples of what others have done: set limits on data use for a period of time - only the institution who generated the data can use it for a period of two years.

Vincius: National Lab, Benefit sharing and inclusion, see as opportunity, one issue, people have access, that in Africa recently funded, facilitate this kind of information

Muzz: Knowledge sharing in a more formalised way, that could be weaved into the code of conduct, so that it's more formalised, capacity strengthening, could be done in partnership with UNESCO in highlighting national level information for access and dealing with access. How to deal with vendors at the national level. Second point: great opportunity to look at disease, genetic diversity, with global representatives, environmental exposure (different) e.g. UNESCO slide on exposome climate exposure, local exposure?, relevant to local needs for the funding, creating a case of need and justification.

Musa: Knowledge management tool builds upon the knowledge that has been acquired from AIDA, data sharing embargoes. Does it reside inside HCA, knowledge management tool, guidance notes, vendor agreements, discussion on HCA

1. What strategies can ensure inclusion of rare, systemic, and neglected diseases alongside high-prevalence global diseases?

Short of time. Not discussed.