ALLEN INSTITUTE *for* IMMUNOLOGY

Using Multi-omic Profiling to Unravel Human Immunity Across Age

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Program Lead, *Immune Health & Aging*

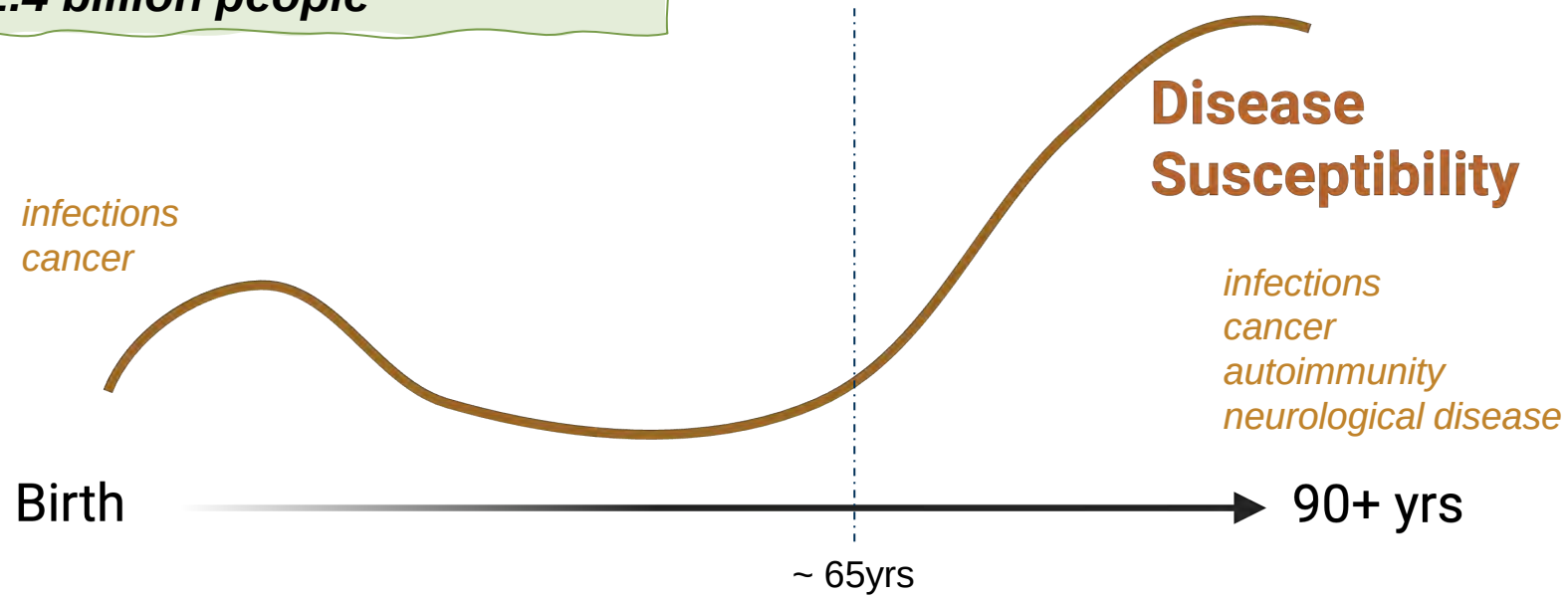
Disclosures

- None

Age and Disease

Humans have differing susceptibilities to diseases across age

By 2100, the WHO predicts that the global population aged 65+ will exceed 2.4 billion people



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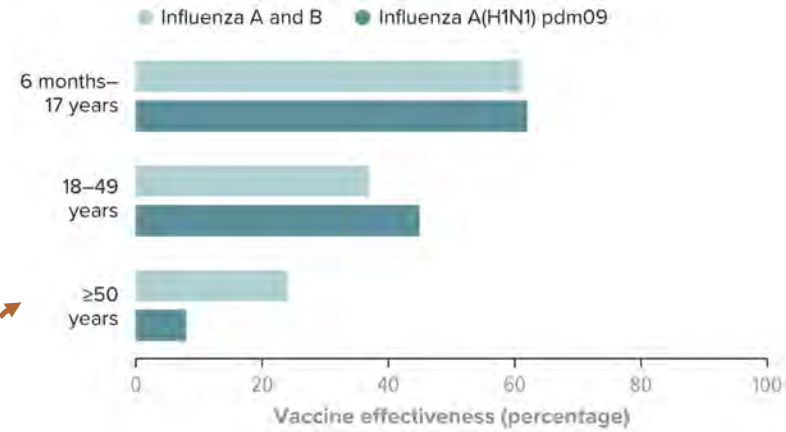
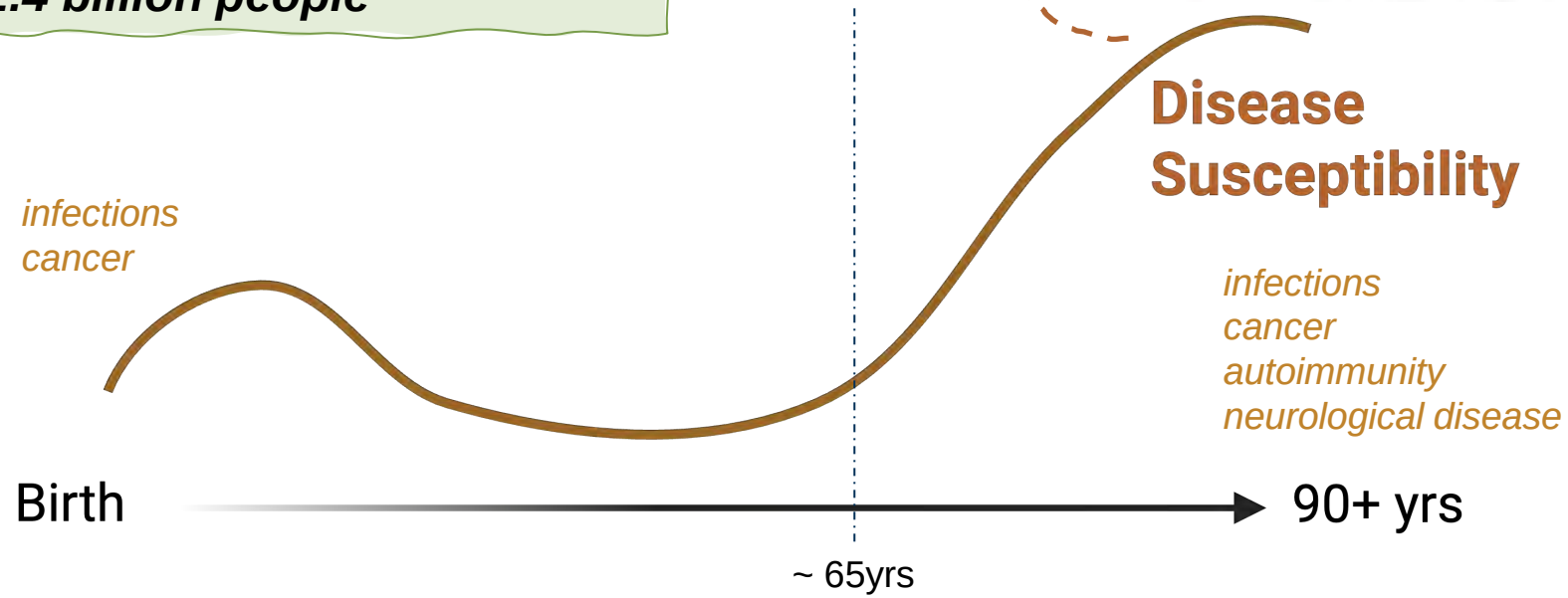
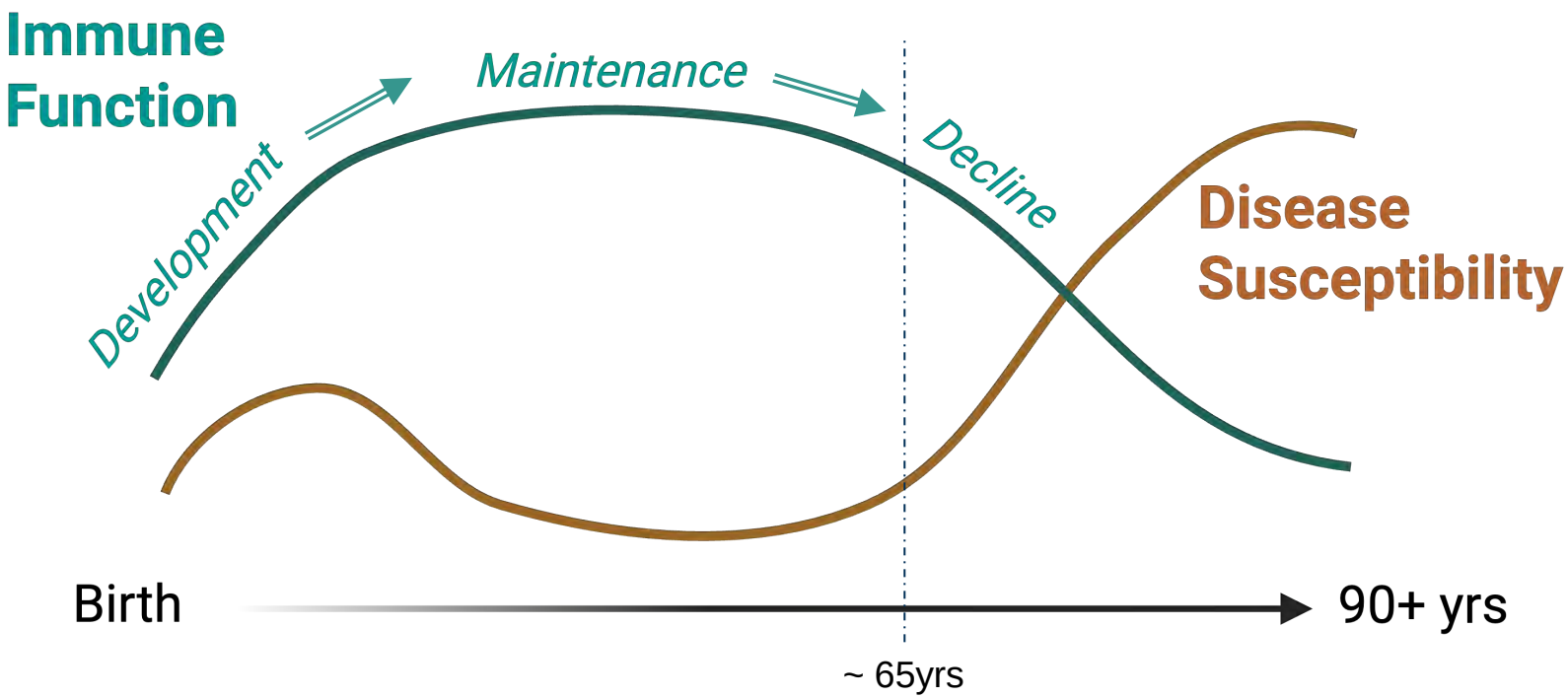


Reduced Protection from vaccines



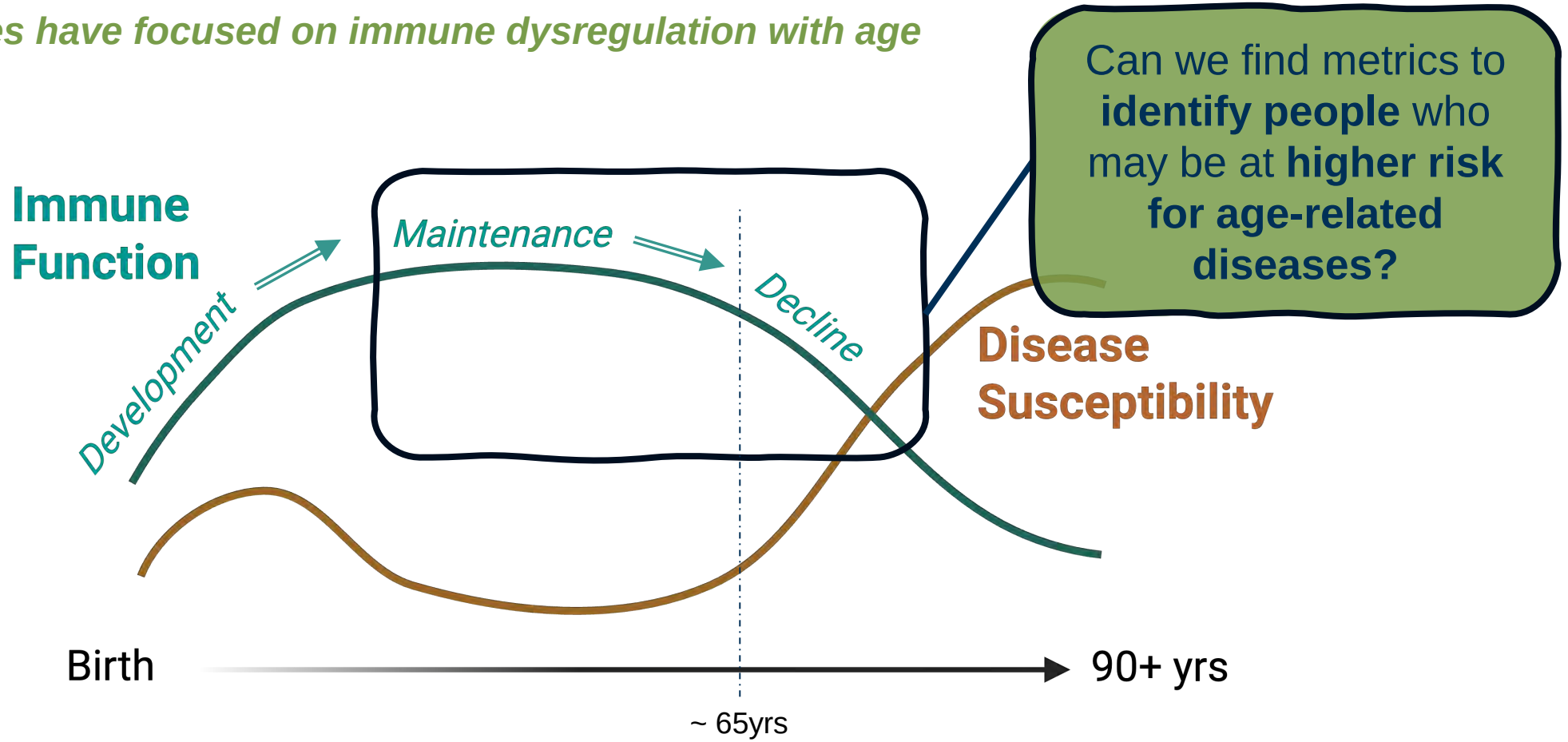
Immunity Across Healthy Age

Age-related susceptibility to disease linked to immune function



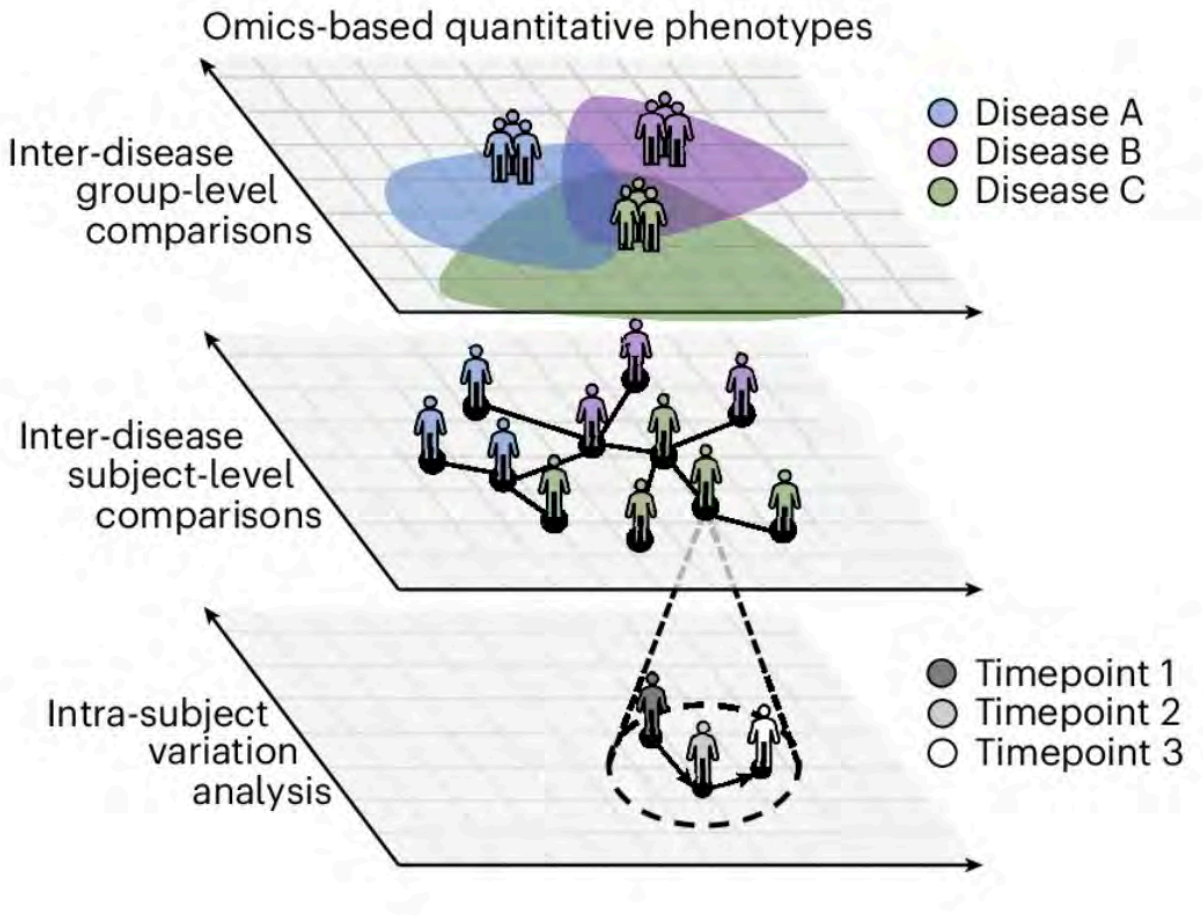
Immunity Across Healthy Age

Many studies have focused on immune dysregulation with age



Omics in Human Immune Variation and Aging

Identify systemic changes in the human immune system with age



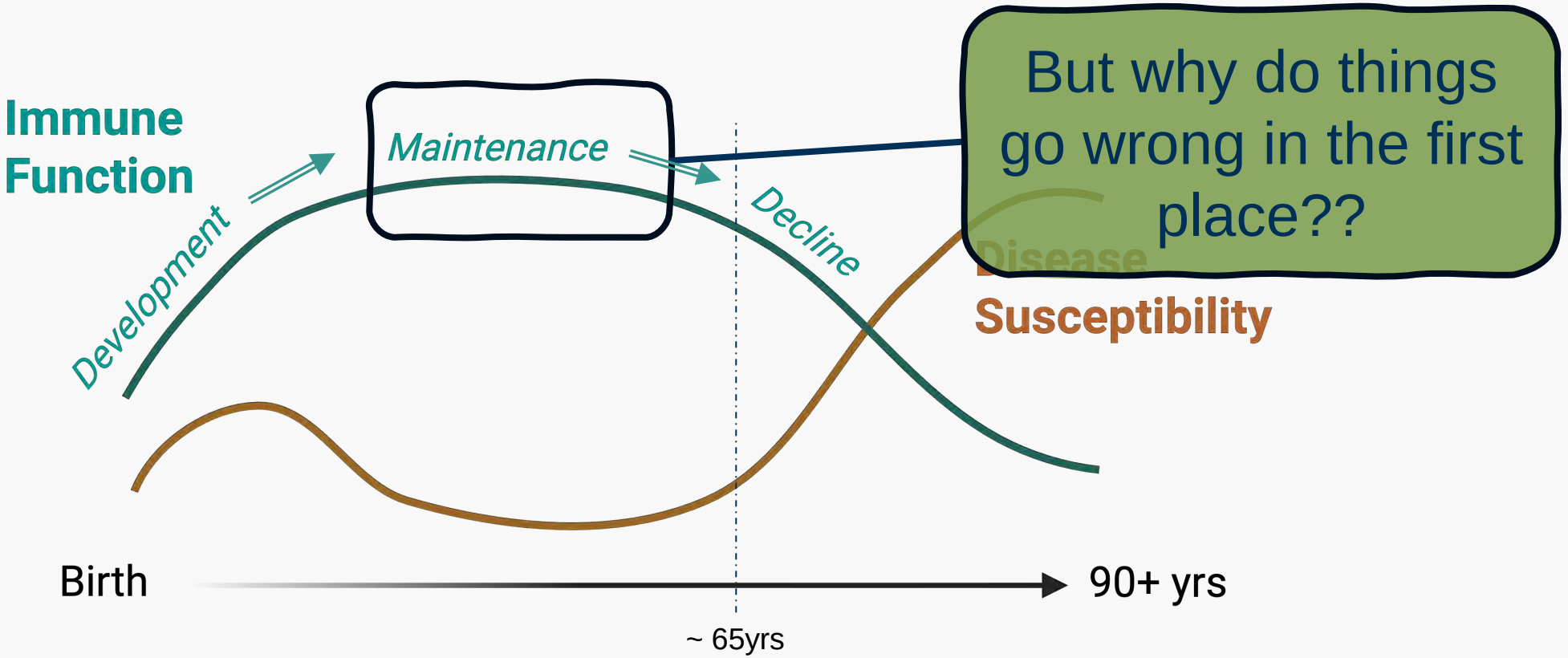
- *Plasma Proteomic*
- *Immune Cell Composition in blood*
- *Broad Molecular Signatures in blood*

Towards common metrics of "immune health"

Sparks et al, Nat Med, 2024

Immunity Across Healthy Age

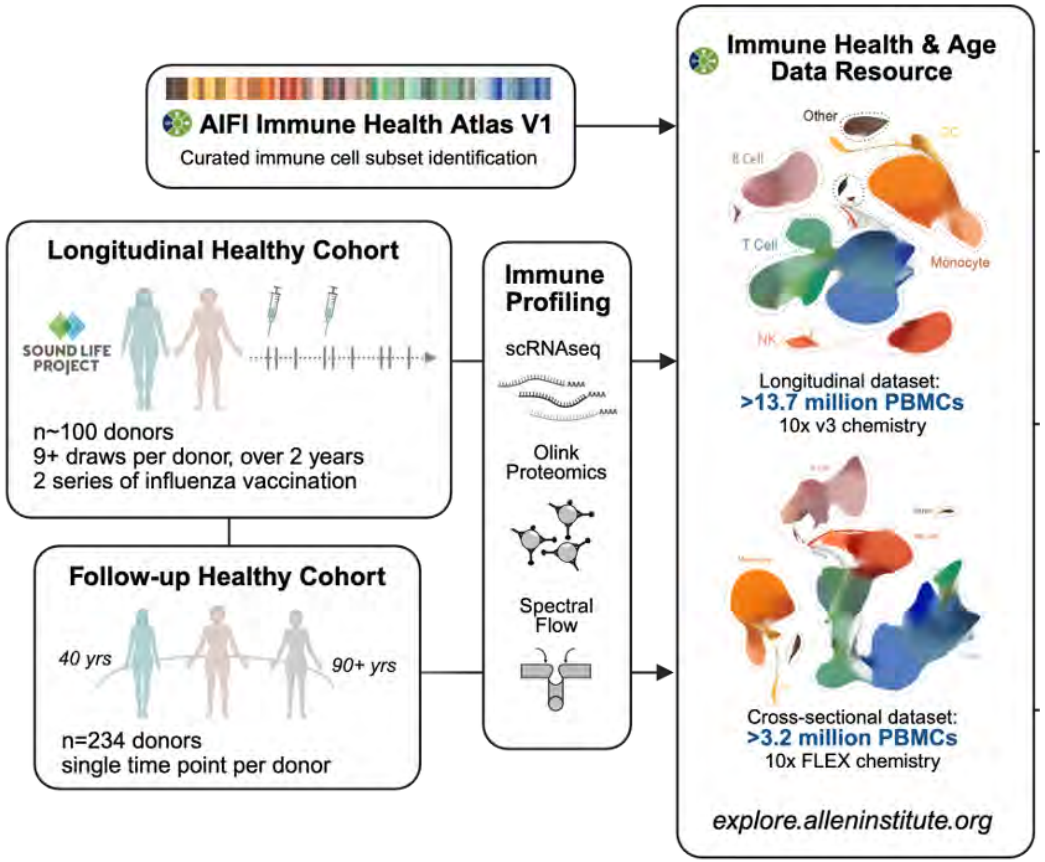
Studying the immune system and its function prior to advanced age - to stop immune aging



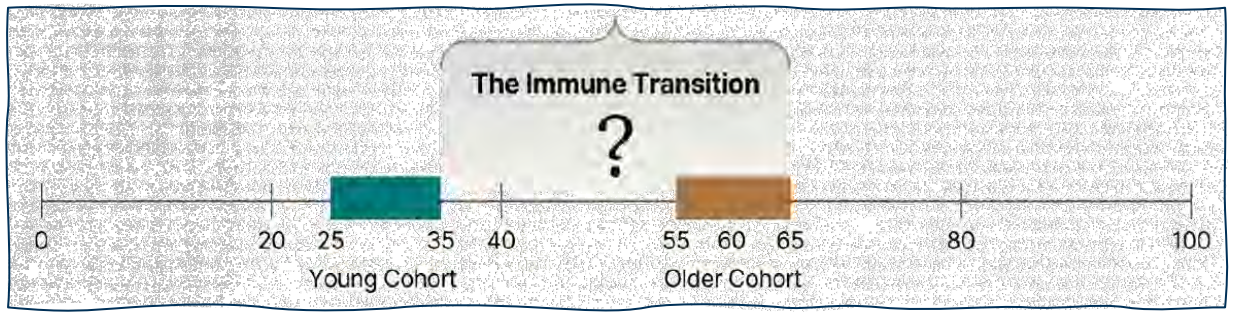
Can we **prevent increasing disease susceptibility** in older adults by **understanding immune function *prior to advanced age*?**

Human Immune Health + Tech Innovation = *Advanced Discovery*

Longitudinal human studies + state-of-the-art multi-omics + vaccine perturbation reveals...



When and why does immune aging start to occur?



Gong et al, Nature, 2025

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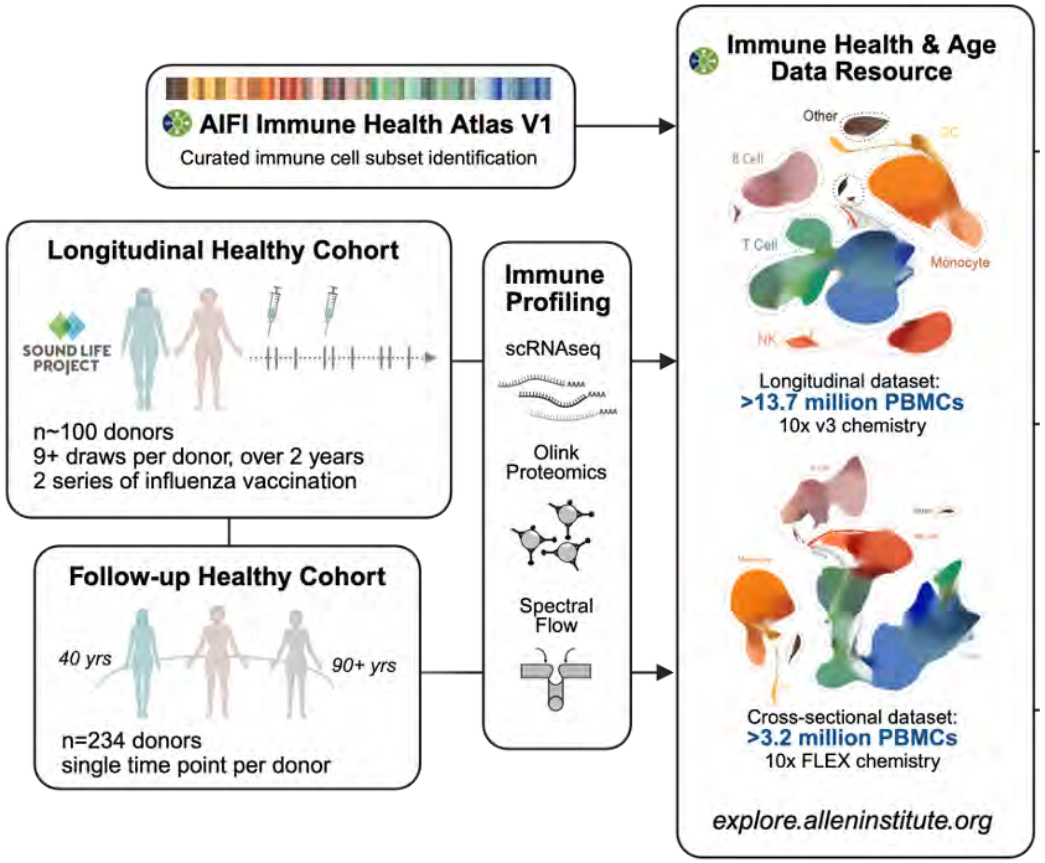
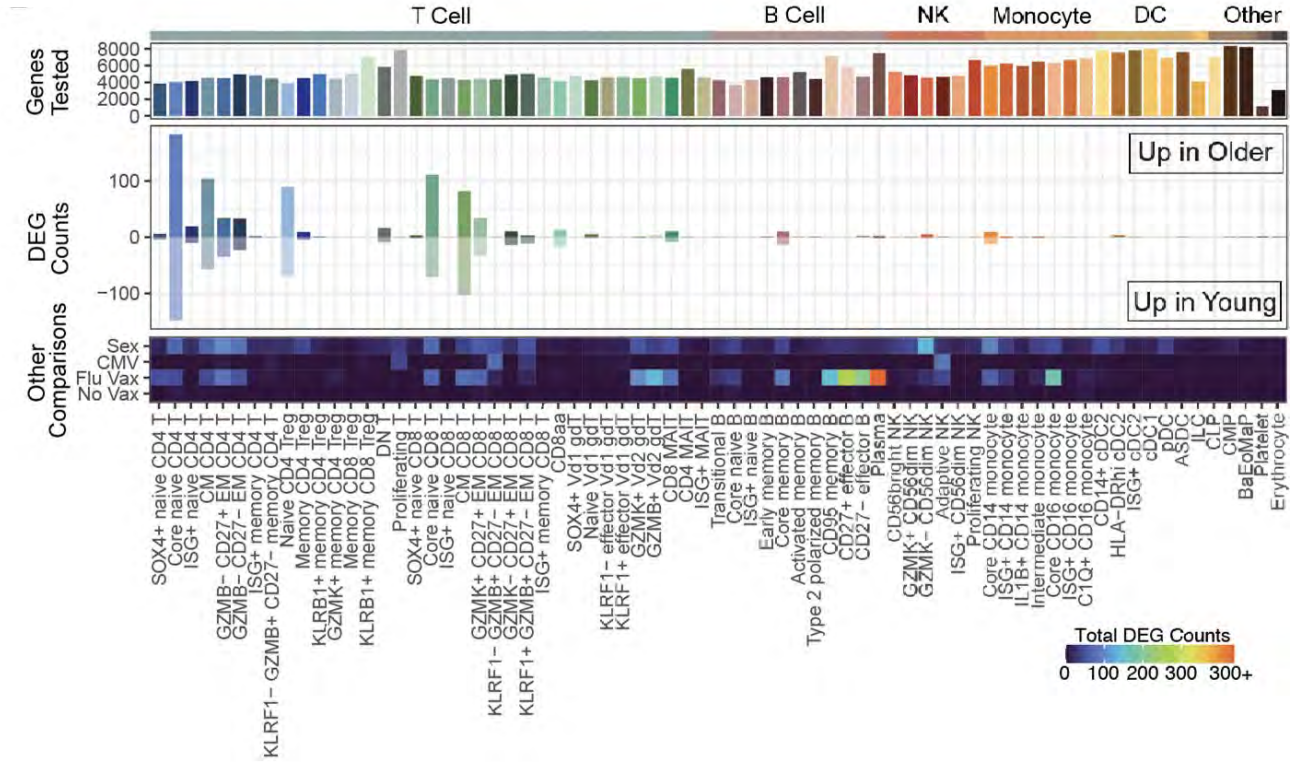




→ ***T cell reprogramming links to altered flu vaccine responses prior to advanced age***

"internal 'software' change rather than wear-and-tear from inflammation"

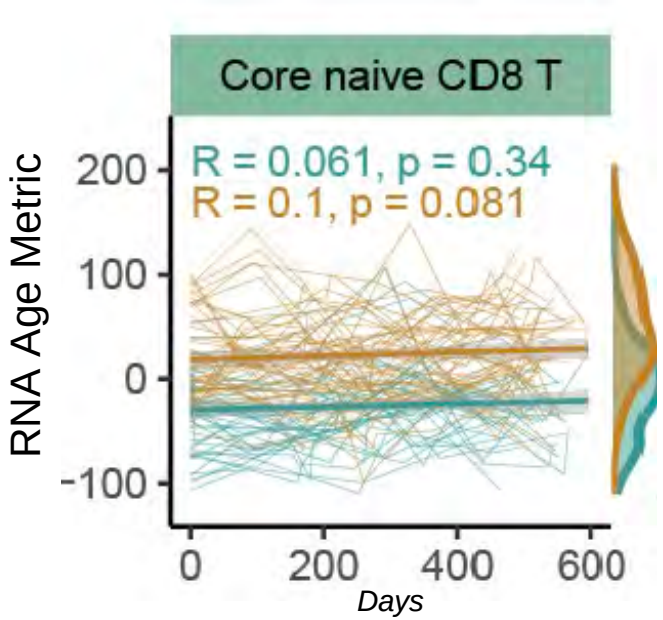
Gong et al, Nature, 2025

The T cell Timer

T cell reprogramming as a conserved feature of aging

Young adult
Older adult

Maintained over time



RNA Age Metric *= Molecular Clock \\ summary metric for age-related RNA expression changes within cells*

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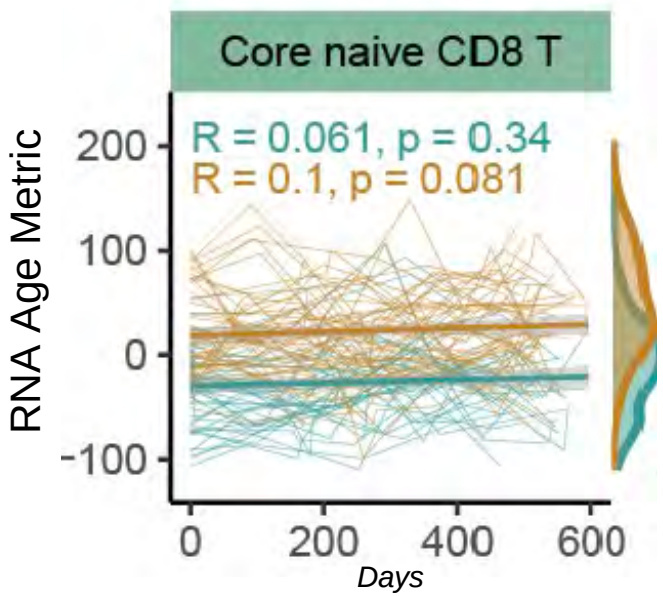
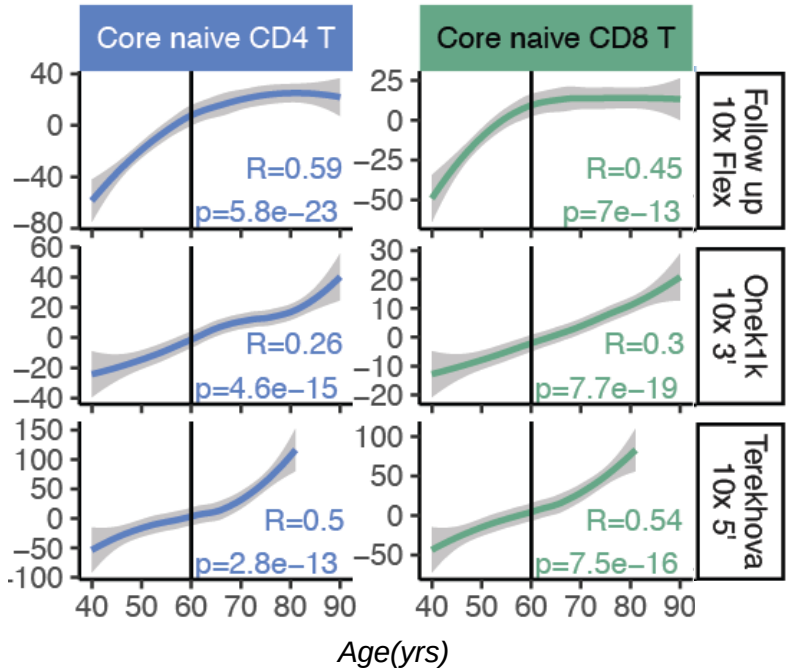


Commonly accumulates across healthy aging (>1300 people)



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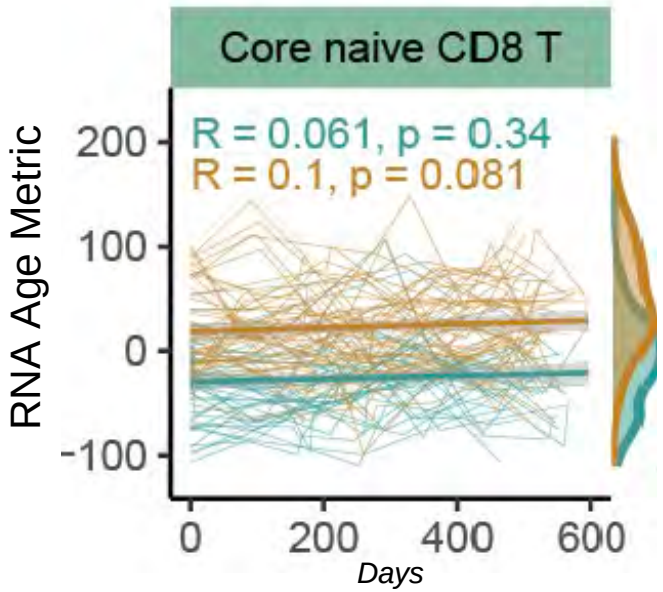

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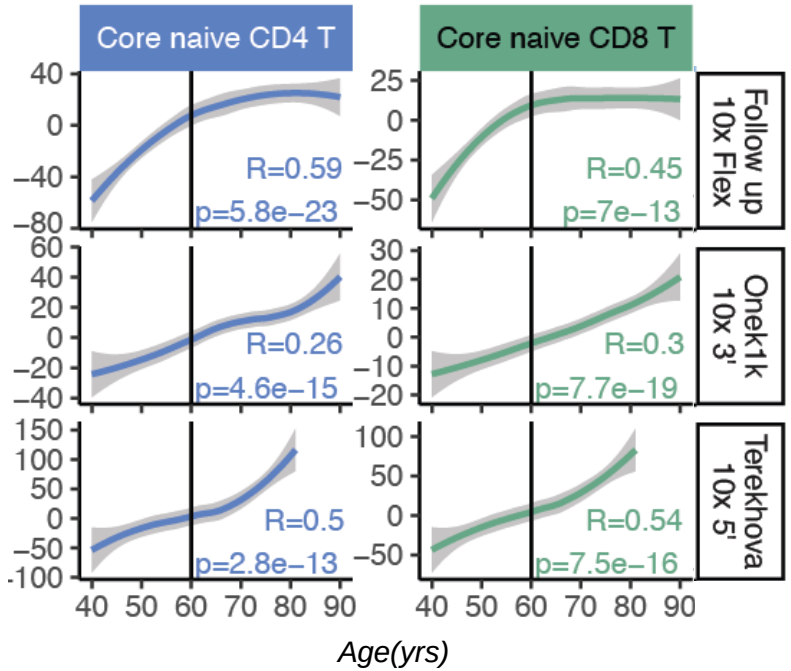
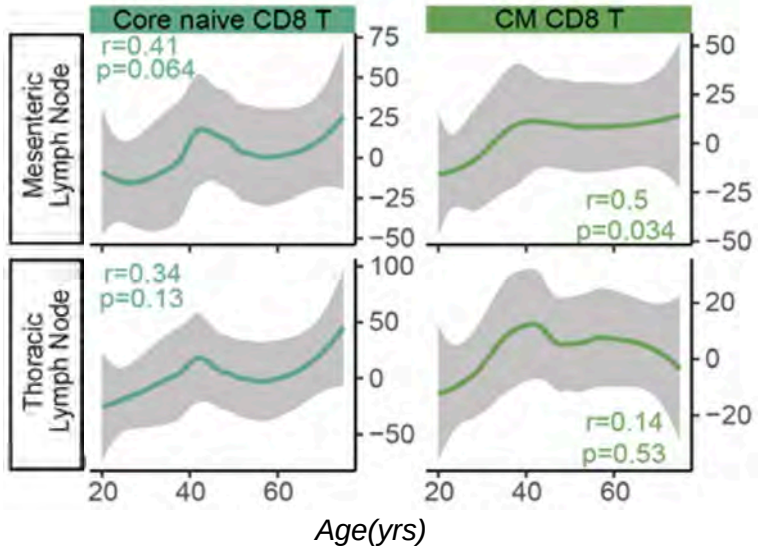


Occurs in tissues

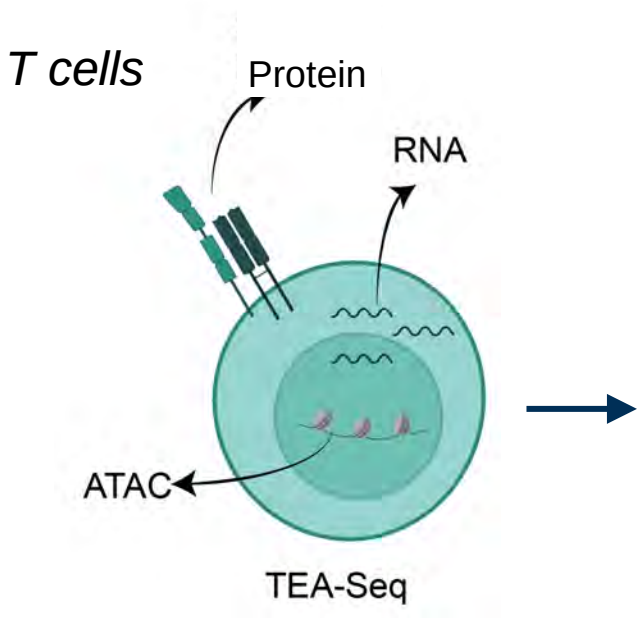


***RNA Age Metric** = Molecular Clock \\ summary metric for age-related RNA expression changes within cells*

Dataset from Wells et al, Nat Imm, 2024

Moving Beyond Baseline Biomarkers…

… into mechanistic and functional insight



Does T cell reprogramming lead to different T cell functionality?

Dataset from Thomson et al, Nat. Immunol, 2023

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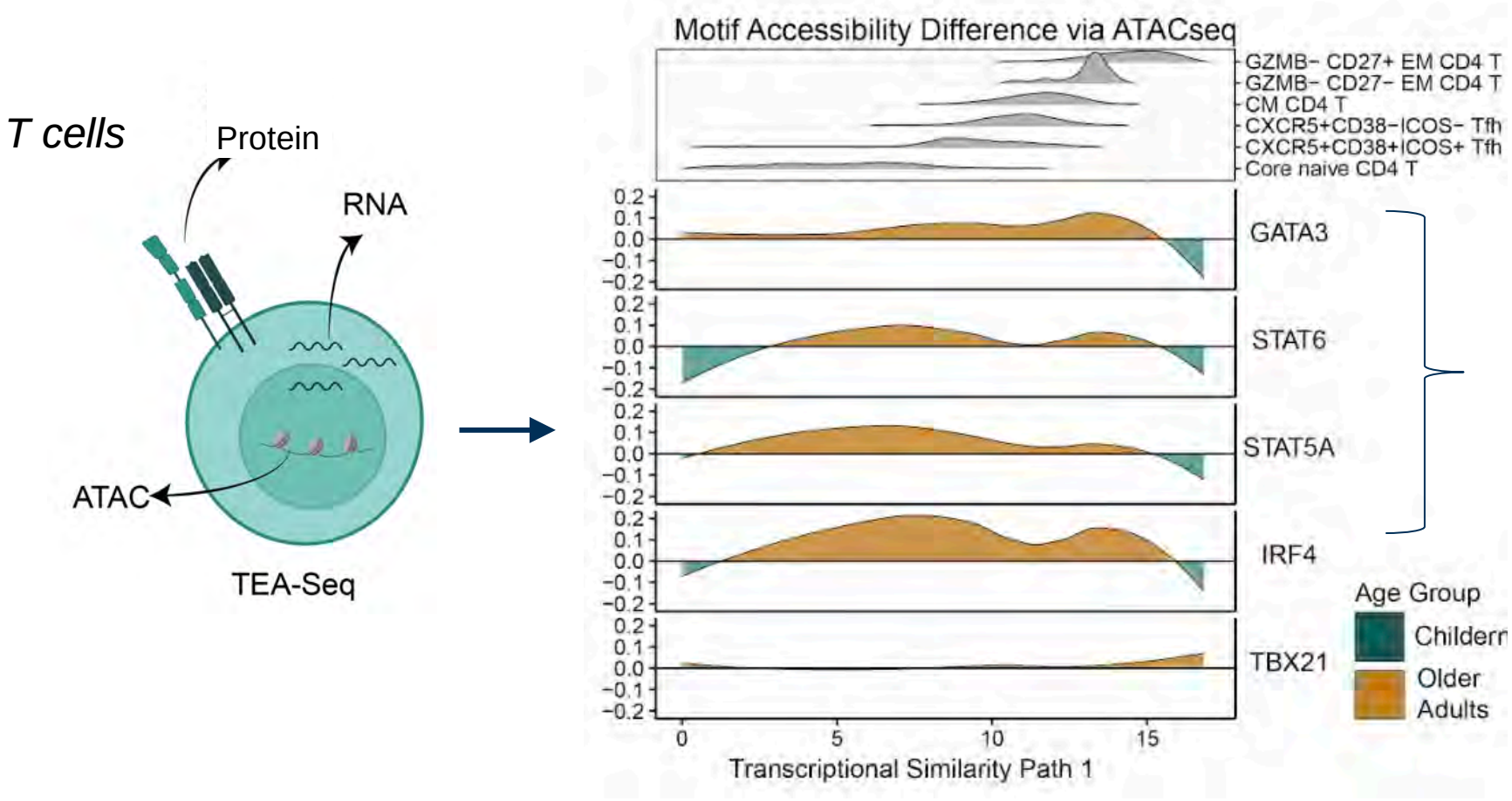
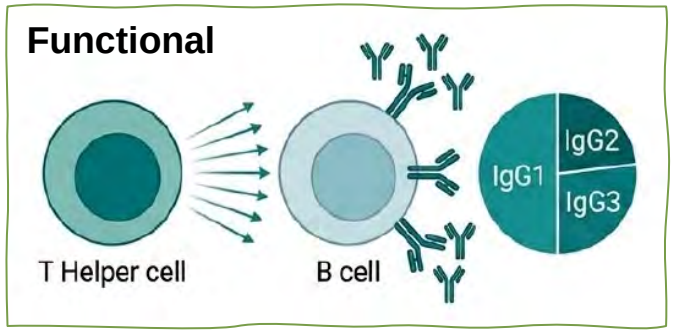
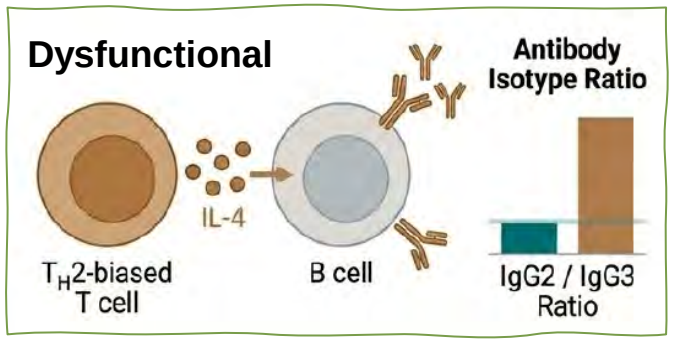


Dataset from Thomson et al, Nat. Immunol, 2023

… T cell reprogramming = broad Th2-ness

Unified Model of Immune Aging: Immune aging is not a steady decline but a dynamic reprogramming of T cells…





Gong et al, Nature, 2025

Memory T cells are qualitatively different in young and older adults (broadly Th2 skewed)

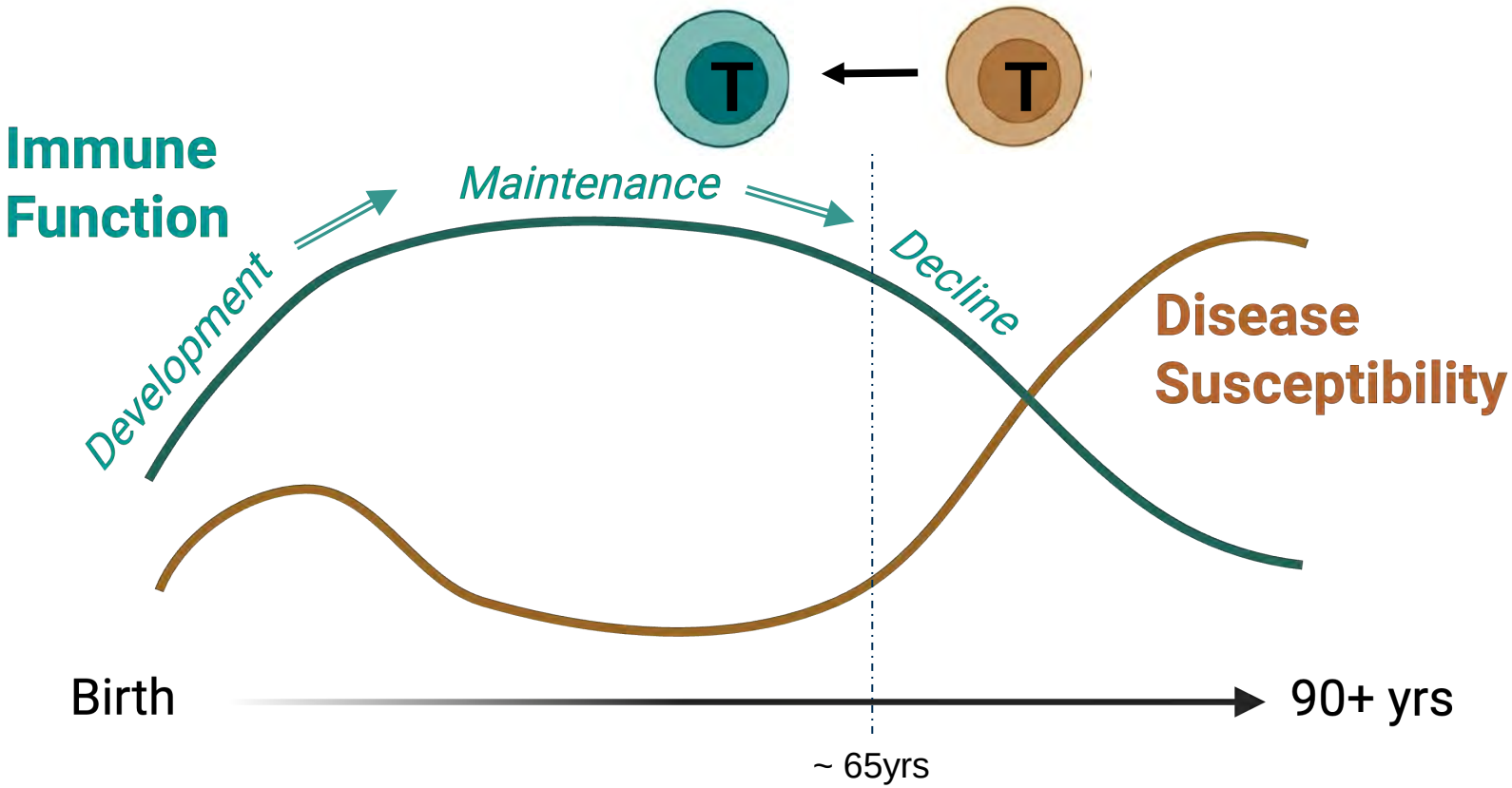
This alteration **occurs prior to advanced age**, and is not driven by *inflammation* or *CMV infection*

T cell reprogramming **impacts functional responses to *highly boosted* influenza vaccine antigen**

Reprogramming is found in tissue and young adults at risk for developing autoimmune disease

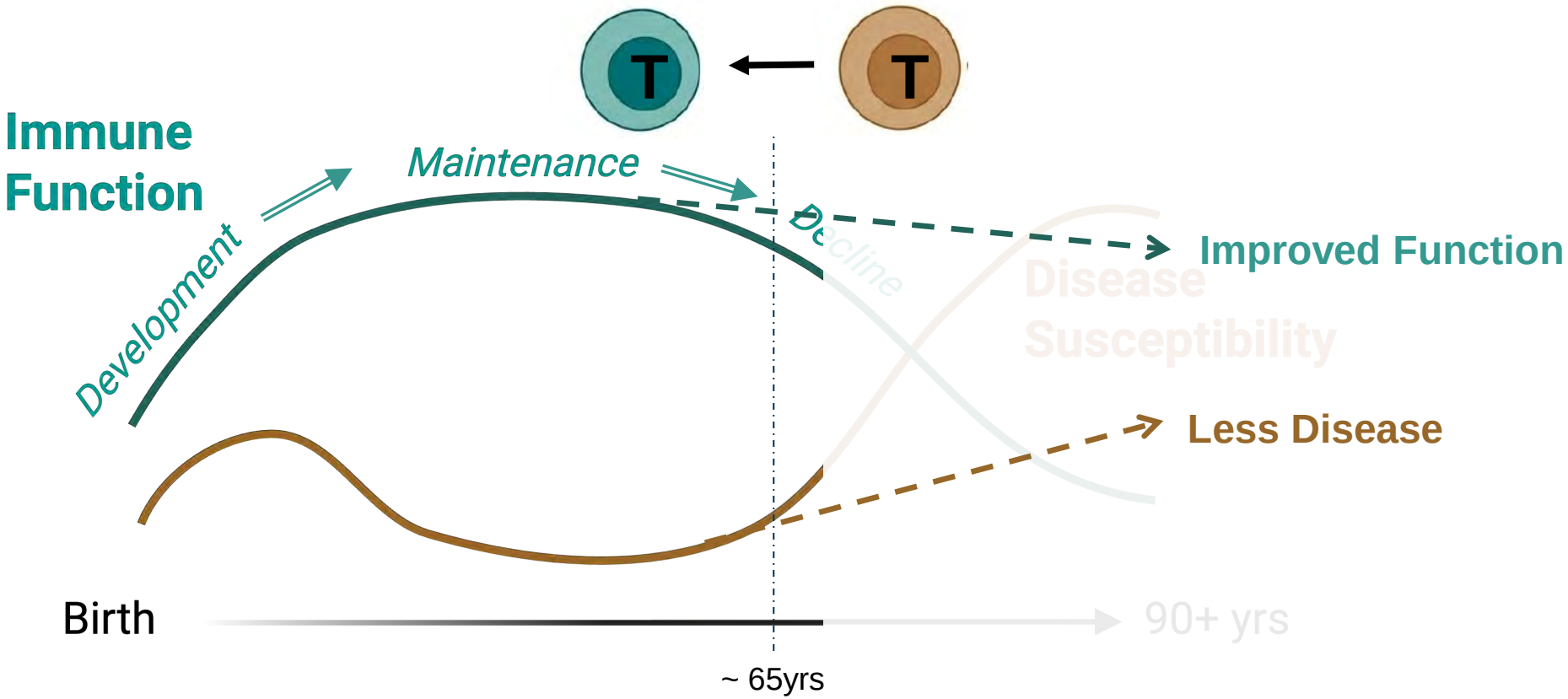
Building Immune Resilience across Age

Can we modulate T cell programming to build immune resilience across age?



Building Immune Resilience across Age

Can we move beyond baseline biomarkers to functional immune response prediction in people?



Knowledge Gaps

… in the casual drivers of human immune dysregulation with age

- **Universality of Immune Aging**: Does immune dysregulation follow a common trajectory in all people everywhere?

  (*Franck, Nat Aging, 2025; Yin, Science, 2026*)

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- **Tissue Specificity of Immune Aging:** Where/how does immune aging start? And what drives specific immune cell dysregulation?
  (*Wells, Nat Imm, 2025*)
- **Functional Immune Capacity with Age**: How do biomarkers of health/age directly link to change in immune cell functional responses?
  (*Gong, Nature, 2025*)

Research Opportunities

… to expand mechanistic insight in human immunity, age-related disease and long-term resilience

- **Inclusion of under-represented populations** across age ranges (*New Rapid Cryopreservation Method: Heubeck, JTM, 2025; Global efforts such as Project Jaguar, CIMA, UK Biobank, HIP, etc*)

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- **Multi-scale AI modeling:** to promote more comprehensive data integration and casual inference of immune dysregulation (New donor-level modeling: Pang, bioRxiv, 2025)

  ➔ To determine ***casual*** drivers of age-related disease susceptibility
  (e.g. functional immune link between viral infection, autoimmunity and dementia)

Explore our data

THANK YOU

We wish to thank the Allen Institute founder, Paul G. Allen, for his vision, encouragement, and support.

+ all the study participants for their time and commitment