Small samples, large questions: how Stanford's Holden Maecker is using immune profiling to study African health

Introduction:

For many clinicians and public health teams, the immune system is visible mainly when something has already gone wrong: a severe infection, a complicated pregnancy, a poor vaccine response, a child with persistent inflammation, or a patient who does not recover as expected. Standard laboratory tests are essential, but they usually capture only part of the immune picture.

A growing field of immune profiling aims to provide a broader view. Instead of measuring one marker at a time, researchers can now measure patterns across immune cells, cytokines and soluble proteins. The aim is to understand the biological state of a patient or study population: how the immune system responds to infection, how pregnancy reshapes inflammation, how nutrition affects immune development, and why some individuals recover while others progress to severe disease.

For African health research, this approach is relevant to several areas, including maternal and child health, HIV, sexually transmitted infections, malaria, dengue, chikungunya, malnutrition and environmental exposure. These conditions are often closely linked to immune function, but advanced immune monitoring has historically been concentrated in highly resourced laboratories.

Holden Maecker, Professor of Microbiology and Immunology at Stanford University and Director of the Human Immune Monitoring Center, has spent much of his career working on how to measure the immune system more comprehensively and reproducibly. The Stanford centre he leads provides immune-monitoring technologies including mass cytometry, flow cytometry, Luminex, Olink and NULISA-based immunoassays, as well as genomic assays such as single-cell RNA sequencing.

"What we'd really like to end up with is some kind of metrics of what constitutes a good human immune system," Maecker said in an interview. That question, he added, can apply to "specific disease risk", healthy ageing, cancer immunotherapy, or whether a patient may be a good candidate for an immune intervention.

The same question can also be asked in global health research: what does a resilient immune system look like in the face of infection, pregnancy, undernutrition and environmental stress?

From single markers to immune patterns

Cytokines are small proteins used by immune cells to communicate. They help coordinate inflammation, antiviral responses, wound healing and immune regulation. In clinical practice, however, cytokine testing is still relatively limited. A single inflammatory marker may suggest that something is wrong, but it rarely explains the wider pattern of immune activity.

Maecker is interested in the pattern itself. "When you start to look at a whole lot of different cytokines or other secreted proteins, you see patterns," he said. "And that's extremely interesting."

This shift from single markers to immune patterns is important because many diseases and health states do not produce a simple on/off signal. Pregnancy, for example, is not an immunologically neutral state. It requires tolerance of the fetus while still protecting the mother and newborn from infection. HIV, even when suppressed by antiretroviral therapy, may influence baseline immune status. Sexually transmitted infections may alter inflammation in ways that affect pregnancy outcomes. In children, a small blood sample may contain information about exposure to mosquito-borne viruses or other infections.

The challenge is to measure enough biology to see meaningful patterns, without making testing so broad, expensive or technically complex that it becomes impractical. That balance matters for health systems and research settings where laboratory resources, staffing and sample logistics can be constrained.

Pregnancy, infection and cytokines in Botswana

One example of this work comes from Botswana. In a 2022 paper in The Journal of Infectious Diseases (2), Maecker and colleagues reported plasma cytokine profiles among pregnant women in Botswana in relation to Chlamydia trachomatis infection, HIV status and gestational age.

The study was small and exploratory, involving plasma samples from 37 women at their first antenatal visit. Researchers measured 80 cytokines using a multiplex immunoassay. Fifteen women had C. trachomatis infection and 10 were living with HIV on antiretroviral therapy with viral load below 400 copies/mL.

The authors reported that 17 of 80 cytokines showed significant findings across the analyses. FLT3 ligand differed by chlamydia infection status, while several cytokines differed by HIV status. Other cytokines were associated with gestational age. The study also identified an interaction between chlamydia infection status and gestational age for resistin, a protein linked to inflammation and metabolism.

The immediate clinical message was not that these markers are ready for routine antenatal decision-making. The authors described the pilot as hypothesis-generating and noted that larger prospective studies would be needed. But the work demonstrated feasibility: plasma samples could be used to study immune mechanisms that may connect infection, inflammation and preterm birth risk.

For clinicians and researchers, this illustrates the value of immune profiling as a research tool. It can help identify

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biological pathways that deserve further study, patient groups that may differ immunologically, and pregnancy-related immune changes that may interact with infection.

Microsampling and children in Kenya

A second Africa-focused example comes from Msambweni, Kenya, where Maecker and collaborators studied immune responses to chikungunya and dengue viruses in children. The 2025 study published in Immunohorizons[1] used a miniaturized automated whole-blood cellular analysis system together with mass cytometry and flow cytometry.

The sample-sparing element is important. The system was designed to process 250 µL of whole blood for high-throughput cellular analysis. In the field study, researchers processed 133 whole-blood samples from a pediatric cohort known to have previous exposure to chikungunya and/or dengue viruses. The samples were analysed under unstimulated conditions and after stimulation with viral peptide pools.

The study found measurable virus-specific immune responses, including cytokine responses in gamma-delta T cells. The authors concluded that the approach could support detailed immune-function assessment in pediatric populations and resource-limited settings where sample volumes are limited.

This type of microsampling, or sample-sparing whole-blood processing, addresses a practical barrier in paediatric and field research. Children cannot be treated as small adults when it comes to blood collection. In many research settings, sample volume, transport, processing time and cold-chain logistics influence what science is possible.

If advanced immune profiling requires large blood volumes and immediate processing in specialised laboratories, its use will be limited. Smaller sample volumes, automated processing and more robust workflows may make such research more feasible in settings where childhood infections are common.

Platforms that make broader immune profiling possible

At the Stanford Human Immune Monitoring Center, Maecker's team uses several platforms for multiplex immune and protein measurement, including NULISA-based assays. The centre's role is not only to provide access to individual technologies, but to support studies that require standardized, reproducible measurement of cytokines and other soluble proteins across many samples.

For Maecker, the value of newer multiplex approaches lies in the ability to measure a focused but informative set of proteins. Rather than attempting to measure the entire proteome in every study, he points to what he describes as "a nice sweet spot with a few hundred proteins" that can cover a biological area such as inflammation or central nervous system disease "without getting so broad and so expensive that it becomes untenable."

In practical terms, this can help researchers move from isolated biomarkers toward biological patterns. In the NIH-supported IMPACC study of hospitalized COVID-19 patients, Maecker said NULISA made it possible to include all interferon alpha proteins as well as other key proteins that were missing from other platforms used in the project. This gave the researchers "a much broader view of what proteins were associated with severe COVID and/or death versus mild infection."

Automation is also relevant for studies that need consistency across many samples. Maecker noted that a fully automated workflow can support reproducibility and reduce technician time. "We've just never had that luxury before of being able to just load the samples and walk away," he said.

These features are particularly relevant when immune profiling is applied to population and global health research. In studies involving infants, children, pregnant women or rural communities, the constraints are often practical: small sample volumes, limited opportunities for repeat sampling, transport conditions, local laboratory capacity and the need for comparable results across sites. Platforms that can generate sensitive, multiplex data from small volumes of plasma or serum may therefore help extend advanced immune profiling beyond large specialist centres, provided that issues of cost, training, maintenance, data analysis and local research leadership are addressed.

Implications for African health research

Immune profiling is not ready to replace routine clinical judgement, microscopy, rapid diagnostic tests or basic laboratory services. Its role, at least for now, is mainly as a research tool that can help explain biological mechanisms and generate better evidence for prevention and treatment.

For this approach to be useful in African health research, several practical factors are important. African cohorts need to be included early and meaningfully, since immune profiles are shaped by geography, infection history, nutrition, age, genetics, environment and health-system context. Sample-sparing and automated technologies need to be evaluated in relation to paediatric blood volumes, field collection, transport, storage, staff time and cost. Capacity building is also important, including local data generation, analysis, interpretation and scientific leadership.

The future is unlikely to be one in which every clinic measures hundreds of cytokines for every patient. A more realistic near-term role is for immune profiling to identify useful patterns, validate them across relevant populations, and help translate selected findings into practical tools for prevention, diagnosis and monitoring.

Maecker's work begins with a broad question: what does a good immune system look like? In African health research, answers to that question may come from studying immune responses in the contexts where they are shaped most strongly in mothers, infants and children facing infection, nutrition challenges and environmental exposures in real-world settings.

If immune profiling can become more sample-sparing, reproducible and locally useful, small blood samples may provide larger insights into maternal, child and infectious disease health.

References:

1. Coker M, et al. Plasma cytokine profiles in pregnant women in Botswana in relation to Chlamydia trachomatis infection, HIV status and gestational age. J Infect Dis. 2022.
2. Maecker HT, et al. Miniaturized automated whole-blood cellular analysis for assessment of immune responses to chikungunya and dengue viruses in children in Kenya. Immunohorizons. 2025.