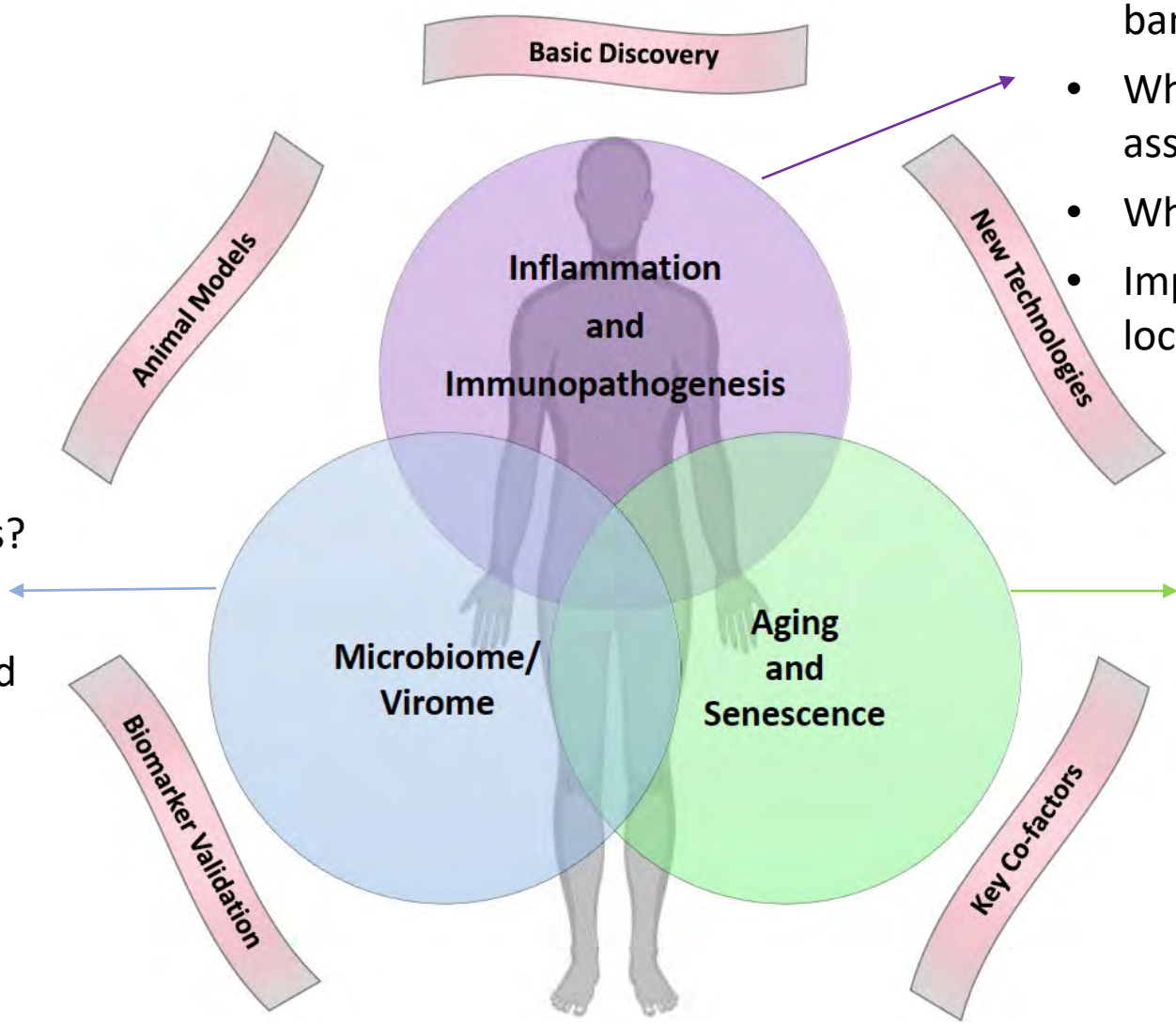
Pathogenesis – Basic Science

- Roots and branches, possibly a banyan tree.
- Which pathways are causally associated with disease?
- Where best to intervene?
- Importance of tissues and anatomic localization of inflammatory stimuli.



- Cause vs. consequence?
- Metaboilic product effects?
- Diet interactions?
- Possible microbial targeted therapy?

- Do “pillars of aging” overlap with those in HIV?
- Shared vs. distinct mechanisms?
- Best places to intervene?

Expanded discussions in working group

- Integrate HIV into HIV- clinical trials, to develop prelim data, samples
- Integrate organ systems (neuro-gut axis, etc) in our work
- Use systems biology to characterize flavors of inflammation
- Develop **Atlas** of molecular/cellular changes that predict multi-morbidity in HIV
- Compare this to similar atlas in aging (TAME trial, MOTRPAC, TOPMED)
- Host genetics and opportunities for Mendelian Randomization

Expanded discussions cont.

- Microbiome: cause or consequence and opportunities for targeting therapy
- Role of co-infections, helminthes in RLS
- Biology of resilience
- Root drivers: HIV silencing, co-infections, microbial translocation
- Animal models – ease of access to tissues, testing interventions, co-infections, control ART timing
- Structural barriers (bureaucracy, multi-institute funding)

Recommendations from the Basic Science WG

- Leverage ongoing large cohort studies of aging and age-related comorbidities (e.g. TAME) by either not excluding HIV+ participants or doing similarly designed parallel studies of HIV+ people so large clinical/lab/biomarker datasets and specimens can be analyzed to understand biological drivers/pathways of aging and comorbidities
- For large longitudinal and therapeutic/intervention studies of HIV+ individuals, make cohort characteristics and data dictionaries publicly available to facilitate new collaborations/analyses, make specimens and data more readily available to other investigators
- Develop funding mechanisms for “add-on” studies and new analyses of existing cohort data/samples to enable analysis of more than one comorbidity
- Genotyping of large cohorts and training more scientists who can analyze these large datasets, provide funding mechanisms to analyze this data

Recommendations from the Basic Science WG

- New funding mechanisms to enhance basic science research on shared drivers/pathways of multi-morbidity –how to get NIH institutes to share/co-fund
- Funding mechanisms for large-scale basic science studies (thousands of samples from same cohort) which could have more added value than only small “piecemeal” studies
- Integration of multiple disciplines, “cross-cutting” studies
- Engage basic scientists early in design of cohort studies so proper methods are used to collect specimens for immunology, microbiome studies etc and the “right specimens” are collected
- Animal model studies
- Big data, ‘omics studies