

Overview of the AIDS Clinical Trials Group

<https://www.actgnetwork.org>



ACTG Mission

- The mission of the ACTG is to develop and conduct scientifically rigorous translational research and therapeutic clinical trials in the U.S. and internationally that:
 - Investigate the viral and immune pathogenesis of HIV-1 infection and its complications
 - Evaluate novel therapeutic agents and the most effective approaches and strategies for the use of existing agents to treat HIV-1 infection
 - Evaluate interventions and strategies to treat and prevent HIV-related opportunistic infections, co-infections, complications of therapies, and other HIV-1-related co-morbidities

ACTG Accomplishments

- Established through randomized clinical trials the standard of care for antiretroviral therapy
- Established the standard of care for treatment and prevention of opportunistic infections
- Developed worldwide infrastructure for conducting state-of-the-art RCT in HIV therapy
 - >6000 subjects enrolled in RLS in the last 5 years
- Developed and standardized quality-controlled laboratory infrastructure for HIV clinical trials
- Trained the majority of US leaders in clinical AIDS research over last two decades
- Developed state-of-the-art biostatistical methods for design and analysis of HIV clinical trials

ACTG Scientific Agenda

- Tuberculosis
- Viral reservoirs and HIV eradication
- Inflammation and end-organ disease
- Viral hepatitis

ACTG Network Components

- Directed by the Network Principal Investigator (Dan Kuritzkes) together with the ACTG Vice Chair (Judy Carrier) and the International Vice Chair (Ian Sanne)
- Domestic Units
 - 19 CTUs
 - 33 CRSs
- International Units
 - 13 CTUs
 - 25 CRS

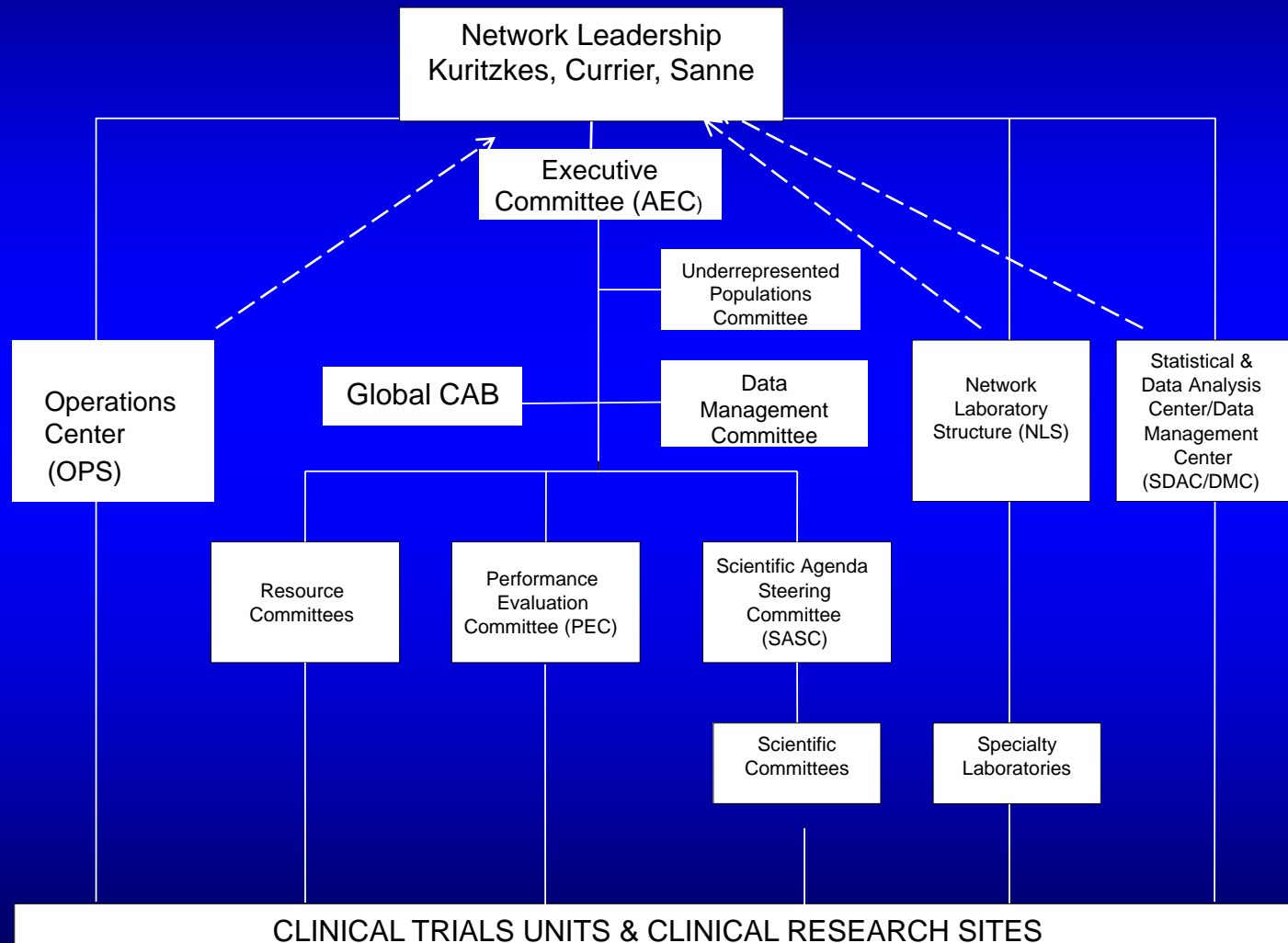
International ACTG CRSs

Country	CRSs
South Africa	7
Kenya	3
Malawi	2
Botswana	1
Uganda	1
Zimbabwe	1

Country	CRSs
India	2
Thailand	2

Country	CRSs
Brazil	2
Haiti	2
Peru	2

ACTG Network Leadership Group (NLG) Organizational Structure



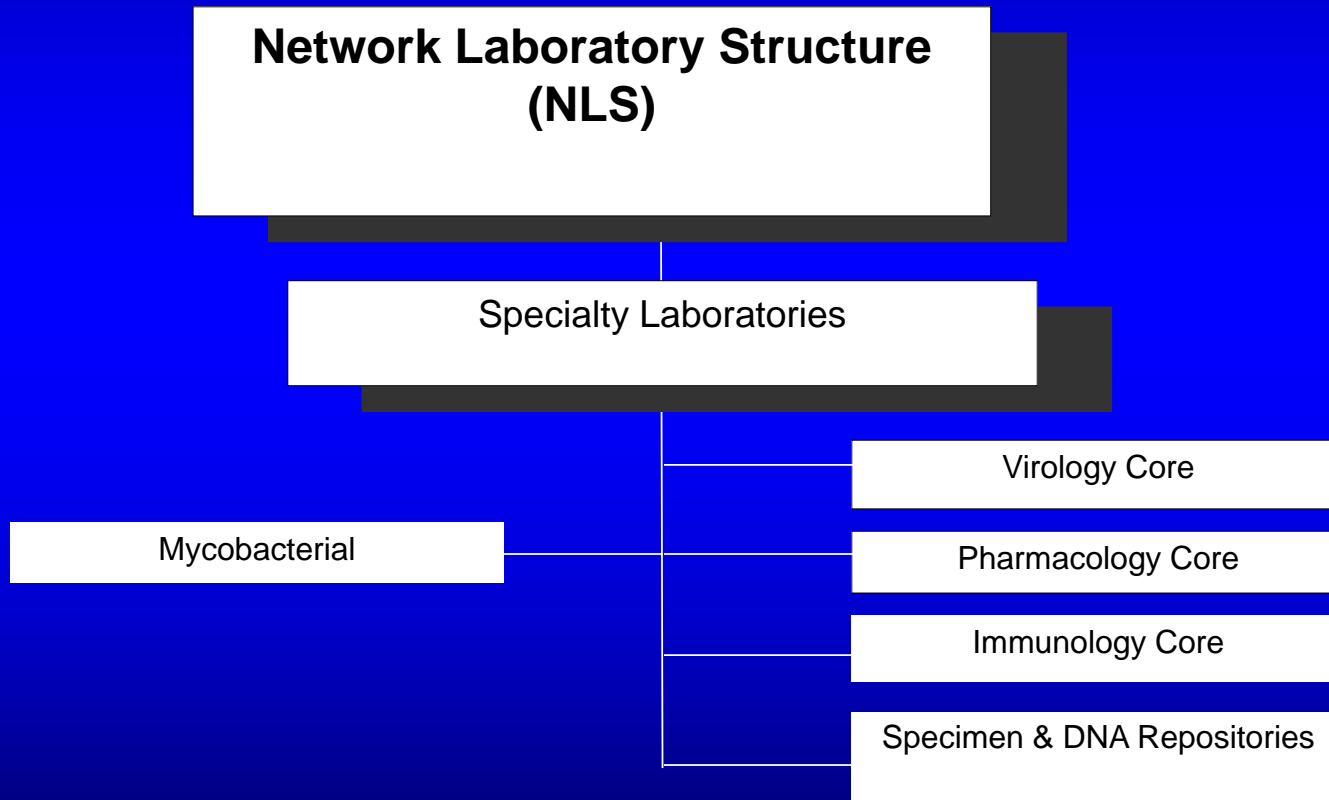
ACTG Coordinating and Operations Center (OPS)

- Serves as the fiscal agent/grantee of the ACTG
- Provides administrative, logistical and coordinating support for major network components
- Supports and manages all protocol development
- Maintains ACTG records and archives
- Prepares regulatory and administrative reports
- Plans and organizes ACTG meetings

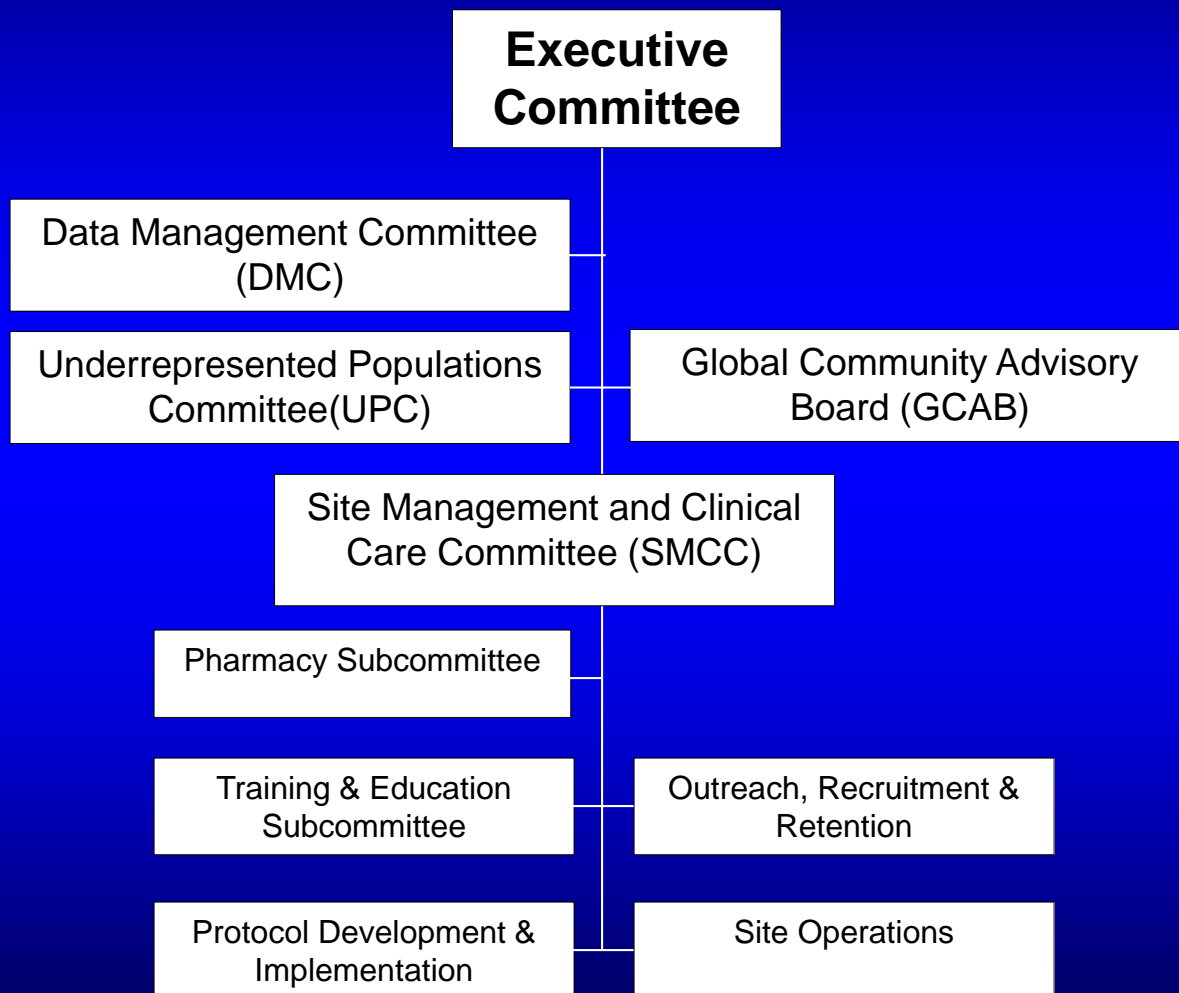
ACTG Statistical and Data Management Center (SDMC)

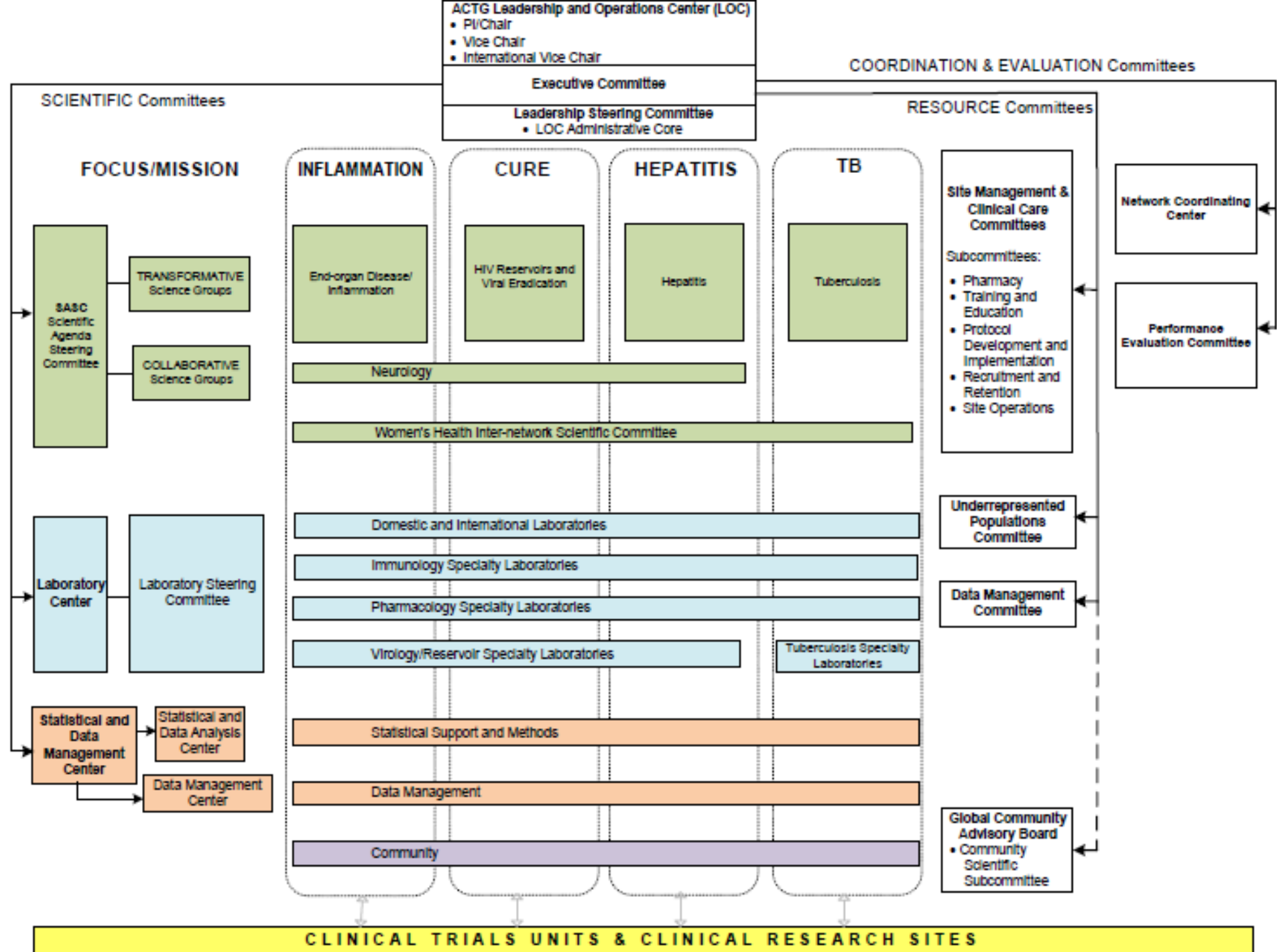
- Comprises the Statistical and Data Analysis Center (SDAC) and the Data Management Center (DMC)
- Provides statistical expertise for study design, data monitoring, and analysis for network clinical trials
- Provides technical expertise in and support for data transfer and management
- SDAC statisticians provide judgment and advice about specific studies, overall research strategies and priorities

ACTG Network Laboratory

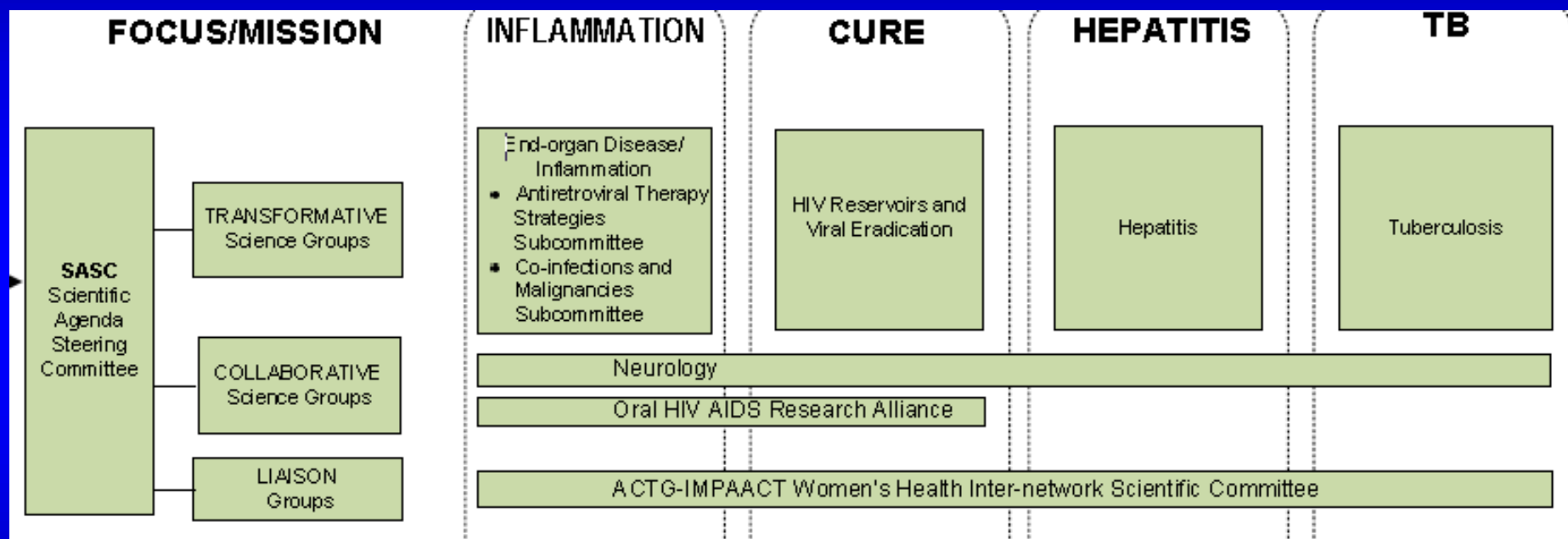


ACTG Resource Committees





ACTG Scientific Committees



Inflammation and End-Organ Disease

- Oversees research to identify biologic markers predictive of immune restoration and occurrence of morbid clinical complications during treated HIV-1 infection; to assess in pilot studies the impact of different treatment strategies on markers of immune dysfunction and end-organ disease; and to test whether promising treatment strategies emerging from pilot studies decrease morbid clinical complications in treated HIV-1 infection in larger clinical endpoint trials.
- Leaders: Drs. Michael Lederman and Peter Hunt

HIV Reservoirs and Eradication ("Cure")

- Oversees research aimed at making substantial progress towards a cure of HIV-1 infection by gaining critical knowledge about HIV-1 reservoirs that persist on current ART and by testing broad therapeutic strategies in clinical trials to reduce and ultimately eliminate replication-competent HIV-1 reservoirs.
- Leaders: Drs. John Mellors and Joseph Eron

Scientific Priorities: Cure

- Quantify HIV-1 reservoirs in blood, tissues (eg. GI tract) and other compartments (e.g.: CSF); assess the correlation among these reservoirs and measure their decay in patients receiving long-term suppressive ART
- Probe the effects of HIV-1 reservoirs of anti-inflammatory therapies directed towards reducing microbial translocation and T-cell activation, in collaboration with the inflammation TSG
- Evaluate the induction of latent HIV-1 expression by novel small molecules, such as the histone deacetylase inhibitor (HDAC) romidepsin or other potent transcriptional activators, and determine whether latently infected cells are depleted as a result.
- Assess the virologic and immunologic effects of monoclonal antibodies to immune exhaustion receptors and their ligands (e.g.: PD-1, PDL-1) on HIV-1 reservoirs.
- Evaluate the effect of HIV-1 reservoirs of other novel immunologic approaches (eg: therapeutic vaccination) that target HIV-1-expressing cells for elimination.
- Design and evaluate combinations of these approaches to delete HIV-1 reservoirs.

Hepatitis

- Oversees research to evaluate novel drugs and drug combinations for the treatment of hepatitis B and C virus and to validate non-invasive markers of liver disease in patients with and without HIV co-infection.
- Leaders: Drs. Marion Peters and Raymond Chung

Scientific Priorities: Hepatitis

- n of anti-TB new drugs and drug combinations
- Treatment of MDR/XDR tuberculosis
- Development of shorter treatment regimens
- Optimal treatment of latent tuberculosis
- Drug-drug interactions TB and ART
- Optimal diagnostic tests and biomarkers
- Optimizing treatment of tuberculosis for patients receiving combination ART
- Evaluating TB vaccines for HIV infected adults

Tuberculosis

- Oversees research that aims to dramatically transform TB therapeutics by optimizing regimens of new and older agents to treat and prevent TB more quickly and effectively in patients with and without HIV infection, and to develop TB biomarkers to facilitate drug development.
- Leaders: Drs. Richard Chaisson, Diane Havlir and Gavin Churchyard

Scientific Priorities: HIV/TB co-infection

- Evaluation of anti-TB new drugs and drug combinations
- Treatment of MDR/XDR tuberculosis
- Development of shorter treatment regimens
- Optimal treatment of latent tuberculosis
- Drug-drug interactions TB and ART
- Optimal diagnostic tests and biomarkers
- Optimizing treatment of tuberculosis for patients receiving combination ART
- Evaluating TB vaccines for HIV infected adults

Co-Infections and Malignancies

Subcommittee- Agenda

–Malignancies

- Opportunistic Infections: Cryptococcus, HPV
- Vaccines to Prevent Co-Infections

Investigator-Initiated Research

- Concept Proposal- to develop a protocol
- New Works Concept Sheet (NWCS)- to access specimens
- Data Analysis Concept Sheet (DACCS)- to access data