

# THE RESEARCH IN THE FIELD: WHERE TO PROGRESS?

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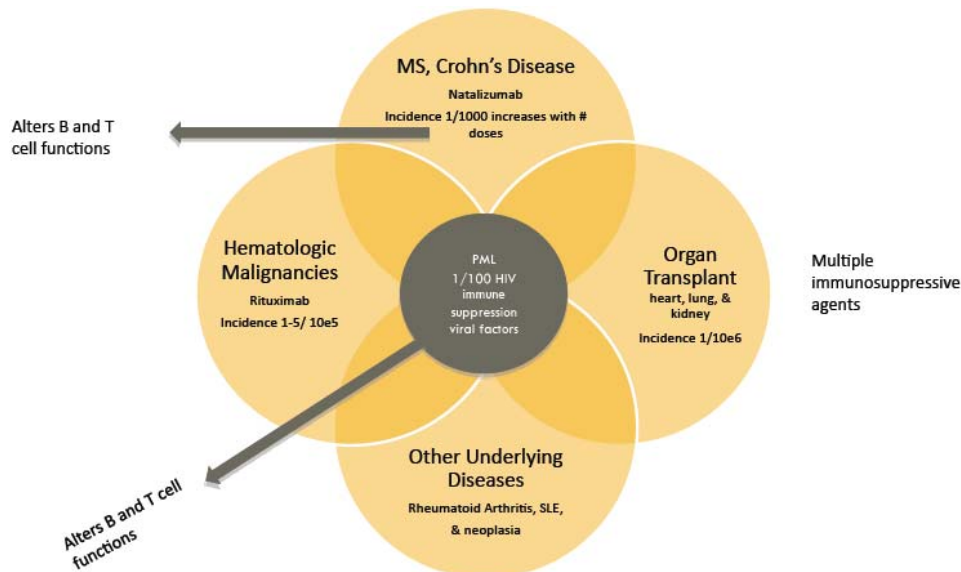
# Major Research Areas

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- Disease incidence
  - ▣ How do we define it?
  - ▣ Who gets it?
- Virus that causes PML
  - ▣ Geographic distribution of the virus
  - ▣ Host range factor
- Patients with the PML
  - ▣ Affected patient populations
  - ▣ Use of genomics
  - ▣ Clinical correlates

# Disease Incidence

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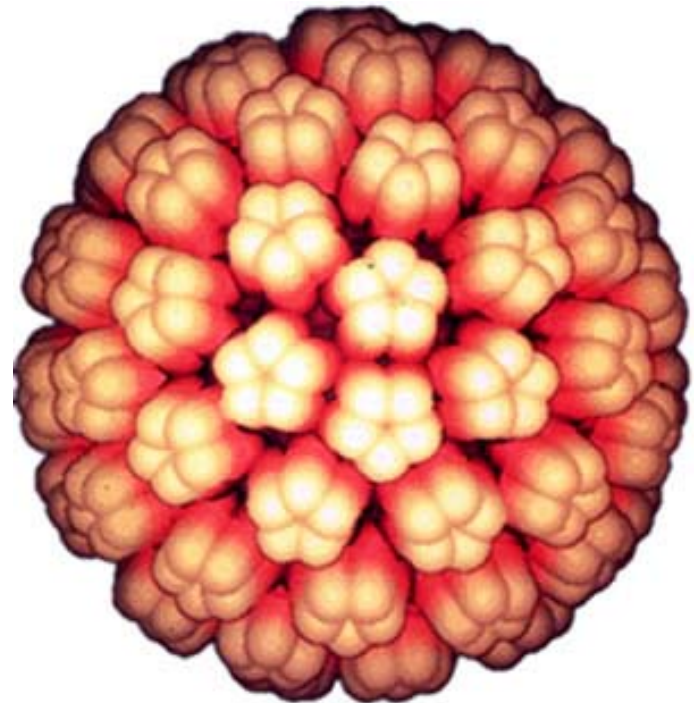


- Better understanding of pathogenesis (translational approach)
- Consensus on diagnostic criteria
  - ▣ American Academy of Neurology PML guidelines
- More information on other non-PML diseases associated with JC virus

# Virus that causes PML

4

- Geographic distribution of the virus (type) and correlation for disease (Is PML in India the same as PML in Europe/North America?)
- Host range factor determined by the receptor and gene sequences (cellular tropism)



# Tools for Translational Opportunities

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- To advance PML research, the community needs a better way to assess information from these correlating factors using an open source. Currently, two data registries are being developed to accomplish this task.
  - NINDS: Laboratory of Molecular Medicine and Neuroscience has convened a steering committee of clinicians and investigators representing patient populations at risk for PML (rheumatology, neurology, epidemiology, transplantation, virology, and oncology) to develop standard diagnostic criteria and other data elements
  - PML Consortium: Representatives from pharmaceutical/biotechnology companies who have come together to coordinate resources to further PML research

# NINDS PML Data Registry

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Main

Patient History

Diagnostic Features

Clinical Information

Reports

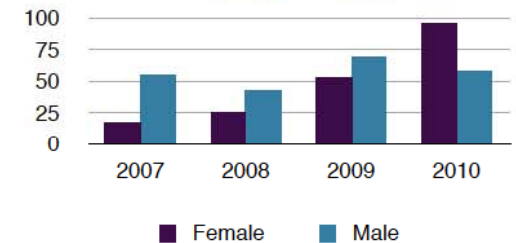
PML Dashboard

## PML DATA REGISTRY DASHBOARD

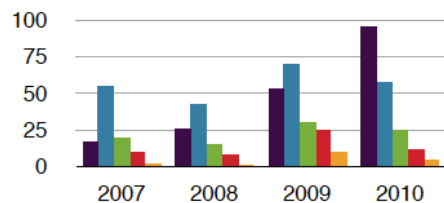


20 REPORTING SITES  
100 PATIENTS

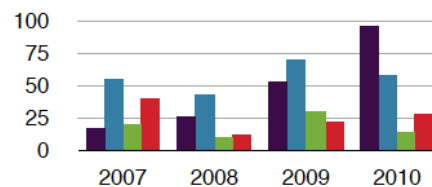
Patients By Gender



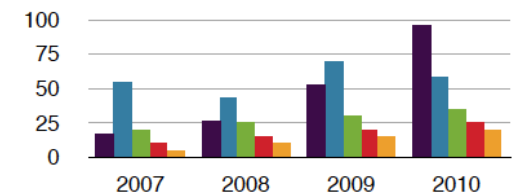
Underlying Disease



Immunomodulatory Drug(s) Used



Patients by Age



■ HIV/AIDS ■ MS ■ RA ■ Transplant ■ Other

■ Drug A ■ Drug B ■ Drug C ■ Drug D

■ 0-15 ■ 16-30 ■ 31-45 ■ 46-60 ■ 61+

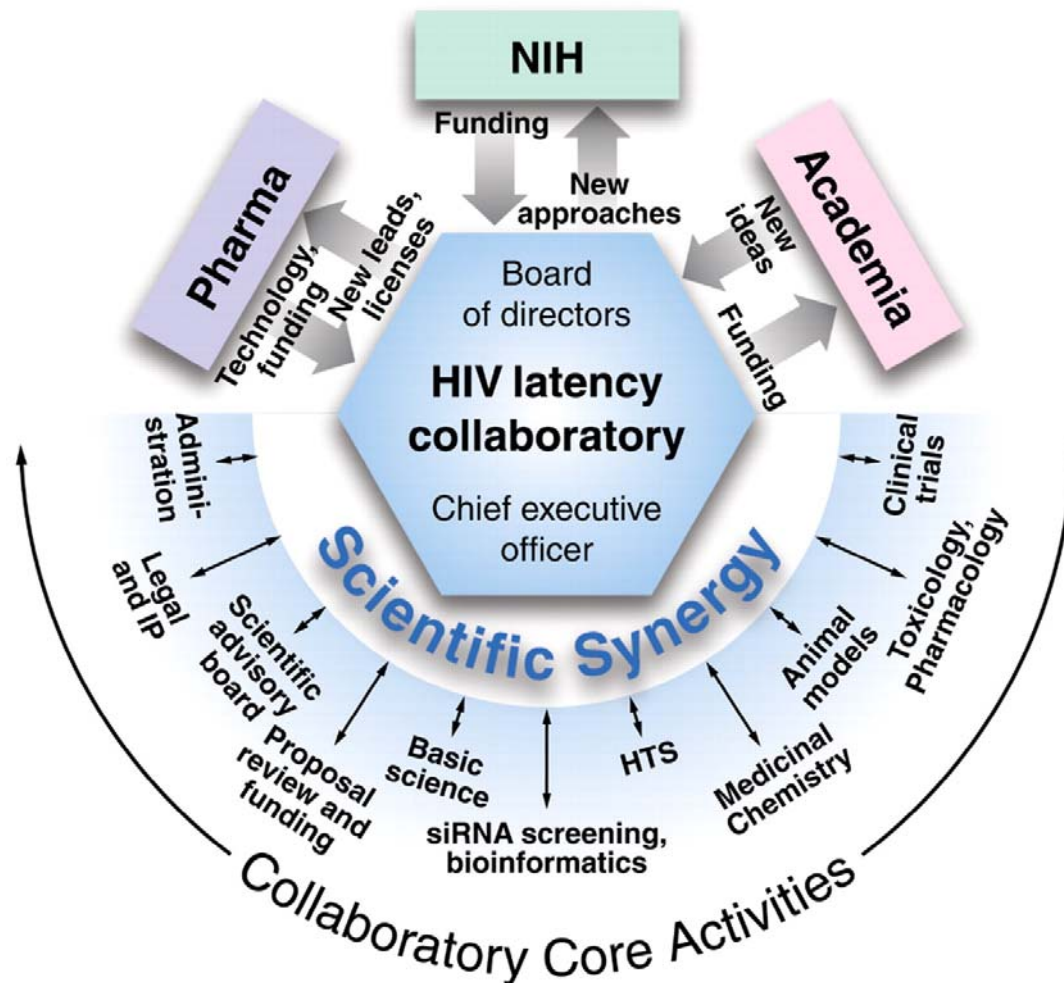
Mock data was used to produce this graphic. Actual data will flow from the registry to populate this dashboard in real-time.

# Tools for Translational Opportunities

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**Fig. 4. Overview of an HIV Latency Collaboratory representing a joint research venture between the U.S. National Institutes of Health (NIH), the pharmaceutical industry (pharma), and academia**



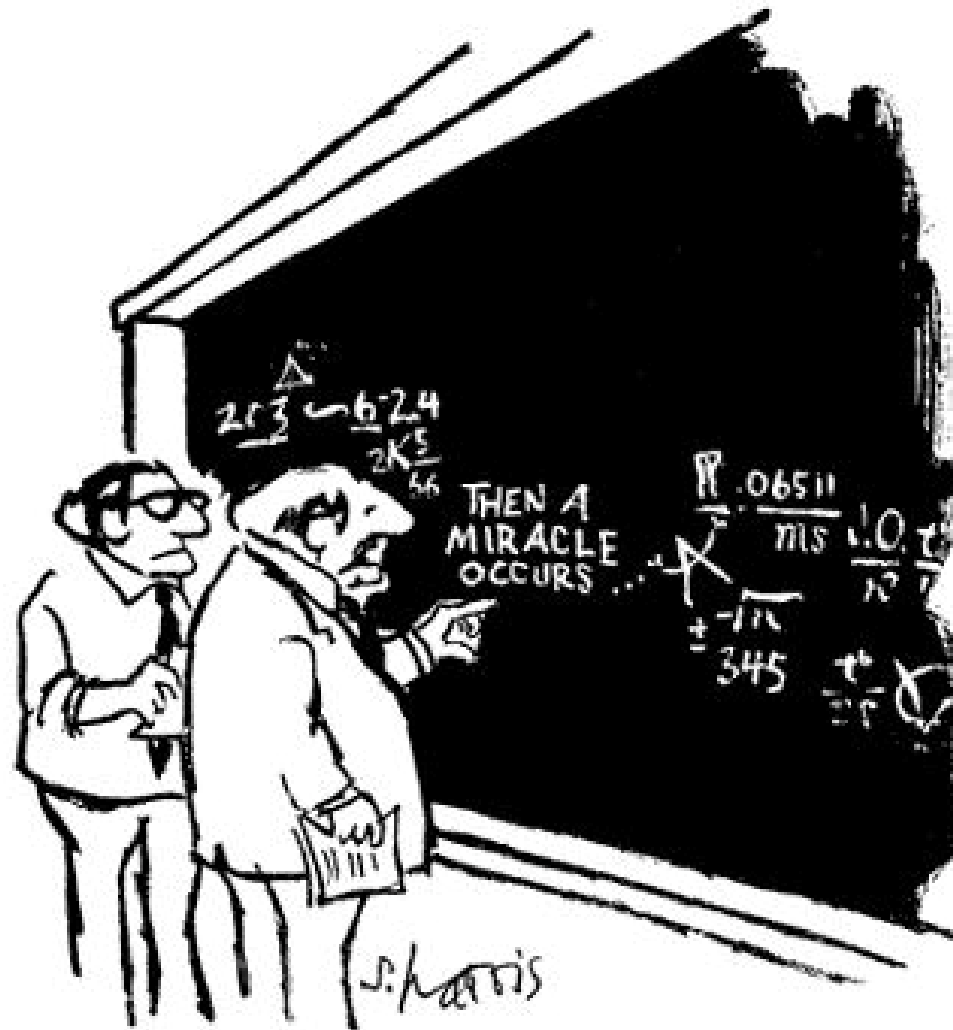
D D Richman et al. Science 2009;323:1304-1307



# What don't we know...

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- ❑ Transmission: vertical/horizontal; some data on maternal transmission
- ❑ Initial site(s) of infection; respiratory, ingestion; cellular site for multiplication and spread
- ❑ Genotype(s) of 'circulating' virus; assumed 'archetype'
- ❑ Cell factors for tropism
- ❑ Establishment of latency (episome or integrated DNA), mechanism of release from latency
- ❑ Traffic of virus to brain; cross blood:brain:barrier
- ❑ Role of humoral immunity
- ❑ Predictive markers for PML; clinical, virological, immune
- ❑ Early stages of PML; progressive/persistent PML
- ❑ Treatment; boost immune response, block viral growth



"I think you should be more explicit here in step two."