A BASIC RESEARCH GOAL:
“SHOCK” HIV OUT OF LATENCY

Andrew P. Rice, PhD
Department of Molecular Virology & Microbiology
Baylor College of Medicine

From Research to the Real World: Sharing Science Symposium
September 28, 2015
Why We Did this Study

• Current anti-HIV medications inhibit viral replication – they target cells that are active

• Current drugs do no cure infection – a silent viral reservoir remains in “resting” CD4 T cells – “Latent Infection”

• If medications are stopped, HIV starts replicating again

• A “shock and kill” strategy has been proposed to cure infection:
  “shock”: develop new medications to activate latent virus
  “kill”: develop methods to enhance immune system’s ability to clear cells with reactivated virus
Why We Did This Study:
To Understand Latent HIV Infection

Latent and Active HIV Infection in CD4 T-cells

(a) Latent infection
(b) Active infection
What We Did

- Previously, we identified key cellular factors that regulate HIV replication and are shut-off when cells are resting. [key factors: CDK9 and Cyclin T1 – an enzyme (kinase)]

- We isolated CD4 T cells from healthy blood donors.

- We infected cells with HIV under conditions where latent infection is established.

- We treated cells harboring latent HIV with small molecules (Histone deacetylase inhibitors) that we thought would activate our key cellular factors.
What We Found

• Treatment of cells with these agents turned on our cellular cofactors (*CDK9* and *Cyclin T1*)

• We observed that latent HIV started replicating to some extent

• Reactivation of these key factors is probably not potent enough by itself to “shock” all latent virus in patients
What Our Results Mean and Why this Matters

• Activation of these key cellular cofactors is essential to reactivate latent HIV

• These key cellular cofactors are an important target for a “shock” strategy

• In combination with other activation agents to potently “shock” latent HIV and an effective “kill” strategy, our work may contribute to a functional cure of HIV infection
Acknowledgments

- Sona Budhiraja, PhD
- Melonie Danels
- Md Saha Jamaluddin, PhD
- Hongbing Liu, PhD
- Penny Hu, MS
- Rajesh Ramakrishnan, PhD
- Edward Siwak, PhD

Funding: NIH (CFAR, individual grants)