

Clinical care, safety, and addictions research in a multi-PI environment

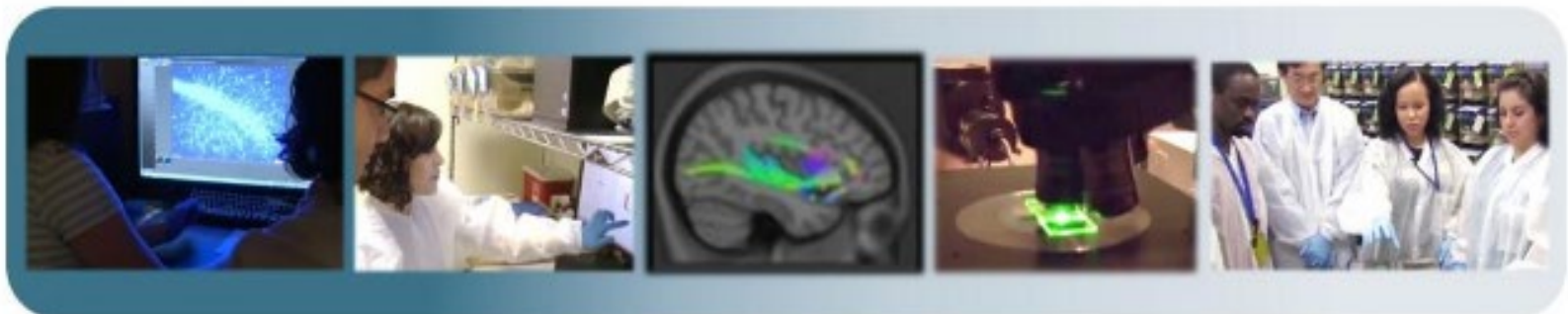
October, 2018

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- ☐ Diverse NIAAA basic and clinical research
 - ☐ Creating a shared framework for clinical research
 - ☐ Progress report
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- ☐ What NIAAA needs to enhance clinical research, clinical care, and safety

Diverse basic research at NIAAA

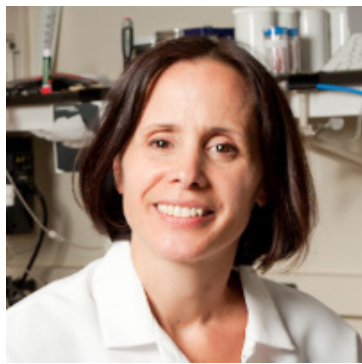
13 Basic Science Labs

Brain: synapse, circuit, behavior, genetics

Other organs: Cardiovascular, liver, metabolism,

Molecules: cannabinoids and other new drugs

Several basic labs are engaged in clinical research
New drugs and probes, physiology, iPSC's, genomics



Veronica Alvarez: Deconstructing circuitry of reward and compulsivity in mice



And other neuroscience labs:
Dave Lovinger
Andrew Holmes
David Goldman

Drinking

operant self-administration

Locomotion, place preference, novel object, rotarod. Other behaviors modeled on DSM5

Behavior

Transgenics
 Optogenetics
 Chemogenetics

Connectivity

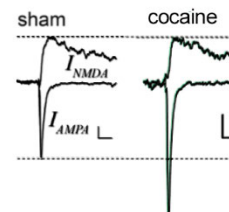
Synapses

DiOlistic labeling
 2-photon microscopy
 Confocal imaging

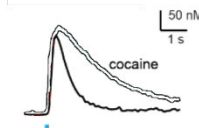
Neuronal morphology

Electrophysiology
 Voltammetry
 Calcium imaging
 Glutamate uncaging

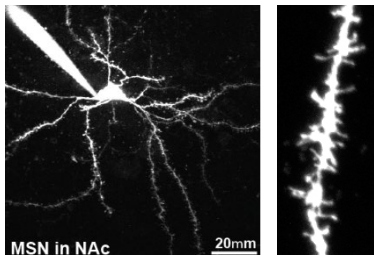
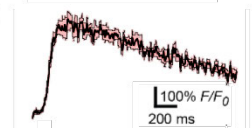
Synaptic responses



Dopamine transients

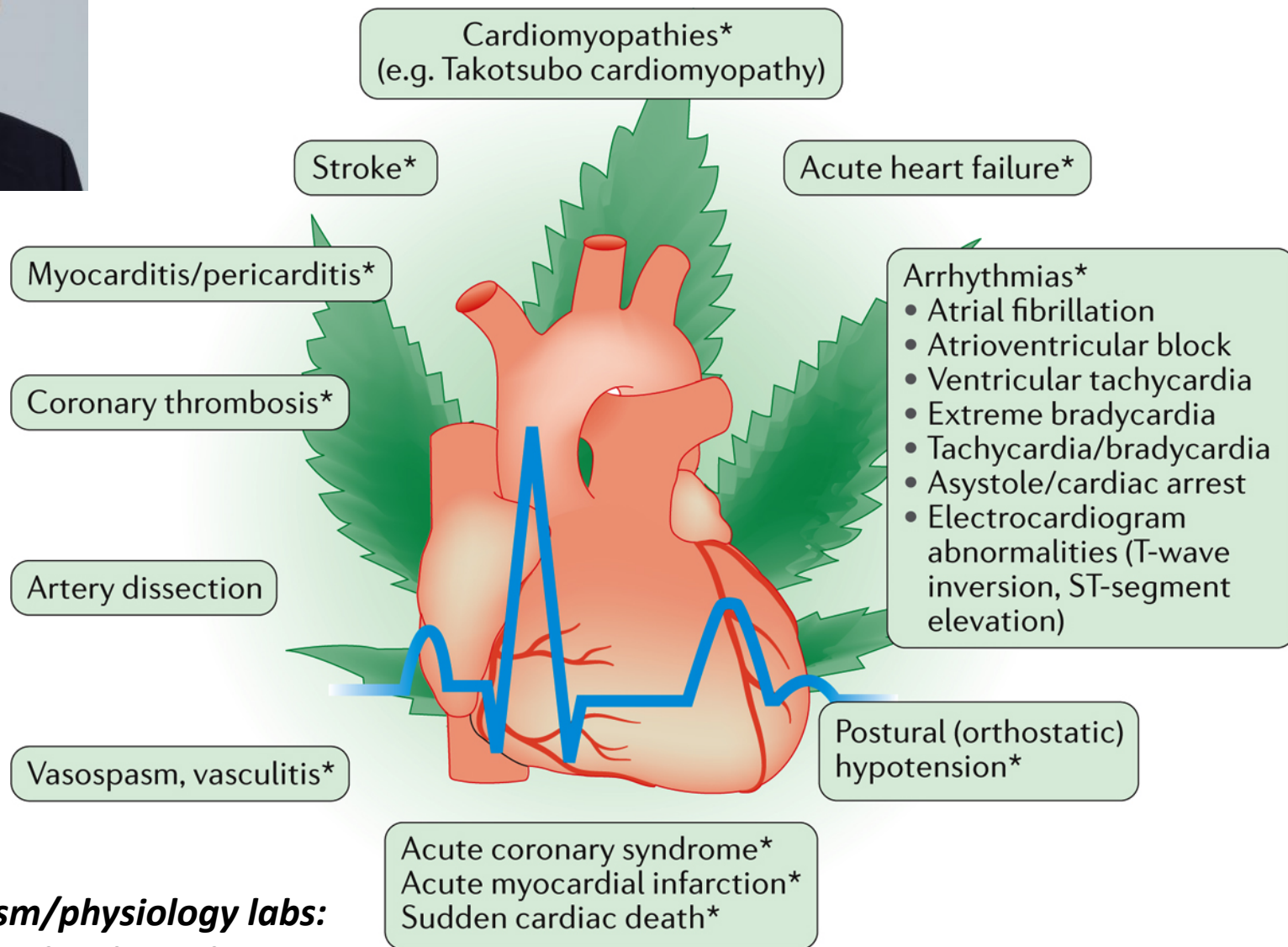


Intracellular Ca²⁺ transients





Pal Pacher: identifying adverse cardiovascular consequences of marijuana and synthetic cannabinoid use



Other metabolism/physiology labs:

George Kunos, Richard Veech,

Hee-Yong Kim, Bin Gao, Klaus Gawrisch

Diverse clinical research at NIAAA

Six clinical labs

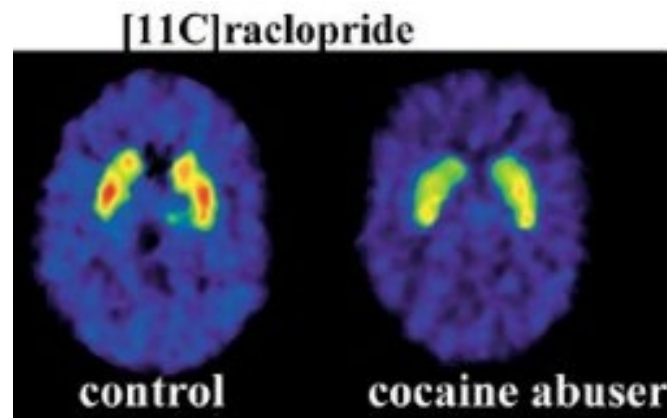
Neurocircuitry of addiction

Gut brain axis: Ghrelin, new drugs

Pharmacodynamics/pharmacokinetics

Ketogenic diet, gut microbiome

Hepatotoxicity: elastography, molecular mediators



Nora Volkow
Lab of Neuroimaging

31 human research protocols

Reviewed, and scored, by *NIAAA/NIDA SRC*



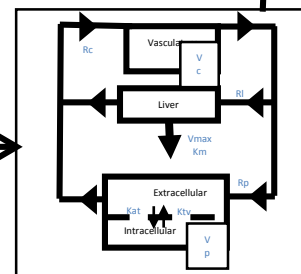
Addictions IRB: 19 protocols, including 4 in data analysis and 1 on clinical hold

CNS IRB: 10 protocols, including 1 in data analysis and 1 on clinical hold

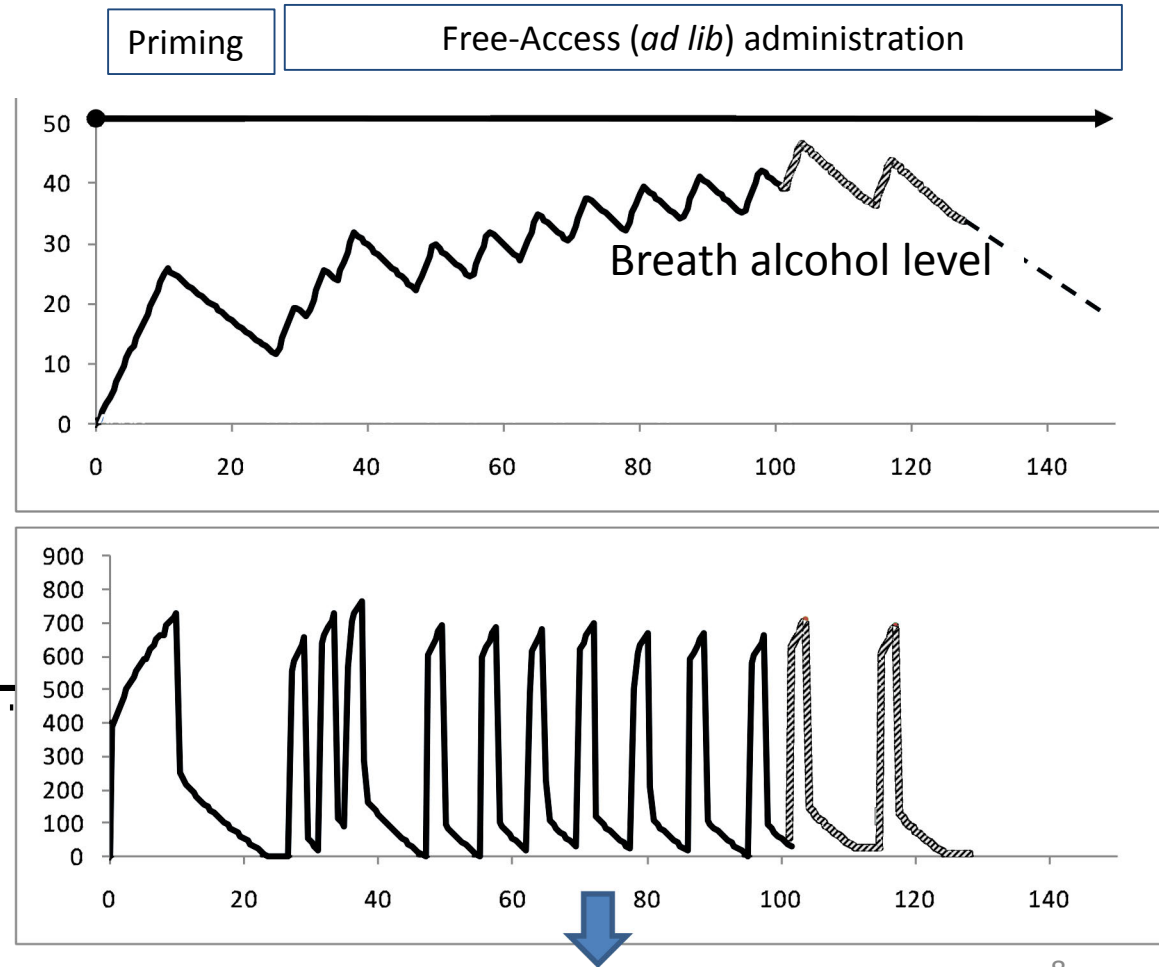


Transitioning to *NIH IRB*

Vijay Ramchandani: Unraveling alcohol pharmacodynamics and pharmacokinetics via Computer-assisted Alcohol Infusion



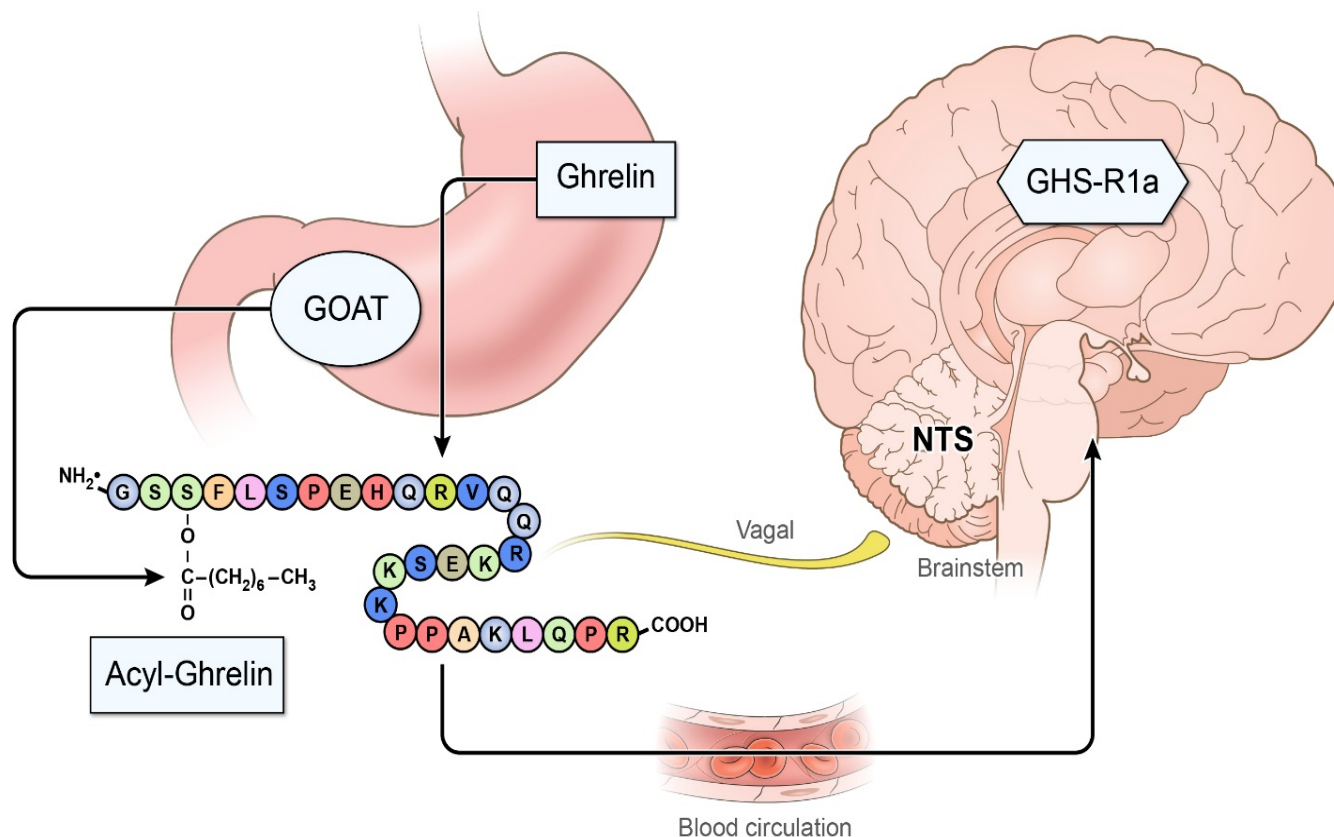
Pharmacokinetic Model





The Ghrelin System

Lorenzo Leggio: developing new addiction therapies by modifying ghrelin in the gut-brain axis

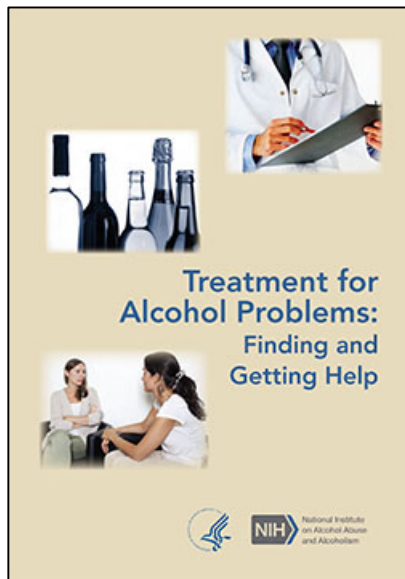


How patients navigate to NIAAA studies

CC Office of Patient Recruitment → normal volunteers

Ads, radio and print, referrals, community outreach

Phone screening → >90% of patients are excluded



Treatment navigator

www.niaaa.nih.gov/
Online resources



Navigator to
intramural
studies



The future? CC partnership with:

www.researchmatch.org

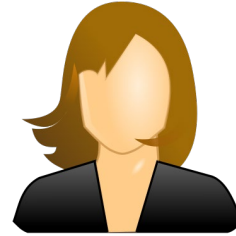


Difficult diseases have met their match.

How is NIAAA different?

Our Patients

Often homeless and using illicit drugs
Diverse problems
Diverse in motivations
Often acute at admission



Physical environment

Restricted access unit
Common areas
Non-alcohol hand wash, minimization of ligature risk

Activity

Median stay: one month
Patients dine and interact together
Patients receive individual and group therapy
Patients often participate in multiple studies



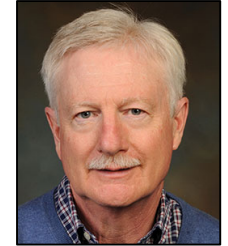
Reinventing NIAAA Clinical Research, Care and Safety 2015→2018

Organizational changes

Nancy Diazgranados
Deputy Clinical Director



David Goldman
Clinical Director



George Koob



George Kunos
Scientific
Director

OCD and six labs replaced one clinical lab

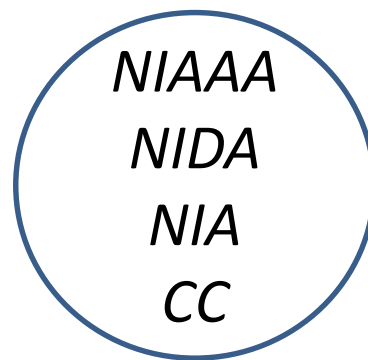
Clinical Director reports to Director.

CD directs clinical research budget, staffing, space

All patients enroll in one Natural History Protocol

Baseline for diagnosis, eligibility, treatment, genomics

Cores: Database, Neuroimaging Core, Clinical Core Lab, Regulatory



PIs

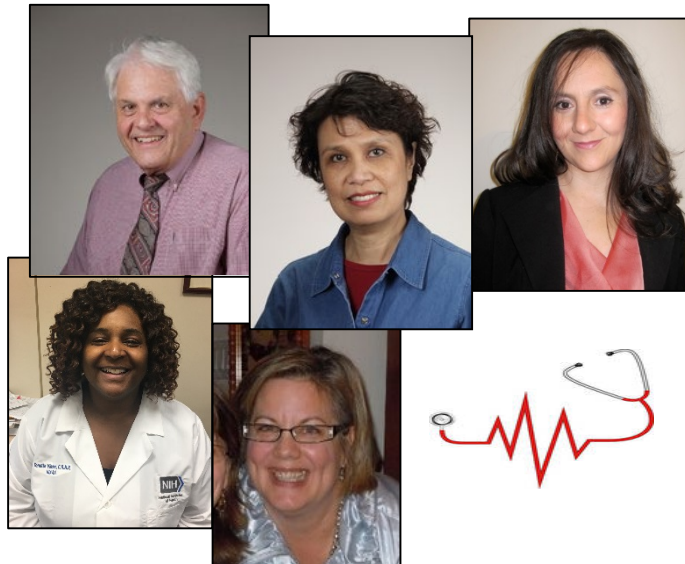
7 groups, 13 PIs, 4 institutes



JOIN A STUDY



Operations
and recruiting

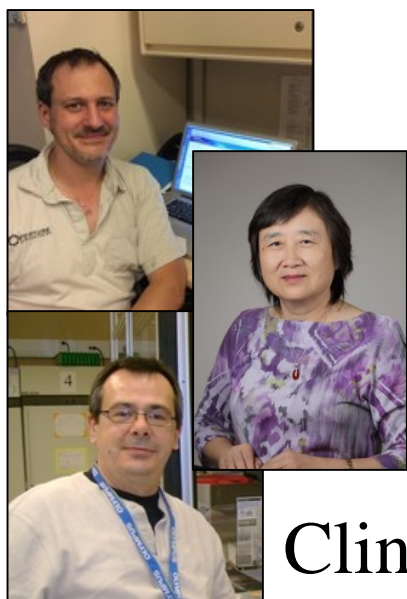


NIAAA clinical team



Regulatory

Core clinical resources



Clinical core lab



Database



Neuroimaging

Reinventing NIAAA Clinical Research, Care and Safety 2015→2018

Regulatory

All protocols have a Monitoring plan
All PIs are annually Audited
UP reporting is emphasized and monitored

Safety Officer and Safety Rounds
SOPs for diverse elements: protocol Monitoring, alcohol administration in studies
Annual training and retraining *pro re nata*

Cheryl
Jones



Betsy Davis



Laura Kwako



Cherie
Bonds-Beeken

Reimagining NIAAA Clinical Research, Care and Safety 2015 → 2018



Clinical



Strengthened partnership with CC

Multidisciplinary rounds with all PIs and CD present

Strengthened consult support, including transfers of patients from other units

Encouraged monitoring: STARS reports, handwashing

Two Med/Surg NPs hired

Internal Medicine/Psychiatrist hired full-time

Two research nurses and a research Nurse Practitioner hired



Ted George



Tonette Vinson



Yvonne Horneffer



Nancy Diazgranados



Sheila
Walsh

Progress report

Science:

Two tenure track scientists recommended for Tenure

New protocols with high merit scores

Core resources

Independent funding

Widening circle of PIs

New clinical technologies

Regulatory:

UP reports are up

Partnership with ORSC

PIs are audited annually, and have generally done well in audits

Clinical:

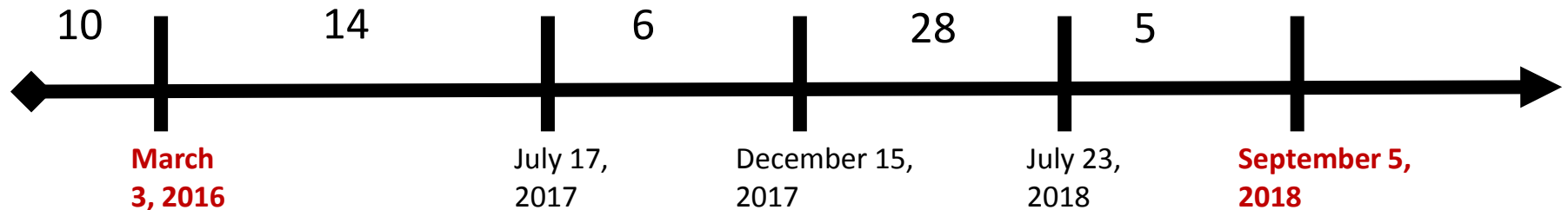
Positive Joint Commission report

Enhanced individual and group therapy

Census is up

Clinical care is better documented and monitored, and is of high quality

Reported Potential PII/PHI/SI Breaches



PII/PHI/SI Training Dates

Dates indicate training for entire NIAAA clinical IRP

What NIAAA needs

503A/B capacity to formulate oral drugs and placebos

Systems solutions to unencrypted electronic PII

Office space in Bldg 10 or elsewhere to move more research staff out of clinical and laboratory areas

Improved utilization of lightly used addictions consult service

More CC med/surg nurses, and enhanced training of nurses in behavioral health