From Bench to Bedside and Back Again:

*Translational bridges in adolescent nicotine dependence research*

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Yale Child Study Center Grand Rounds
September 30, 2014
Nicotine Dependence: Big Picture

• Tobacco use remains the leading global cause of preventable disease and premature death (World Health Organization, 2011)

• Over 80% of adults with nicotine dependence started smoking tobacco during adolescence (USDHHS, 1994)

“In the case of smoking, children and adolescents hold the key to progress toward curbing tobacco use in future generations”

- U.S. Surgeon General, 1994
Translational Approaches: Bench to Bedside and Back Again

**Mineur Laboratory:**
- preclinical/animal studies of nicotinic acetylcholine receptors ($\alpha_7$ and $\beta_4$) and feeding behaviors

**Krishnan-Sarin Laboratory:**
- Early and Late stage clinical trials, neural (fMRI) and behavioral (impulsivity) correlates of treatment

https://www.ctsi.ucla.edu/about/pages/featured
Translational Implications: Better Treatments and Targeted Interventions

Using translational approaches to better understand the molecular mechanisms behind the nicotine receptor system will assist in:

- Mechanism-based Drug Targets for Nicotine Dependence (e.g. α4β2), Obesity (e.g. β4 or α7), and subgroups of smokers who smoke to lose/maintain weight

- **Personalized Medicine**: *Pharmacogenetics* = Genotype-targeted treatments to Improve Outcomes in subgroups
  
  - Example: CHRNA5, CHRNA4, CHRNB2 gene SNPs and Treatment Response to Varenicline (Chantix) in smoking adults (King et al. 2012)
Translational Implications: Development of Biobehavioral Markers

• A major challenge for the field of addiction moving forward is the development of biobehavioral markers that convey addiction vulnerability in at-risk populations and that are associated with treatment-response, prognosis, and recovery in addicted youth.

• Candidate intermediate phenotypes:
  – Impulsivity, delay discounting, stress-reactivity/responsiveness, fMRI, & EEG biomarkers

• In vivo neuroimaging ‘challenge’ studies involving behavioral challenges that require cognitive control in the presence of appetitive cues or affective stimuli may be useful assays

Translational Implications: Neurobiologically-Informed Behavioral Interventions and Public Policy

- Prevention and interventional strategies should take into account the specific biological vulnerabilities and strengths of adolescents.
- Adolescents are biologically **more responsive to rewards** and **less responsive to aversive stimuli/losses**, relative to adults:
  - Positive reinforcement > punishment or negative reinforcement
  - Providing access to exciting activities under controlled settings may help replace or limit harmful risk-taking opportunities (Casey, 2008)
  - Contingency management using positive reinforcers for prosocial behavior, engagement, and negative urine drug tests (Budney et al. 2009)
- Attempting to enhance cognitive control by cognitive training or cognitive behavioral therapy (CBT)

*Hammond, Mayes, Potenza. Adolescent Medicine: STARS, 25(1), 2014*
Understanding Recovery: *Neurodevelopmental implications*