Catalyzing Innovation: NIH National Center for Advancing Translational Sciences

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Division of Pre-Clinical Innovation (DPI)

- Therapeutics for Rare and Neglected Diseases (TRND)
- Toxicology in the 21st Century (Tox21)
- Bridging Interventional Development Gaps (BrIDGs)
- Molecular Libraries Probe Production Center
- Assay Development

DPI currently has 300+ collaborations with investigators across the U.S. and around the world.
DPI is Different in Science and Operation

- DPI is administratively intramural
  - No independent PIs, no tenure system; 80% of staff ex-industry
  - All projects are collaborations, 90% of which are with extramural investigators/foundations/companies
  - Projects are selected via solicitation/review
- Science is intermediary between mechanistic research and commercialization
  - Each project has tangible deliverable and technology/paradigm development components
- It is disease agnostic, works across disease spectrum
  - Common mechanisms and principles to make translation better/faster/cheaper for all
- Focuses on new technologies, enabling tools, dissemination
NCATS DPI: A Collaborative Pipeline

**Project Entry Point**: Unvalidated target, Validated target

**Target**: Target Validation

**Assay Dev**: Probe/Lead Development

**Lead Optimization**: Preclinical Development

**Preclinical Development/Trnd**: Clinical Trials

**RNAi**: Preclinical Development/Trnd

**Probe Dev./NCGC**: Preclinical Development/Trnd

**Assay, Chemistry Technologies**: RAID/BridGs

**DPI**:

- FDA Collaboration
- Systems Toxicology (Tox21)
- Repurposing
- Paradigm/Technology Development

**Deliverables**:

- Genome-wide RNAi systems biology data
- Chemical genomics systems biology data
- Leads for therapeutic development
- Approved drugs effective for new indications
- New drugs for untreatable diseases
- Small molecule and siRNA research probes
- Predictive in vitro toxicology profiles
- Drugs suitable for adoption for further development
- Novel clinical trial designs

More efficient/faster/cheaper translation and therapeutic development

**NIH**
National Center for Advancing Translational Sciences
Bridging Interventional Development Gaps (BrIDGs) Program

- Model: Contract access collaboration between DPI and extramural labs (Formerly NIH-RAID Program)
- Projects
  - Enter with clinical candidate identified
  - Any disease eligible
  - Gap analysis followed by data generation using DPI contracts to generate data necessary for IND filing
  - Exit at or before IND
  - Milestone driven
  - Therapeutic modalities: any (small molecules, peptides, oligonucleotides, gene therapy, antibodies, recombinant proteins)
- Eligible Applicants
  - Academic (US and Ex-US), Non-Profit, SBIR eligible businesses
BrIDGs Highlights

- 180 applications submitted since 2005
  - 34 approved

- 19 completed projects (two in FY12)
  - 12/12 submitted INDs approved
  - 5 projects in Phase 1, three in Phase II
  - 5 agents licensed during or after BrIDGs involvement
<table>
<thead>
<tr>
<th>Applicant</th>
<th>Organization Name</th>
<th>Org Type</th>
<th>Agent</th>
<th>Disease</th>
<th>Funding</th>
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<tbody>
<tr>
<td>Au, Jessie</td>
<td>Optimum Therapeutics</td>
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<td>Small Molecule</td>
<td>Pancreatic Cancer</td>
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<td>Aromatic L-amino acid decarboxylase</td>
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<td>Hyperinsulinism</td>
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<td>Parion Sciences, inc.</td>
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<td>Niemann-Pick C</td>
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<td>Turner, Scott</td>
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<td>Peptide</td>
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* indicates that the investigator is partnered with a company
Therapeutics for Rare and Neglected Diseases (TRND) Program

- Model: Comprehensive drug development collaboration between DPI and extramural labs with disease-area / target expertise

- Projects
  - May enter at various stages of preclinical development
  - Disease must meet FDA orphan or WHO neglected tropical disease criteria
  - Taken to stage needed to attract external organization to adopt to complete clinical development/registration, max 2a
  - Milestone driven
  - Therapeutic modalities: small molecules, proteins
  - Serve to develop new generally applicable platform technologies and paradigms

- Eligible Applicants
  - Academic, Nonprofit, Government Lab, Biotech / Pharma
  - Ex-U.S. applicants accepted
TRND Highlights

- 14 projects through pilot phase & 2 public solicitations since 2009
  - Mix of small molecules and biologics
  - Two innovative platform technologies
- 3 investigational drugs taken into humans
  - CLL: IND filed with US FDA 7/12/11, approved 8/5/11
    - Phase I trial commenced 9/11
  - SCD: IND filed 10/14/11, approved 11/10/11
    - Phase I trial commenced 12/11
  - HIBM: Complete response filed 7/27/12, approved 8/24/12
    - Phase 1 trial in patients commenced 9/13/12
- Initiated first natural history study
  - HIBM: NIH Clinical Center, 1st patient enrolled September 2011
- Every project is a unique Public-Private partnership
  - Many include foundation and patient advocacy input
<table>
<thead>
<tr>
<th>Collaborator</th>
<th>Organization Name(s)</th>
<th>Partner Type(s)</th>
<th>Agent</th>
<th>Therapeutic Area / Disease</th>
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<tbody>
<tr>
<td>TRND Pilot Project</td>
<td>NPC-SOAR, Washington Univ., Einstein College of Medicine, NICHD, NHGRI</td>
<td>Disease Foundation, Academic, DIR</td>
<td>Repurposed Approved Drug</td>
<td>Niemann-Pick C</td>
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<td>TRND Pilot Project</td>
<td>New Zealand Pharmaceuticals, NHGRI</td>
<td>Biotech, DIR</td>
<td>Intermediate Replacement</td>
<td>Hereditary Inclusion Body Myopathy</td>
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<td>TRND Pilot Project</td>
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<td>Biotech, DIR</td>
<td>NME</td>
<td>Sickle Cell Disease</td>
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<td>Disease Foundation, Academic</td>
<td>Repurposed Approved Drug</td>
<td>Chronic Lymphocytic Leukemia</td>
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<td>Reeves, Erica</td>
<td>ReveraGen BioPharma</td>
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<td>NME</td>
<td>Duchenne Muscular Dystrophy</td>
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<td>Nucleotide Analog Pro-drug</td>
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## Comparison of BrIDGs and TRND

<table>
<thead>
<tr>
<th>BrIDGs</th>
<th>TRND</th>
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<tbody>
<tr>
<td><strong>Contract Resource</strong></td>
<td>Team–based Collaboration</td>
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<tr>
<td><strong>PI must have identified lead agent</strong></td>
<td>PI may start with lead optimized</td>
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<tr>
<td><strong>No clinical trial support provided</strong></td>
<td>Some clinical trial support provided</td>
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<tr>
<td><strong>IP retained by owner</strong></td>
<td>TRND may generate IP</td>
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<td><strong>Universal disease scope</strong></td>
<td>Rare and neglected diseases only</td>
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<tr>
<td><strong>Investigator prepares IND</strong></td>
<td>Regulatory affairs assistance provided</td>
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