COVID-19 Drug Repurposing Efforts

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Outline

1. Drug repurposing and real-world data to address emerging infectious disease threats
2. Launching the private-public partnership
3. Capturing real-world data using the CURE ID data platform
4. COVID-19 pilot and drug relabeling
COVID-19 and emerging threats

• SARS-COV-2 shows our vulnerability to control new and emerging diseases and the public health response to mitigate transmission

• Medical and scientific community is at a disadvantage
  – Biology, immunology, epidemiology
  – Political will

• Virus-specific therapeutic options are years away

• Major barrier is the lack of tools for COVID-19

• Ideally patients enrolled in randomized clinical trials
  – Are not close to a clinical trial site
  – May not meet inclusion/exclusion criteria
  – May not be interested due to the risks
Off-label drug treatment

- Upon regulatory approval, drugs are labeled for those indications or diseases sought by the drug sponsor for which there is substantial evidence of effectiveness.
- Once a drug is approved, based on knowledge and professional judgement, physicians may take the responsibility for prescribing drugs for a different indication.
- Patients treated with drugs for another indication outside of a clinical trial:
  - Off-label prescription
  - Expanded Access Programs (early access, compassionate use...)
  - Emergency Use Authorization
What is drug repurposing?

• A strategy predicated on the reuse of (1) existing licensed drugs for new indications or (2) investigational drugs that have failed to meet their efficacy requirements

• Growing list of drugs being used off-label for the treatment of diseases
  – 1500 FDA approved drugs for about 2500 diseases
  – Many more diseases where there is very little investment in finding a cure
    • 7000 rare diseases
    • Anti-infectives
Data sources for drug repurposing

**Experimental**
- Mass spectrometry
- High throughput phenotypic assays

**Computational**

**Pathway mapping**

**Target** + **Ligand** = **Molecular Docking**
Real-World Data (RWD)

• Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources

• What can we learn by collecting RWD in a standardized way
  – New ways of treating diseases
  – New combinations of drugs
  – New dosing regimens and durations of therapy
  – New populations that can benefit from existing treatments
  – Discover that unapproved uses do not work or are harming patients

• Currently, no organized way to capture the important safety and effectiveness information from RWD to:
  a. Inform design of future clinical trials
  b. Formulate hypothesis that can be addressed in clinical trials
  c. Generate RWE to help support drug relabeling
Launched a public-private partnership with FDA and NCATS/NIH in June 2020 to bring stakeholders together and address how drug repurposing can be accelerated

**Mission**
• Become the central **global** source of validated real-world data to advance drug repurposing for diseases with the highest levels of unmet medical need

**Rationale**
• A platform for physicians to share their unusual treatment experiences in a systematic manner with the **global** clinical community

**Strategy**
1. Capture high level information “off-label” drug use
2. Identify drug leads through advanced analytics
3. Generate hypothesis to inform design of RCTs of existing marketed drugs for new indications
4. Work with regulators to update labeling changes
CURE Drug Repurposing Collaboratory

https://c-path.org/programs/cdrc/

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For more information
A Platform to Capture Novel Uses of Existing Drugs

• Web-based tool
  - Computer, smartphone or mobile device
  - https://cure.ncats.io/explore

• Capture and share real-world experiences treating patients through a simple online case report form

• All data collected is HIPAA compliant and contains no PII

• Newsfeed

• Link to www.clinicaltrials.gov
CURE ID case report: Quick submit

1. What disease did your patient have?
2. How did you make the diagnosis?
3. **What made your patient’s infection difficult to treat?**
4. What drug(s) did you use to address this difficult to treat infection? *
5. What was the patient’s outcome?
6. Did the patient experience any adverse events? *
7. Would you like a follow up reminder?
8. ...

* Free text
Use of CURE ID for COVID-19 Case Collection

• C-Path, along with FDA, NIH (NIAID and NCATS), CDC, and IDSA are now collaborating to promote the use of CURE ID as a tool to collect cases on the treatment of patients with COVID-19, in conjunction with ongoing clinical trial efforts.

• Activities are also being coordinated with the World Health Organization (WHO) through the existing FDA-WHO CURE ID partnership.

• The case report form has been tailored to COVID-19 and data fields have been harmonized with other RWD and clinical trial platforms.

• A COVID-19 pilot project to accelerate the deployment of the CURE ID app as a critical source of real-world data:
  - Reach out and incentivize clinicians to submit COVID-19 case reports to CURE ID
  - Capture case reports from the literature
  - Collaborate with health networks to extract data from EHRs to CURE ID case report form
  - Partner with COVID-19 disease registries to explore data sharing initiatives
Registry and health network partners

- Virus Registry (Mayo + Soc. Crit. Care Med.) 100+ sites
- UC BRAID (University of California medical schools) 5 sites
- Keystone Health (Pennsylvania outpatient clinic)
- Summa Heath (Ohio Health Network)
- Zuckerberg San Francisco General
- Wellspan (10 hospital system in Pennsylvania)
- Emory School of Medical
- U. Miami Miller School of Medical
- Johns Hopkins University School of Medicine
- BJ Medical College (India)
Bioinformatic data flow

- **ETL**
- **Glue**
- **Amazon Athena**
- **Analytics/Al**
- **SageMaker**
- **Amazon QuickSight**

**Data Flow Diagram**

1. CURE ID database
2. ETL
3. Glue
4. Amazon Athena
5. Analytics.AI
6. SageMaker
7. Amazon QuickSight

**Key Components**

- CURE ID database
- ETL
- Glue
- Amazon Athena
- Analytics.AI
- SageMaker
- Amazon QuickSight

**Processes**

- Data
- Insights
- Identified Signals and generated hypotheses
- Free text
- Features
- Comprehend Medical
How CDRC is contributing to finding a treatment for COVID-19

• Identify signals in existing data sources that can be used to inform clinical trials for potential treatments using repurposed drugs
  – Data collected during an outbreak can be improved and coordinated
  – This may allow us to find possible treatments to help ease this pandemic and prepare us to better fight the next one

• Provide a clear pathway, for stakeholders working collaboratively, to identify the potential of an existing marketed drug and pursue label expansion
  – Facilitate labeling change that accurately reflects a how a drug is used in clinical practice, harnessing a combination of traditional trials and real-world evidence
Challenges in drug repurposing

• Process must be initiated by the drug sponsor
  – Is the repurposing effort aligned with pharma business strategy? (incentives, exclusivity, ROI)

• Intellectual property and patent protections
  – Legislation impede obtaining a patent for second or further medical uses (it is possible to protect a drug for a repurposed medical use)
  – Repurposing uses have already been reported in the literature or are already being exploited in clinical practice as off-label, the information is already in the public domain and affects novelty and, consequently, patentability

• Older drugs that are off patent
  – Patent for the new indication can be obtained but enforceability could become an issue if the new indication makes use of already available strengths and dosage forms
  – Exclusivity may not be enough of an incentive
Summary

• Drug repurposing is a fast and efficient way in which to secure treatments for diseases that have no or limited options

• C-Path has partnered with FDA and NIH to launch the CURE Drug Repurposing Collaboratory (CDRC)
  – Piloting COVID-19 initiative
  – Deploying CURE ID globally to capture how drugs are used by physicians
  – Collate data and analyze using cloud-based bioinformatic pipelines
    • Clinician submitted case reports
    • Literature
    • Electronic health records
    • COVID-19 registries

• To generate hypothesis using RWD, inform clinical trials, and work with stakeholders to advance the regulatory approval of repurposed drugs through relabeling
Acknowledgements: Advisory Committee

Core Committee Members

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  - Leonard Sacks (Associate Director: Office of Medical Policy)
  - Heather Stone (Science Policy Analyst: Office of Medical Policy)
  - Ameeta Parekh (Senior Advisor: Office of Translational Sciences)
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  - John-Michael Sauer (Biomarker Program Officer)
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External Committee Members

• David Aronoff – Vanderbilt U
• Greg Deye – DMID, NIAID, NIH
• David Fajgenbaum – U Pennsylvania (Patient advocacy)
• Dan Hartman – Bill & Melinda Gates Foundation
• Jaclyn Levy – Infectious Diseases Society of America
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