Teaching Old Drugs New Tricks

Drug Repurposing to Accelerate Disease-Modifying Treatment for CFS

The CFIDS Association of America

Biovista
Overview

The CFIDS Association

- Patient-centered and funded
- Participated in development of current research case definition
- Risk factors include being female, infection/environmental, genetic
- Described by signs & symptoms
- Multiple system perturbations
  - CNS, HPA, immune, GI, cardiovascular, musculoskeletal
Overview

CFS
• 5,000 publications
  • 1 million people in US and 17 million worldwide
  • $51 billion annual direct and indirect costs
• >$150 million spent
  • No diagnostic marker or FDA-approved treatment
  • FDA considers CFS a “serious and life-threatening condition”
  • No standardized clinical guidelines
• Patients describe their symptoms
  • Physicians treat most severe symptoms

Incremental Symptom Relief

[Table with symptoms: Fatigue, Mood, Fitness, Sleep, Pain]
The Challenge

• How to treat a phenotype that may have multiple poorly understood etiologies?
  • Conventional approaches have not worked
    • By 2011 there were 20 RCTs on pharmacological treatments for CFS with little to no effect for treatment
      • Reasons for lack of success: small sample size, heterogeneous patient sample, lack of organized knowledge archive
    • PLM: 8,351 patients using 753 Rx drugs, 173 OTC drugs, 667 supplements
  • CFS is not unique
    • 4,000 diseases with known molecular basis, but just 250 with treatments
Strategic Shift

- Our Innovation Pathway
- Patient-centered research to de-risk and foster CFS treatment R&D = RIWW
  - An infrastructure that makes it faster, easier, cheaper
    - Literature repository
    - Patient registry, biobank, consent
    - High-quality, curated data in a platform that enables sharing, collaboration
    - Novel dynamic patient-generated data
    - Regular posting and reporting of results
- New research avenues
  - Drug repurposing
Strategic Partnership

A drug that is well seasoned is an excellent starting point for innovation.
—Aris Persidis, Biovista

- Biovista is a pioneering biotech company specializing in drug repurposing
- Computational tools to mine biomedical literature to reveal non-obvious relationships
- Verification with cheminformatics simulations + in vitro/in vivo

Disease-defining concepts: core signs, symptoms and decrements in function

The CFIDS Association

New and Novel IND
• Well suited to multifactorial diseases
• Drug safety is known, this accelerates development and reduces costs
• Ideal for orphan disease space – where efficient treatments are lacking and research spending is not adequate
• The scientific methodology of drug repurposing and the research approach followed by the RIWW approach can be replicated in many different diseases areas
• Lessons learned – bring together stakeholders (researchers, doctors, patients, KOLs, Regulators, NIH), regular communications, need quick “success”
Strategic Approach

COSS™ Platform
- A mixture of simulations, animal model testing and a literature discovery module that helps point our scientists in “promising regions of the biological search space”
- Creates multi-dimensional profiles of over 1 million biologically relevant entities (such as genes, drugs, diseases, pathways) and compares these against each other to come up with novel uses of existing drugs
Accomplishments

- Drugs most strongly correlated with CFS are related to the regulation of neurotransmitters (mostly monoamines)
- In order of decreasing bibliographical association: serotonin > dopamine > acetylcholine > histamine >= epinephrine
Counterintuitive: serotoninergic & noradrenergic drugs cause fatigue more frequently than neuroleptics
Accomplishments

• We have developed a web-based platform for clinical experts to contribute their treatment practices and clinical intuition

• **Goal:** to collect and mine this data for better disease characterization and treatment identification
State of affairs in treatment development

A collection of specialist bodies of knowledge
… often loosely connected …

Where we want to be

a complete understanding of biology and disease mechanisms

framework for healthcare in the 21st century
A New Model for Development

Ingredients we need:

1. Drug repositioning gives a 30,000-foot view that encourages us to know what we know... ... and make effective use of it...

2. RIWW + drug repositioning provide:
   - Incentives and direction
   - Framework to connect R&D silos
   - Mechanism to integrate disparate data from many research groups
   - ...

the big picture
“glue”
Future Milestones

Pre-clinical validation:
• SolveCFS BioBank and RIWW

Proof-of-Concept Clinical Trials:
• Design (define endpoints/metrics, protocol, IRBs)
• Execution (recruitment, intervention, follow-up)
• Analysis & interpretation
Venture Philanthropy At Work

- Support for the RIWW is made possible with generous donations from individuals.
- RIWW funded with $100,000, 18-month grants intended to de-risk and validate research.
- 2009-2010 grantees begin to accumulate follow-on support -- $637,000 ➔ $7+ million.
- SolveCFS BioBank – revenue generating resource.
Key Partners/Players

• Scientific Advisory Board composed of clinical, academic, pharma, strategic and legal experts.
• Funded RIWW investigators who use and contribute to SolveCFS BioBank
• Federal partners from the CDC, NIH and the FDA
• Strategic and inspirational partners: Bernard Munos, Russell Bromley
• Looking for pharma partners willing and able to work with us
Summary

- FDA considers CFS a “serious and life threatening condition” and a candidate for accelerated approval.

- The CFIDS Association has built a robust patient-centric resource that can be used to define core signs, symptoms and decrements in function.

- Biovista has identified a “short list” of counter-intuitive drugs that target specific pathways.

- **Seeking phase II partners**