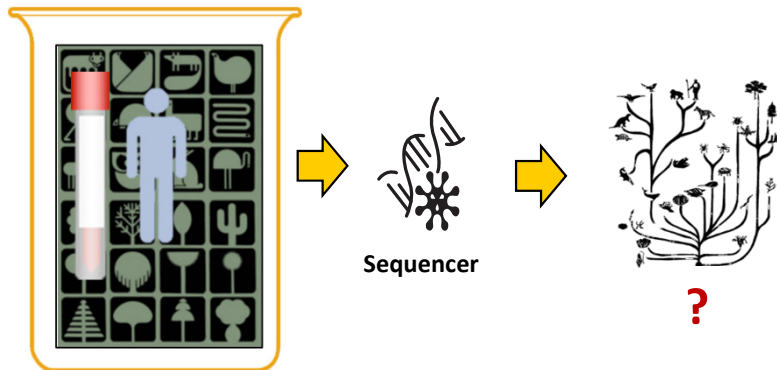# ID by DNA: harnessing genome technologies for diagnosis of infectious disease
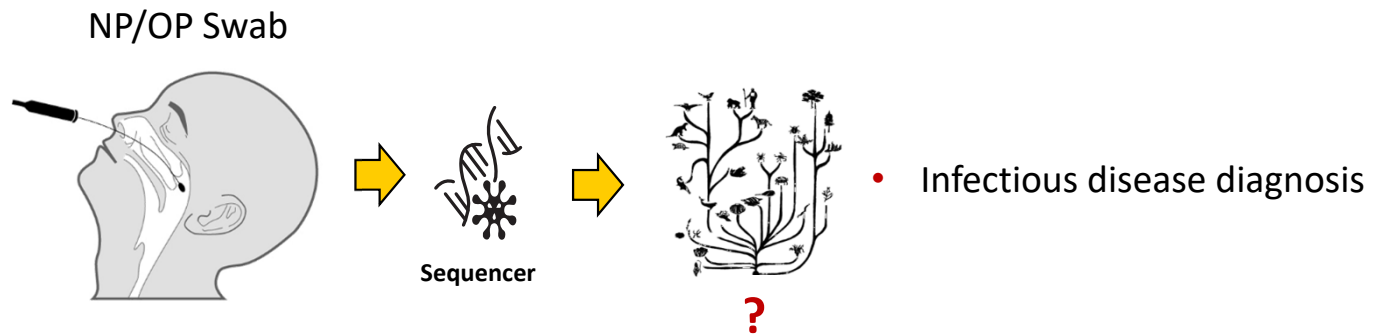
Mark Yandell, PhD.
Professor, Human Genetics
HA & Edna Benning Presidential Chair
Co-director USTAR Center for Genetic Discovery
Assoc. Director Program in Personalized Health
University of Utah

THE UNIVERSITY OF UTAH

Utah Center for Genetic Discovery

What is Metagenomics ?

Any Source

Sequencer

?

What is Metagenomics ?

NP/OP Swab

Sequencer

?

- Infectious disease diagnosis

Robert Schlaberg, MD, PhD, MPH
Department of Pathology, U of Utah
Medical Director, ARUP Laboratories
CMO IDbyDNA Inc.

"I've got 8000 or so pediatric pneumonia samples. Can you analyze them for me?"
-- 2014

Taxonomer is an *ultrafast* metagenomics tool designed to overcome this computational challenge

What does *ultrafast* mean?

- Search **every read** in a typical NGS sample, $\sim 1 \times 10^7$ reads

- Against **millions** of reference sequences, all organized hierarchically, e.g. phylogeny

- Identify all organisms in the sample, at the best possible **taxonomic resolution**
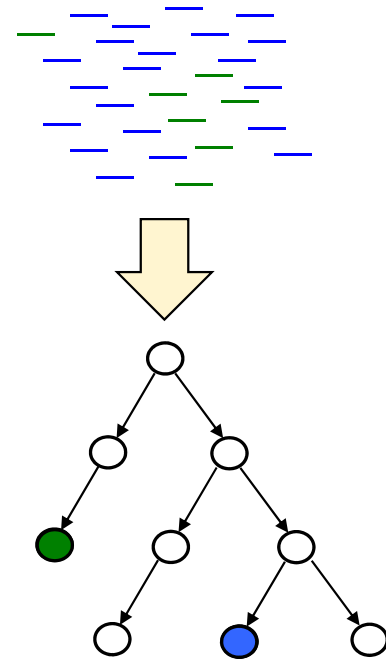
- In ~ 1 **minute**
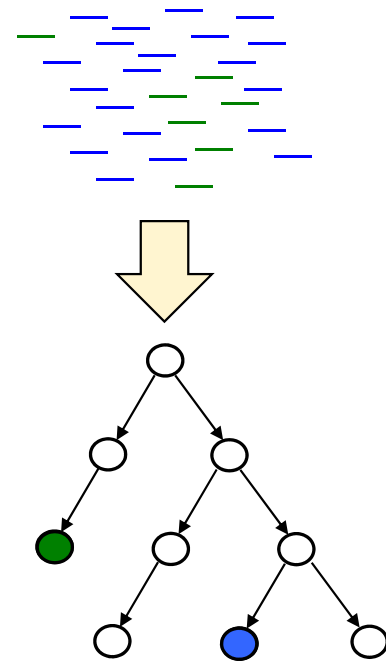
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Steven Flygare, PhD
Head of Bioinformatics, IDbyDNA Inc.

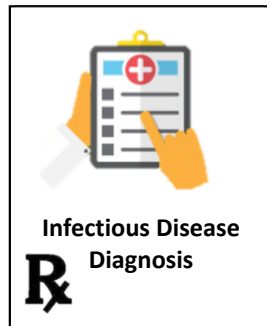# Taxonomer is also web-based, highly visual and interactive

Any Source

Any Sequencer

Pan-Kingdom Taxonomic Analysis

TAXONOMER

www.taxonomer.com
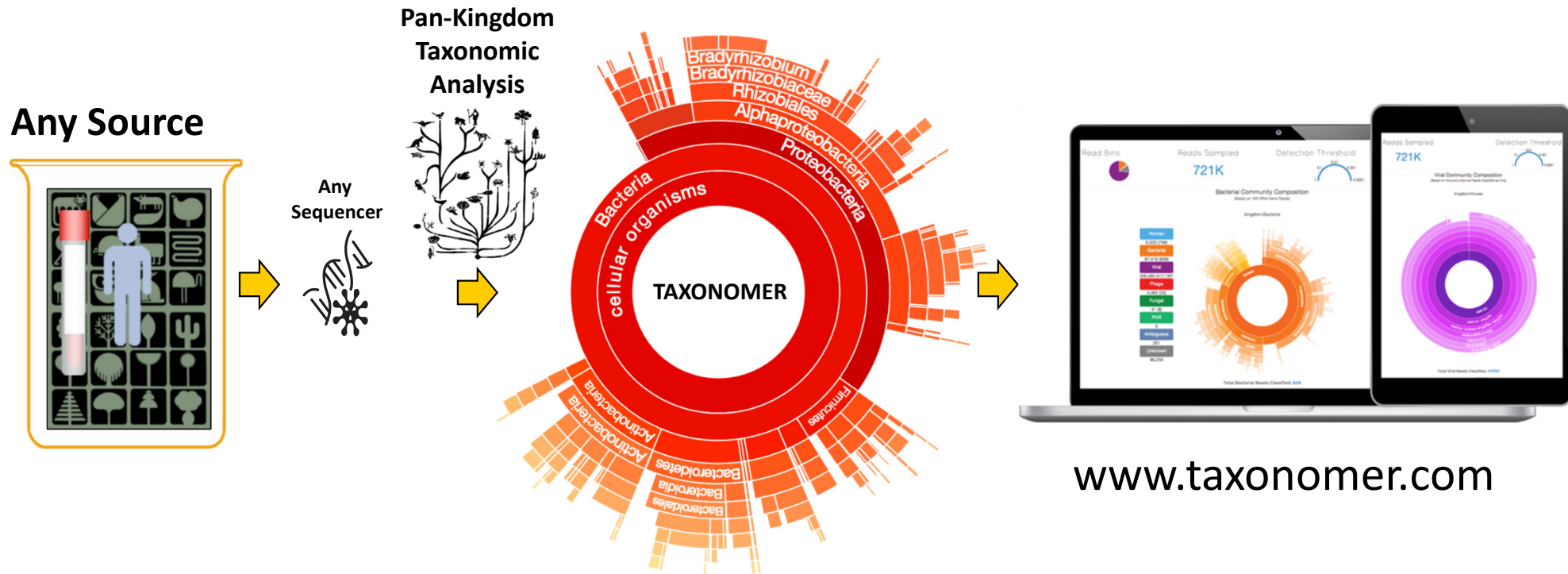
Freeing users from costly hardware and analysis infrastructure requirements

Disruptive

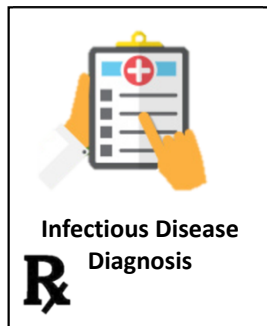# What's so *disruptive* about ultrafast metagenomics technologies?

Infectious Disease Diagnosis

- ***Hypothesis free*** clinical testing and discovery

Google-like DNA Discovery Engine

- 'Google like' ***exploration*** of even the largest NGS datasets *over the web.*

What's so *disruptive* about ultrafast metagenomics technologies?

Infectious Disease Diagnosis

R̲x

- ***Hypothesis free*** clinical testing and discovery

What is **Hypothesis-free** testing and discovery?

- **Traditional clinical testing** is a *Usual Suspects* activity. Does patient have X? If not, '*How about Y?*', and so on.

- **Hypothesis-free testing** checks for presence of every organism A-Z, even ones that are not yet known to be disease causing.

- **Real need**. For example, using all existing clinical tests, the cause of pneumonia remains unknown in >60% of cases.

- **Great Potential**. Diagnose many more cases, discover new disease-causing organisms, better tailor treatments for precision medicine.

The technological challenge

The *translational* challenge

High profile, peer reviewed publications validate the science

Validation of Metagenomic Next-Generation Sequencing Tests for Universal Pathogen Detection

Robert Schlaberg, MD, MPH; Charles Y. Chiu, MD, PhD; Steve Miller, MD, PhD; Gary W. Procop, MD; George Weinstock, PhD; the Professional Practice Committee and Committee on Laboratory Practices of the American Society for Microbiology; the Microbiology Resource Committee of the College of American Pathologists

Archives of Pathology & Laboratory Medicine, Early Online Release, doi: http://dx.doi.org/10.5858/arpa.2016-0539-RA
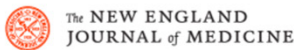
Fatal Zika Virus Infection with Secondary Nonsexual Transmission

Sankar Swaminathan, Robert Schlaberg, Julia Lewis, Kimberly E. Hanson, Marc R. Couturier

New England Journal of Medicine, DOI: 10.1056/NEJMc1610613

Diagnosis Ex Machina – A new software tool may improve upon current infectious disease diagnosis methods to return faster, more accurate results

Robert Schlaberg

The Pathologist, September 2016

Taxonomer: an interactive metagenomics analysis portal for universal pathogen detection and host mRNA expression profiling

Flygare S, Simmon KE, Miller C, Qiao Y, Kennedy B, Di Sera T, Graf EH, Tardif KD, Kapusta A, Rynearson S, Stockmann C, Queen K, Tong S, Voelkerding KV, Blaschke A, Byington CL, Jain S, Pavia A, Ampofo K, Eilbeck K, Marth G, Yandell M, Schlaberg R
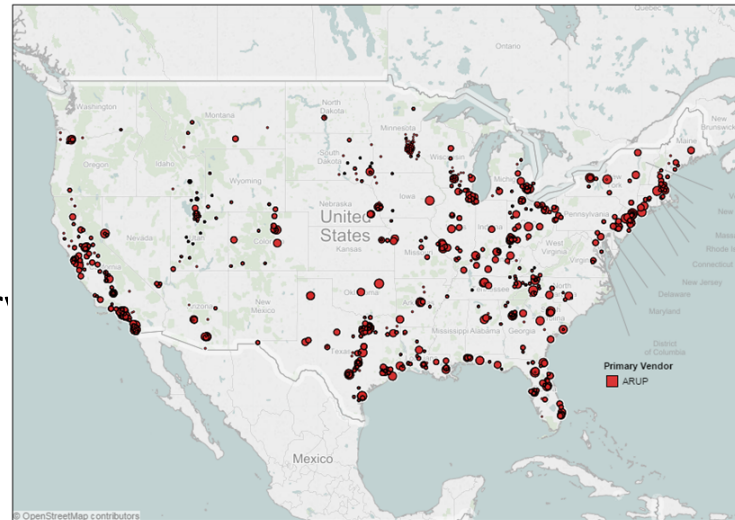
Genome Biology 2016 17:111

Unbiased Detection of Respiratory Viruses by Use of RNA Sequencing-Based Metagenomics: a Systematic Comparison to a Commercial PCR Panel

Graf EH, Simmon KE, Tardif KD, Hymas W, Flygare S, Eilbeck K, Yandell M, Schlaberg R

J. Clin. Microbiol. 2016 vol. 54 no. 4

Go to market strategy :

- Partnered rollout with reference laboratory

You need a product

First product: Hypothesis-free test for Pneumonia of unknown cause

- Most common reason for hospital admission of children

- Problem:
  - → Caused by dozens of different pathogens.
  - → Pathogen never identified in 60% of cases, despite exhaustive testing.
  - → Effective treatment depends upon diagnosis.

- Urgent need for hypothesis free testing
  - → *Increase rate of diagnosis*
  - → *Discover new disease-causing organisms*
  - → *Better tailor treatments*

http://www.jems.com/articles/2009/08/ treating-children-respiratory.html

A product is good

But you will also need $

But you will also need $

Taxonomer

Metagenomic
Analysis

But you will also need $

Workflow Management — Metagenomic Analysis (Taxonomer) — Clinical Review — QA / QC — Report Generation

But you will also need $

Workflow Management · Metagenomic Analysis (Taxonomer) · Clinical Review · QA / QC · Report Generation

COLLEGE of AMERICAN PATHOLOGISTS
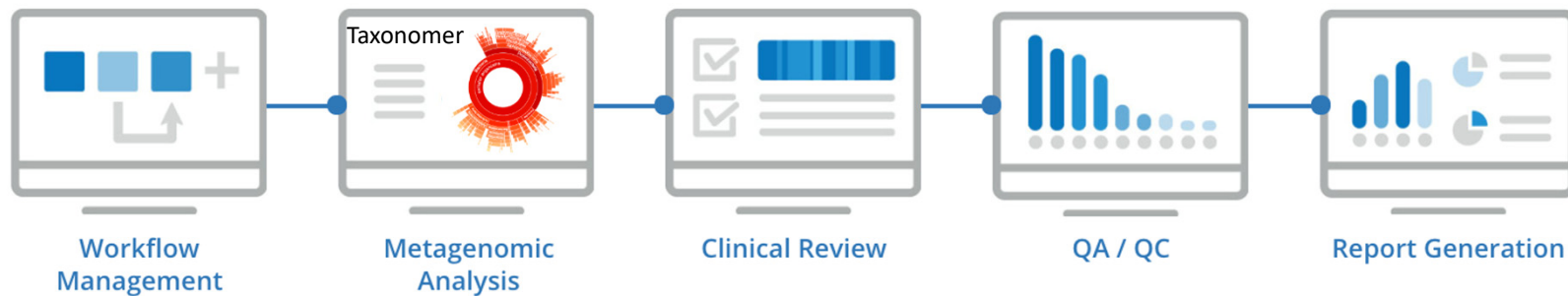
But you will also need $

ID by DNA ➡ IDbyDNA Inc.

USTAR Center for Genetic Discovery: Technology Commercialization Efforts

FABRIC GENOMICS

- Opal clinical genomics platform based on VAAST & PHEVOR
- $23M Series B (06/2016)

IDbyDNA

- Infectious disease diagnostics based on Taxonomer
- Partnership between U of Utah, UCGD, and ARUP
- $9M Series A (09/2016)

FRAMESHIFT visually driven genomics

- Visually driven genomics platform based on iobio
- Phase 1 STTR funded 9/2016

base2 genomics

- Commercial-grade whole genome analysis based on GEMINI
- Currently seeking funding and commercial partners

THE UNIVERSITY OF UTAH

USTAR Center for Genetic Discovery

Explify® Respiratory identified pathogens in 44% of previously Test-Negative (0% by all available tests)*, immunocompromised children with suspected respiratory infections

*NOTE: These pan-negative tested patients received >15 conventional Dx tests (i.e. culture, PCR, PCR panels, serology etc.)

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- 'Google like' **exploration** of even the largest NGS datasets *over the web*

Thanks