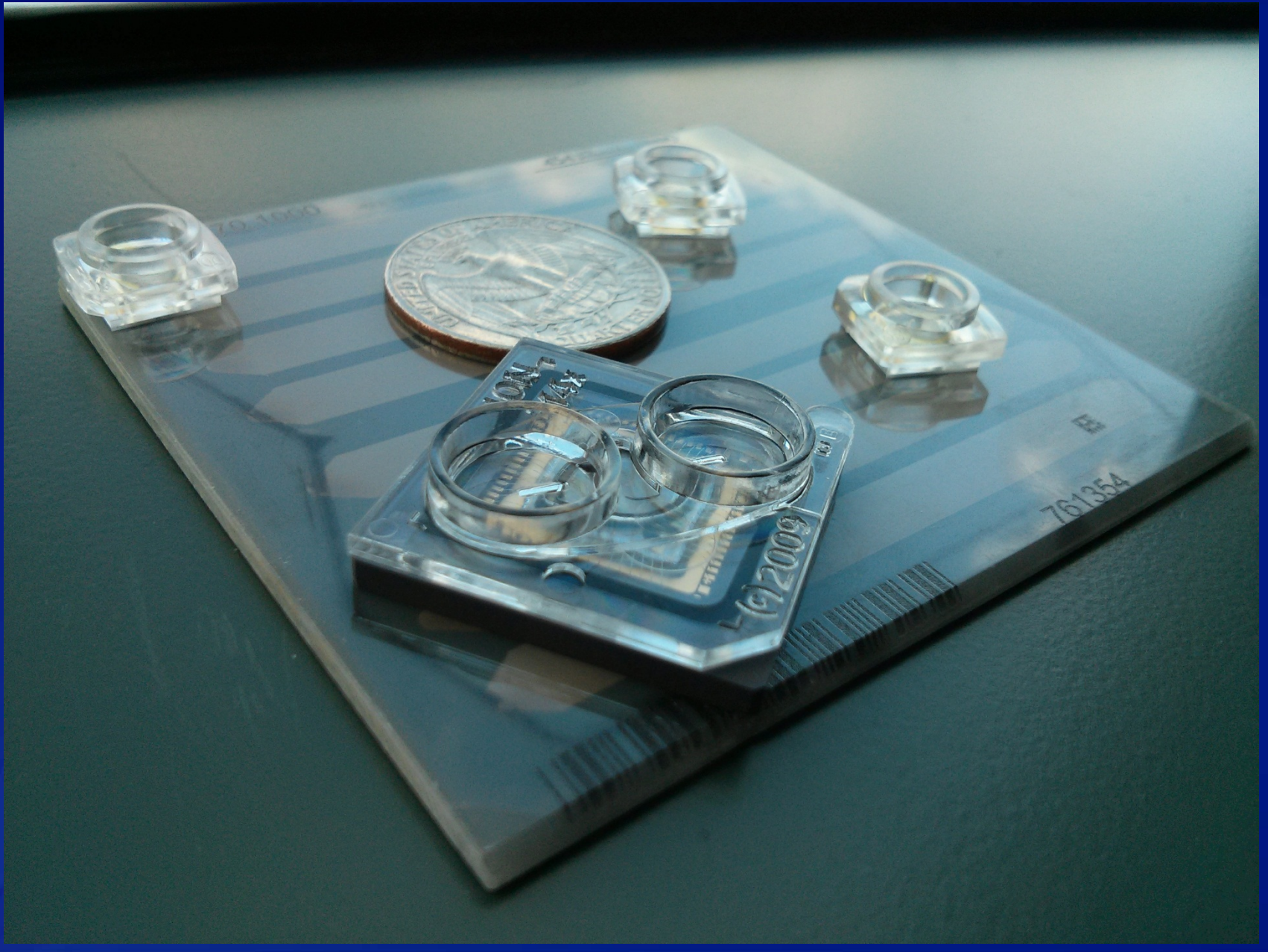# Advanced Molecular Detection

**Duncan MacCannell, PhD**

Clinical Laboratory Improvement Advisory Committee
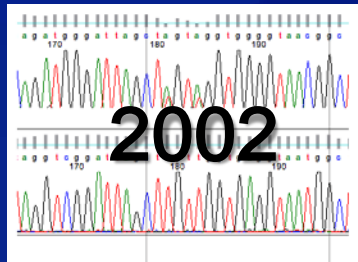
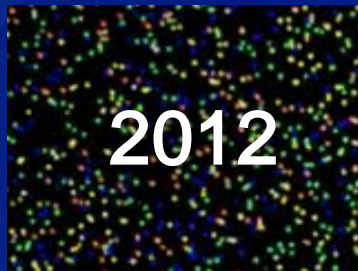March 5th, 2014

Roche 454 PTP plate, Ion Torrent 314, Pacific BioSciences SMRT cells (x 3)

**1992** — **500** basepairs/day
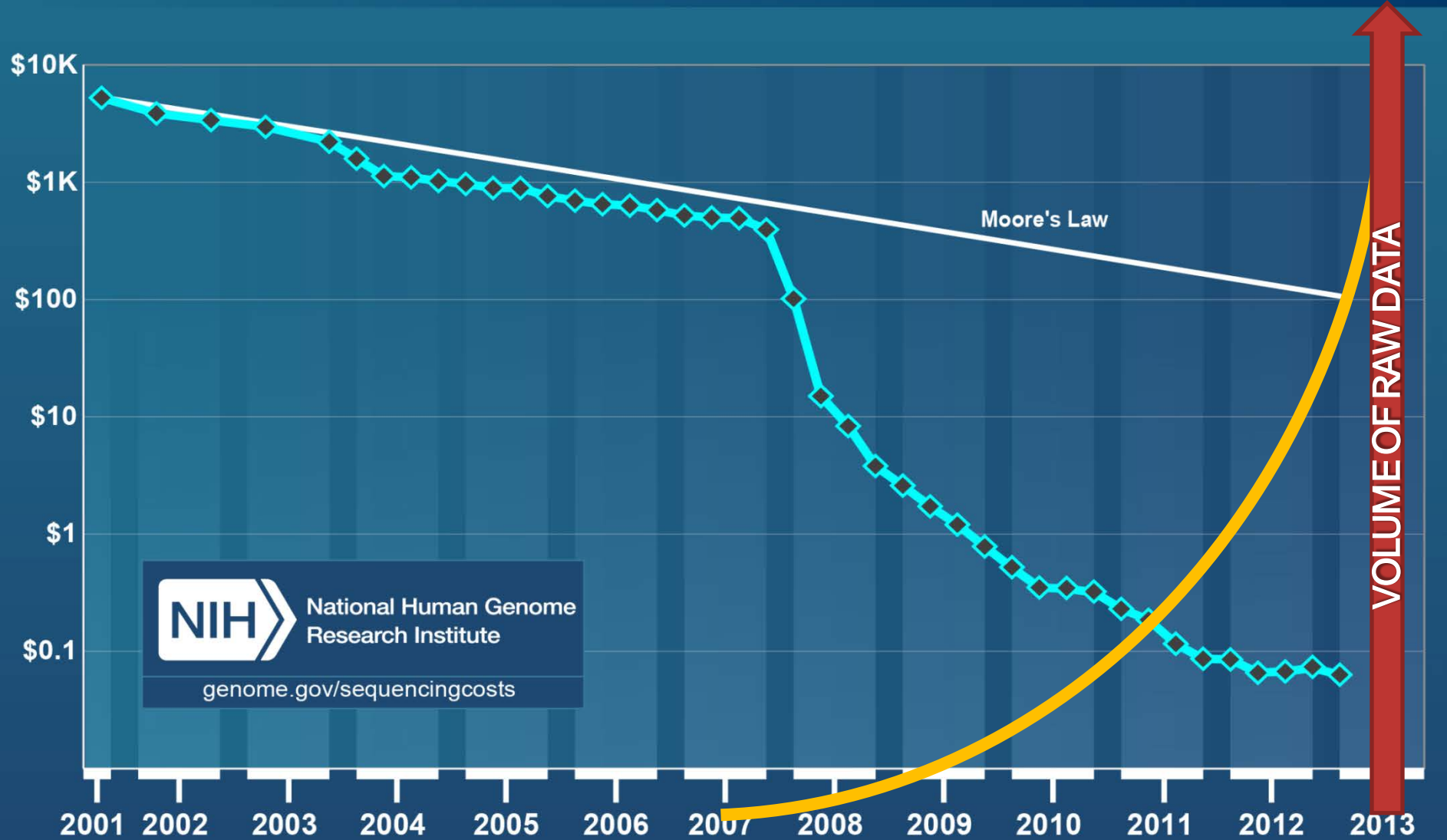
**2002** — **50,000** basepairs/day

**2012** — **50,000,000,000** basepairs/day

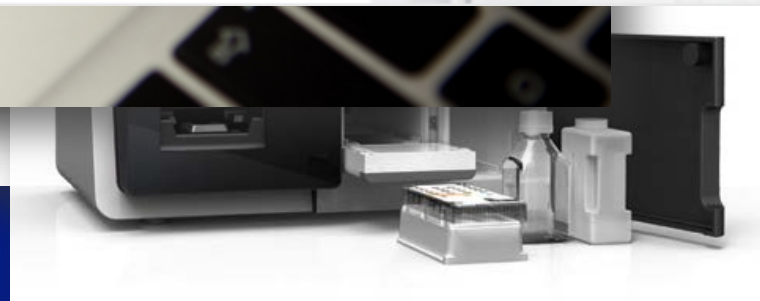Human genome: 3,000,000,000bp

Cost per Raw Megabase of DNA Sequence

NOW FDA-CLEARED

Seek flexibility.

Develop your own diagnostic tests with the MiSeqDx.

**Input: DNA/RNA**

Source:
Genomic
Amplicon
Whole sample

Host/vector/
pathogen/
environment

…

**NGS**

Workflow:
Platforms
Chemistry
Perf. char.
Labor/TaT
Cost

**Bioinformatics**

Workflow:
Hardware/software
Specialized skillsets
Algorithms/pipelines
Pathogen databases
Data analysis/interpret/
Integration/visualization

**Output: Information From Sequence Data**

**Comparative Genomics**
HRS straintyping/Subtyping
Cluster identification
Molecular evolution
Genotypic characterization
Virulence, AR, signatures
Functional annotation
Diagnostic dev/validation

**Metagenomics**
Pathogen identification/discovery
Culture-independent diagnostics
Microbial ecology/diversity
….

**Increasingly Universal Workflows**
Established sequencing workflows for a wide range of pathogens.

**A Moving Target**
Rapidly evolving technology space. Changing hardware and COTS/OSS capabilities. Lots of choice, but lack of consistent standards. BIG DATA. New workforce and skillset is required.

**Objective, "Future-Proof" Data**
Intrinsic quality metrics. Ability to back-test retrospective sequence data in silico for genes/markers identified at a future date.

Sample intake    Conversion          File hashes/versioning
Prep/staging     Library prep
Extraction       Sequencing          Process logging/audit

**Pathogen- and application-specific, CLIA-compliant assays**

**MANY RESULTS POSSIBLE FROM A SINGLE DATASET!**

# Advanced Molecular Detection

Proposed **$30M FY2014** budget request to:

1. *Improve pathogen identification and detection*

   **Outcome**: Rapid progress toward modernizing PulseNet and other critical lab-based surveillance systems

2. *Adapt new diagnostics to meet evolving public health needs*

   **Outcome:** Enhance CDC's ability to detect outbreaks early, develop new test during outbreaks, and better characterize infectious disease threats

3. *Help states meet future reference testing needs in a coordinated manner*

   **Outcome:** More effective and better integrated outbreak response activities

4. *Implement enhanced, sustainable, and integrated laboratory information systems*

   **Outcome:** Labs inside and outside CDC can share information quickly and seamlessly, including with other CDC databases, such as MicrobeNet and PulseNet

5. *Develop prediction, modeling, and early recognition tools*

   **Outcome:** Better equipped to prevent, detect & respond to infectious diseases.

EPI **+** NGS **+** BIOINFO **=** AMD
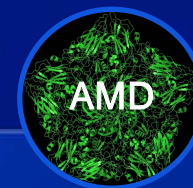
# AMD Initiative: Strategic Investments (1)
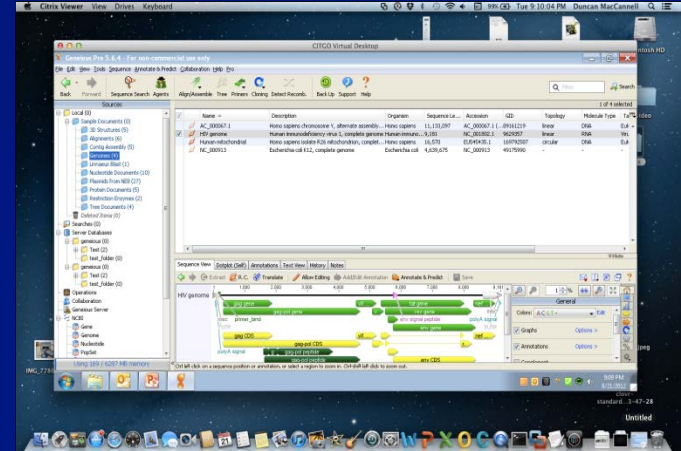


- ❑ Scientific Infrastructure:
    - ▪ Critical laboratory and bioinformatics infrastructure at CDC, state/local PHL, and key overseas laboratories.
        - • Sequencers, mass-spec, other instrumentation, reagents.
        - • High performance computing, workstations.
        - • Data storage, networking; data integration, knowledge management.
        - • Service contracts, software licensing, etc.

# AMD Initiative: Strategic Investments (2)
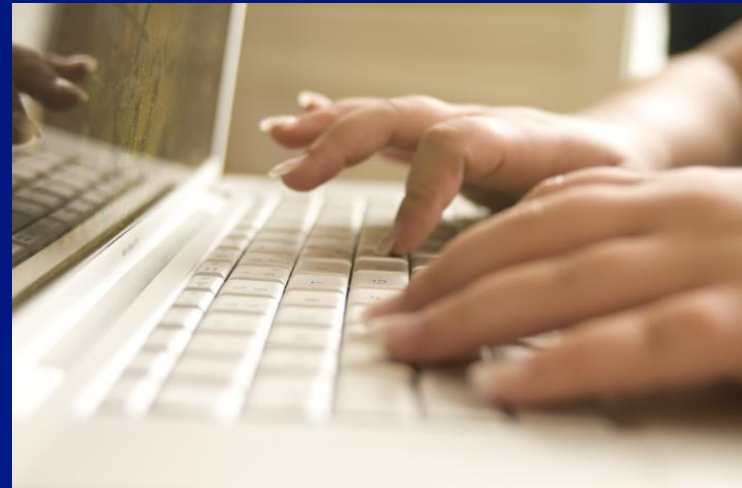


- ❑ Workforce development:
  - Training for CDC and PHL staff (bioinformatics, genomics, -omics)
  - New or re-tooled fellowship programs (bioinformatics, genomics)
  - Recruitment of new staff and skillsets (bioinformaticians, data scientists, lab specialists, …)

# AMD Initiative: Strategic Investments (3)

- **Consortia, partnerships and alignment of efforts**
  - Academic institutions
  - State, Federal (NIH, FDA, DHS, DoD, DoE/National Laboratories)
  - Non-Profit/NGO
  - International community
  - Commercial/For-Profit
  - Clinical laboratories
- **Pilot projects with state/local and other partners.**
  - Outbreak detection, investigation and response
  - Leverage existing laboratory-based surveillance systems

# Conclusions

- Emerging laboratory technologies, such as next-generation sequencing, represent a fundamental change in the practice of clinical and public health microbiology alike.

- CDC's Advanced Molecular Detection and Response to Infectious Disease Outbreaks (AMD) initiative will help implement these advancements in public health.

- Working with "big data" in the laboratory, and applying it effectively to patient care, will require new skills and capabilities, including bioinformatics and data science.

- As benchside protocols become increasingly standardized, laboratories must also consider the importance of the underlying bioinformatics methods, reference databases, data management and reporting processes.

# Questions and Discussion

**For more information please contact Centers for Disease Control and Prevention**

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.