Report from
Unifying the Evaluation and Implementation of Genomic Medicine
AKA
The Payer Engagement Workshop

Toni I. Pollin, MS, PhD, CGC
Daniel Mullins, PhD

Attendance: Unifying the Evaluation and Implementation of Genomic Medicine

- August 18th, 2016 @ 8:30 AM – 5:30 PM in Bethesda, MD
  - 66 people at one large table and 36 remote attendees
    - NHGRI program staff and network (IGNITE, CSER, NSIGHT, eMERGE, UDN) members
    - Patients
    - Care and technology providers
    - Researchers
    - Payers
  - Payer Panel
    - Suzanne Belinson, PhD (BlueCross BlueShield [BCBS])
    - Joshua Plavin, MD (BCBS Vermont)
    - Cheryl Reid, MD (Aetna)
    - Kenneth Schaecher, MD (SelectHealth)
    - Heather Shappell, MS, CGC (Beacon Laboratory Benefit Solutions)
    - Deborah Smith, MD, MPH (BCBS Federal Employee Program)

Unifying the Evaluation and Implementation of Genomic Medicine

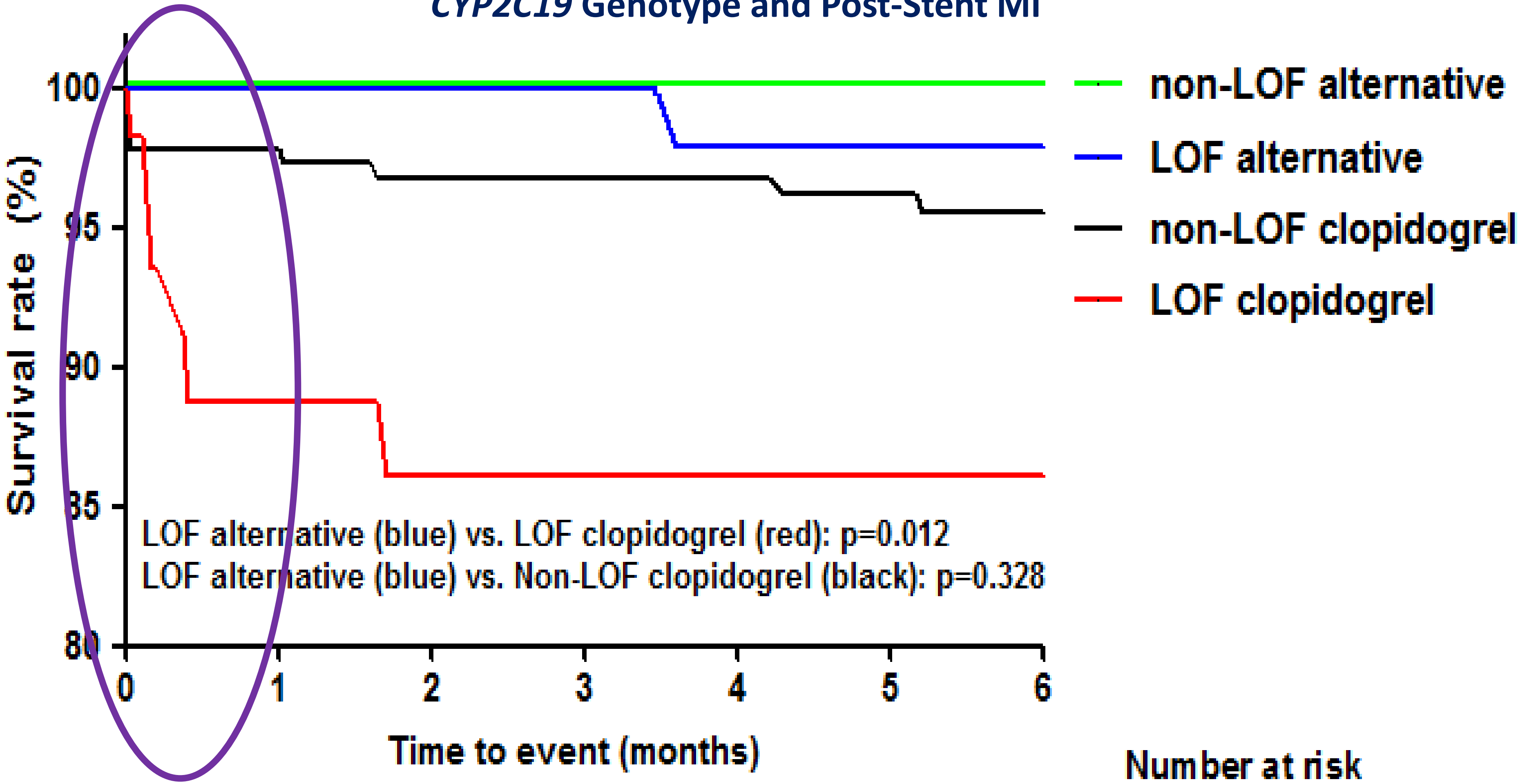
- Brief introduction to the value of IGNITE and Genomic Medicine by Eric Green
- Objectives presented by Toni Pollin and Daniel Mullins
  - To begin to build a process for communication among patients, providers, insurers, and researchers for a team-oriented approach to evaluating and implementing genomic medicine
  - To understand what evidence is needed and how it should be disseminated for all
  - To identify protocols that will help to provide evidence needed to make the application of genomic medicine sustainable

Keynote: The Future is Now

- **John Brumsted, MD**: CEO, UVM Medical Center and President/CEO, UVM Health Network
  - Investment in genomics as powerful tool to improve patient care and control cost that can be linked to quality parameters
  - Vermont is considering statewide whole genome sequencing to assist in developing lifelong care plan for all patients

- **Joshua Plavin, MD, MPH**: Medical Director, BCBS Vermont
  - December 2015 CPT code 81445 (5 – 50 targeted genomic sequence analysis pane for solid organ tumors) was created and reimbursement approved

Case Study 1: Targeted Genotyping
CYP2C19 Genotype and Post-Stent MI



							Number at risk
58	37	32	29	26	24	22	LOF clopidogrel
272	205	185	175	162	148	139	Non-LOF clopidogrel
68	59	54	51	47	45	40	LOF alternative
10	8	6	6	5	5	5	Non-LOF alternative
408	309	277	261	240	222	206	Total

Larisa Cavallari Circulation 2015;132(Suppl 3):A11802.

Discussion Points: Targeted Genotyping

- Pre-emptive vs. reactive PGx testing
  - Challenges in keeping genomic information in EHR
  - Clinical utility data needed
  - Genotype vs. phenotype testing
  - What constitutes medical necessity
  - How to define who and when a patient gets tested
- Clinical utility vs. clinical validity
- Communication of results
  - Variants not related to prescribed medication
  - How to develop and discuss gene-related treatment plans
  - Transferring information between systems/ payers

Case Study 2: Targeted sequencing panel based genetic testing
Diagnosing highly penetrant genetic forms of diabetes

IGNITE
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Patient completes questionnaire

- Diagnosed before 1 year?
- Diagnosed before 30 years?
- Age of diagnosis ____
- Hearing or visual impairment/birth defects/ kidney disease?
- Extremely overweight at diagnosis?
- Type 1 diabetes?
- Parent or child with type 1 diabetes?
- 2 or more people related by blood with diabetes?

Further workup as indicated

- C-peptide Positive?
- IA-2 Antibody negative?
- Consistent family/ medical history elicited by genetic counselor

If indicated…

- Sequence 40 monogenic diabetes genes for mutations

If pathogenic/likely pathogenic variant found:

- Confirm, disclose and add to electronic health record and customize treatment
- Make genetic counseling and testing available to family members

If variant of unknown Significance found:

- Segregation in family
- Functional studies


THE BALTIMORE SUN

baltimoresun.com

WEDNESDAY

"It just didn't make any sense"

House leaders hope to aid city

Plan would provide jobs, education in wake of April unrest

Aiming to correctly diagnose rare diabetes

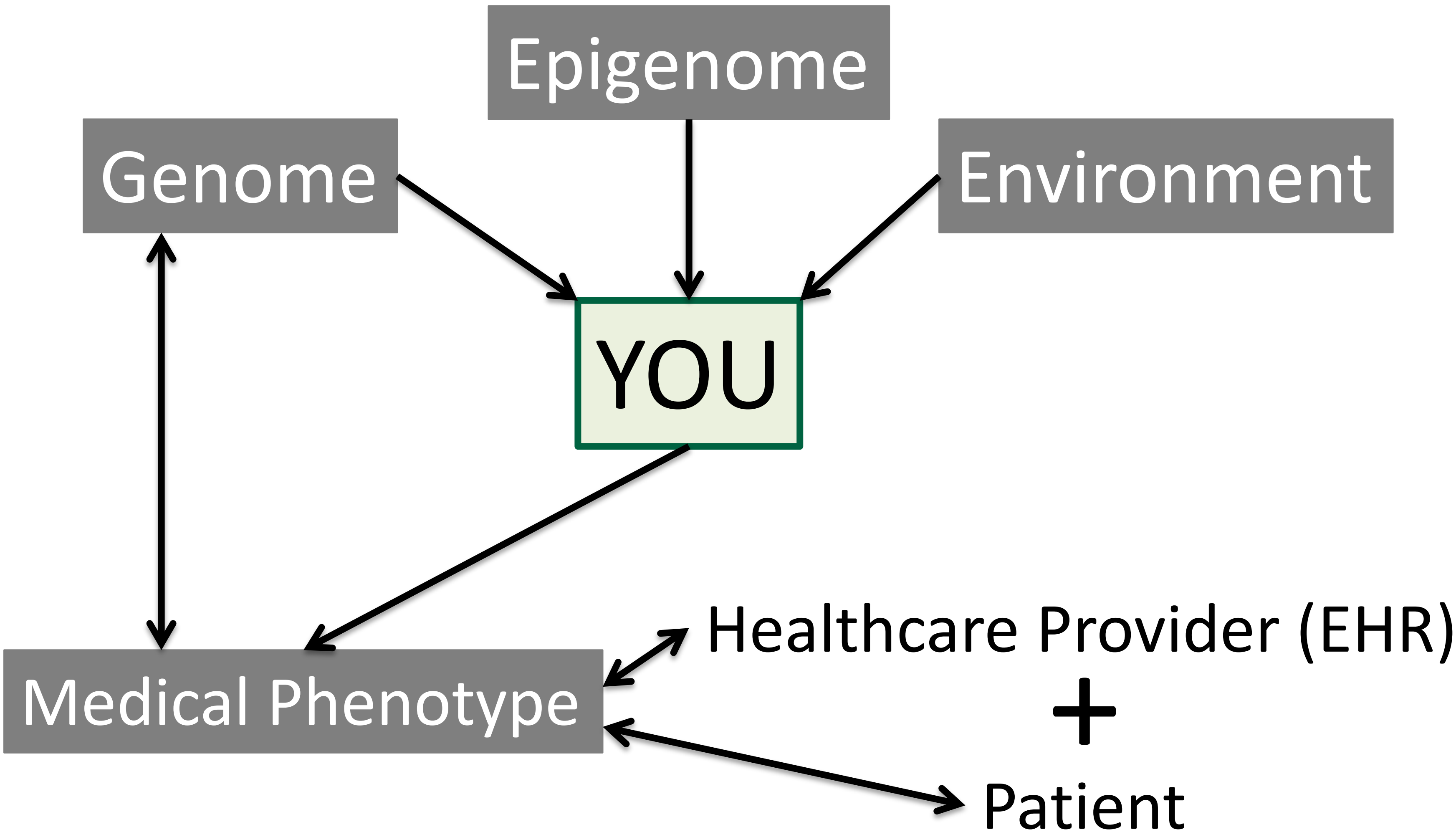
UM researchers study form of disease caused by genetic mutation

http://www.baltimoresun.com/health/bs-hs-monogenic-diabetes-20151203-story.html

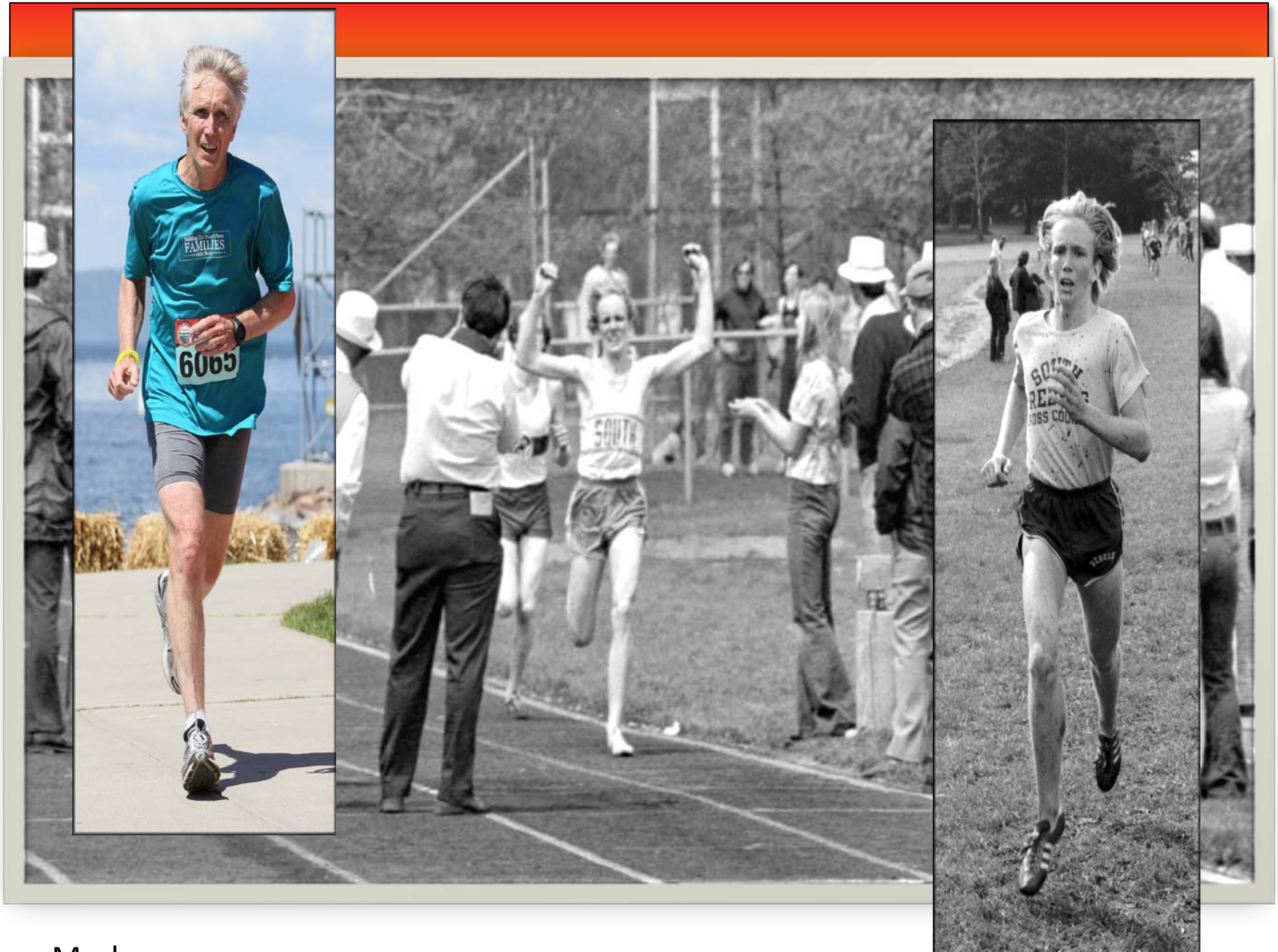
Discussion Points: Sequencing Panel-Based Testing

- Clinical utility and value: how defined and evaluated
  - Costs vary between institutions; may be better to measure resource utilization than costs
  - RCTs have limitations in scope and patient compliance
  - Information available to payers for making decisions may be limited/ unclear
  - Difficult to make informed decision without molecular technology background
  - Coding issues (e.g., non-specific/ ambiguous CPT codes) being addressed
  - How to use existing outcomes and knowledge to inform future decisions
  - Economic data add weight but do not solely drive medical policy decision-making

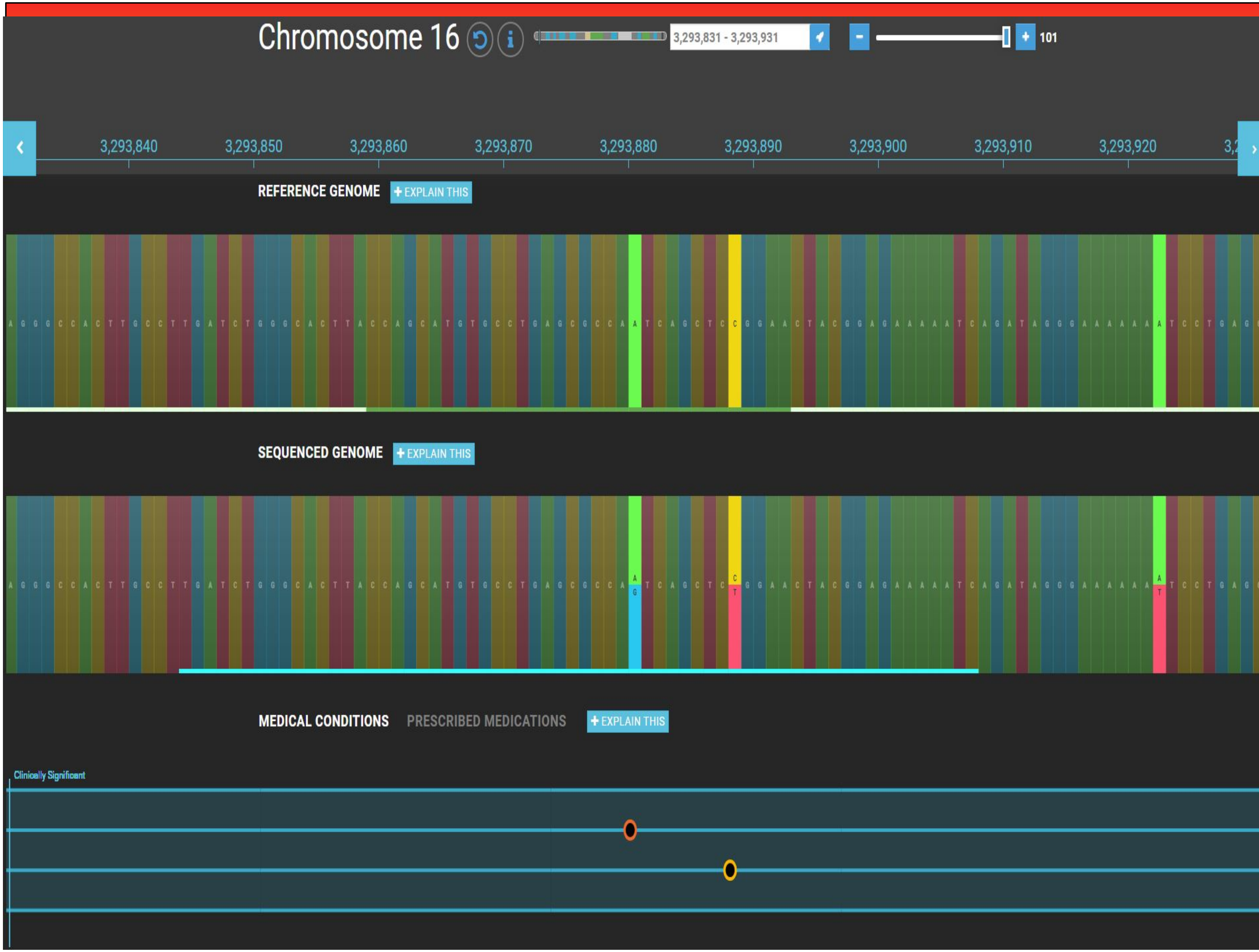
Case Study 3: Genome-wide methods
Shifting paradigms

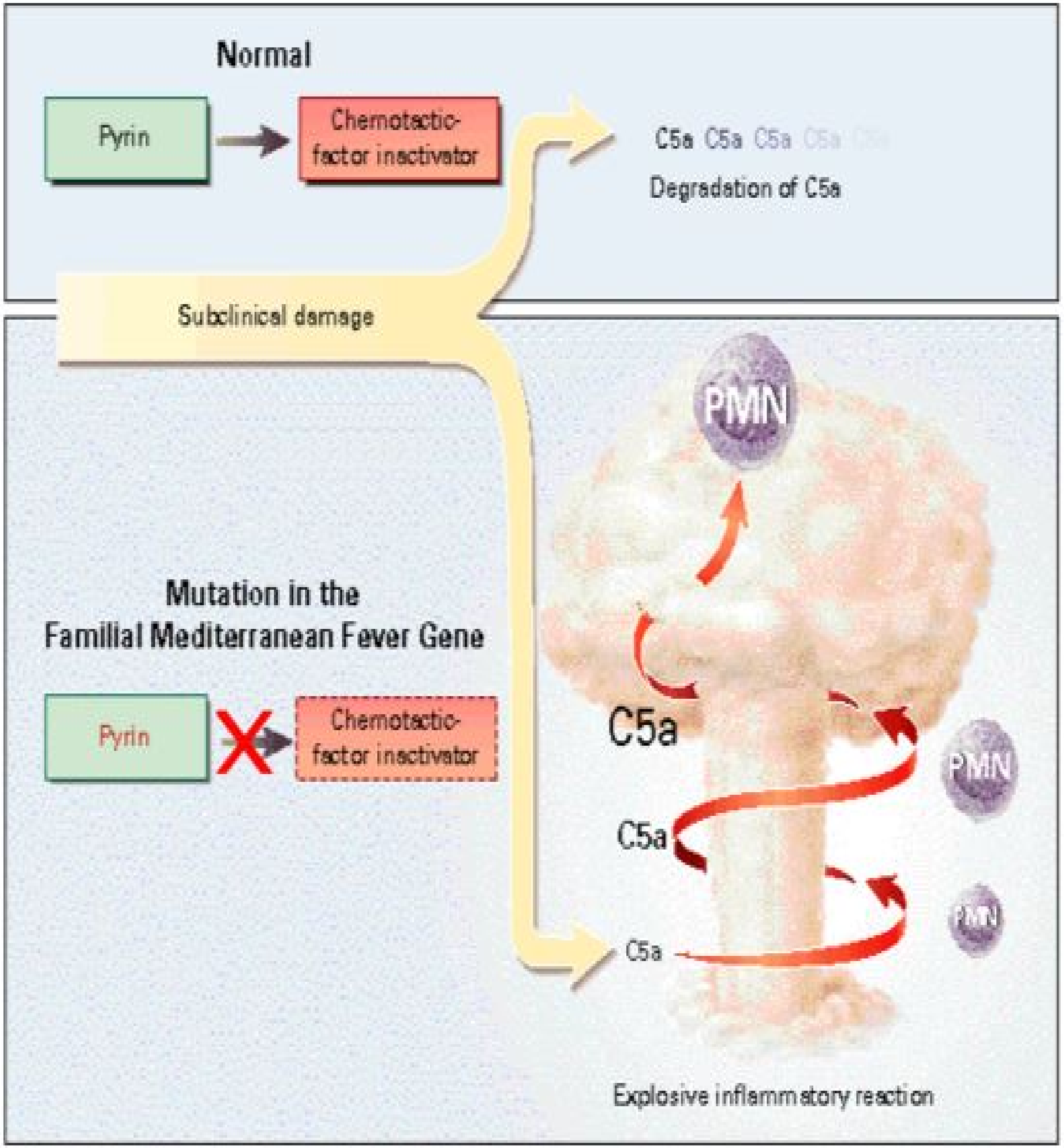


Debra Leonard



Greg Merhar


Chromosome 16
3,293,831 - 3,293,931
101
3,293,840
3,293,850
3,293,860
3,293,870
3,293,880
3,293,890
3,293,900
3,293,910
3,293,920
REFERENCE GENOME
+ EXPLAIN THIS
SEQUENCED GENOME
+ EXPLAIN THIS
MEDICAL CONDITIONS
PRESCRIBED MEDICATIONS
+ EXPLAIN THIS
Clinically Significant


Normal
Pyrin
Chemotactic-factor inactivator
C5a C5a C5a
Degradation of C5a
Subclinical damage
PMN
Mutation in the Familial Mediterranean Fever Gene
Pyrin
Chemotactic-factor inactivator
C5a
PMN
C5a
PMN
C5a
Explosive inflammatory reaction

Discussion Points: Genome-wide Methods

- Genome/exome sequencing as a first vs. last resort
- Need to have a time element linked to clinical utility
- How many sequences do you have to do to get a significant clinical aberration that needs attention?
- 3% of healthy Geisinger MyCode patients had clinically significant variants in the Geisinger 76 (ACMG 56 + 20)
- Cost of genome sequencing chemistry does not capture costs associated with interpretation and therapy changes
- Mechanism for maintenance in EHR payment for and re-interpretation of genome sequence: variant, gene and phenotype level
- Future ideal is that genome sequencing could be done once to inform future care; current reality is that technology is evolving and coverage is not perfect and sequencing will likely have to be repeated

Lunch Roundtable Report-Out 1: Building a Coalition

IGNITE
Implementing GeNomics In pracTicE

- Need to clarify what the coalition is trying to accomplish
- What existing organizations can be built upon?
- Who are the stakeholders?
- Payers don't have the resources to drive the coalition but need to be active participants

Lunch Roundtable Report-Out 2: Evidence Needed

- Need more evidence on downstream costs
- Looking to guideline-setting organizations
- Peer-reviewed publications are critical
- Large payers gather/analyze own evidence to make decisions
- In vitro dx manufacturers could support studies to generate evidence
- How is "change in care" defined?

Lunch Roundtable Report-Out 3: Designing Research and Clinical Protocols

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Implementing GeNomics In pracTicE

- RCT not often possible
- Need to focus on high clinical value conditions or diseases vs. gaining reimbursement
- Challenging to get payers and manufacturers to share the risk
- Use modeling before starting study
- Work closely with payers up front
- Economic analysis not the most critical factor in study design but should be considered
- Look at dx not as an end but how affects patient care

Lunch Roundtable Report-Out 4: Disseminating the Evidence

- Need for a central database
- Letters of medical necessity clearinghouse
- Payers make decisions based on guidelines, publications and national meetings
- Medicaid takes input from patients and advocacy groups
- Regular newsletter with updates on genomic evidence advances would be of value—more than quarterly

Preliminary Summary of Key Recommendations

- A standardized process for providing genomic clinical utility information is needed
- Coverage considerations should include communication of genetic results
- Coverage and EHR models should promote utilization of existing genomic information including whole genome sequence as an ongoing resource

Next Steps in Payer Engagement Process To Work on in the Next 6 Months

- Proceedings to be published at ignite-genomics.org
- Manuscript will be submitted to a peer-reviewed journal
- Strategic plan for
  - Ongoing efforts to engage stakeholders and address challenges
  - Obtaining resources to support these efforts