Cores in Support of Impactful Innovation: the Healthy Oregon Project

JACKILEN SHANNON, PHD, & CHRIS HARRINGTON, PHD
WESTERN ASSN OF CORE DIRECTORS
ANNUAL MEETING 2023
Healthy Oregon Project (HOP)
A Resource for Research
Presented by: Jackilen Shannon, PhD
I have no financial disclosures, real or perceived conflicts with the work I am presenting today.
What is the Healthy Oregon Project?

HOP is a research project that aims to involve >100,000 Oregonians in a large, sustainable cohort.

To learn about how a person’s genetics, health, behaviors and environment, affect risks of cancer and chronic diseases.

Data saved to a secure and privacy-protected repository of information that can be used to answer many different questions about health.
Supporting Collaboration and Innovation by Design

**Recruitment Assistance**
HOP as resource to engage participants

**Ancillary Studies**
Collect additional data Existing and new participants

**Healthy Oregon Project**

**Driver Projects**
Drive HOP recruitment

NCI Moonshot
Population-based screening for HBOC & Lynch
HOP Driver Scientific Project  #1
Funded as a Moonshot Project by the National Cancer Institute:

MPI – Paul Spellman, Jackilen Shannon

**Question:** Is screening the general population effective and sustainable.
- **Effective** == do screened individuals alter their health care to reduce their risk of dying from cancer
- **Sustainable** == are the costs per QALY under $50,000 and is the health care system capable of meeting demand

Comparing HOP participants to patients receiving standard guideline based genetic screening, and existing cancer patients offered screening

1. Adherence to current guidelines for screening and prophylactic intervention.
2. Efficiency of cascade testing.
HOP Genetic – Our First Driver Project
WHY?

~1 M People Have HBOC, Lynch or another Significant Inherited Cancer Syndrome

- Only about 20-30% are aware of their syndrome
- HBOC >50% lifetime risk of breast cancer
- HBOC > 30% lifetime risk of ovarian cancer. >20% die of ovarian cancer
- Lynch > 50% lifetime risk of colon cancer
- Knowing you are Lynch + can result in 14 QALY saved
- Currently only high-risk families are tested because of real and perceived costs and significant limitations in clinical service because of limited # of counselors
- Clinical trial to test efficacy of screening all adults for HBOC and Lynch
NCT04494945: Approaches to Identify and Care for Individuals With Inherited Cancer Syndromes

Aim: Evaluate the effectiveness and sustainability of heritable cancer syndrome testing in the two novel testing populations as compared to current practice.

• Enrollment via Healthy Oregon Project App
• Population 1: Everyone
• Population 2: Those with cancer
• Test: 90% sensitive. Very low-cost.
• NOT for those who meet current genetic testing guidelines.

Success Will Change Standard of Care
WHAT Is HOP Screening For?

Inherited Cancer Syndromes
(5-10% of all cancers)

Population-based **genetic testing** for known cancer-related genetic mutations.

- **32 genes** associated with increased risk of cancer
- Medically actionable per NCCN guidelines
## HOP Gene Panel

Genes chosen based off of Color's/Myriad's Hereditary Cancer Panels and by HOP team

<table>
<thead>
<tr>
<th>Gene</th>
<th>Chromosome</th>
<th>Coordinates</th>
<th>Notes</th>
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<td>chr3</td>
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<tr>
<td>TSC2</td>
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*Only 2 probes covering a specific site:
- **CDK4**: chr12:g.58145429-58145431 (codon 24)
- **MITF**: chr3:g.70014091
- **POLD1**: chr19:g.5090713
- **POLE**: chr12:g.133250250

**Only probes covering areas known to contain large deletions**
- **GREM1**: 2 probes every 2.5KB from GREM1 5' UTR to **SCG5** and coding exons of **SCG5** and **GREM1**. See Myriad Approach
- **Extra Region**: Chr15:g.32988815-33021692

***Exons 12-15 not analyzed in **PMS2** due to high homology with pseudogene

Hg19 coordinates. Refseq Annotation
Return of Genetic Screening Results

NEGATIVE: provided via a notification letter that is provided in the Healthy Oregon Project App.

POSITIVE: any participant with a positive result will be contacted by an OHSU genetic counselor. Results will be explained in detail, including recommendations during a phone consultation.
Receiving Positive Results

OHSU Genetic Counselor

Kelly Hamman
Amelia Mulford

Consult for Results

HOP Participant Navigator
Ryan Lutz

Resource Connector
**How to participate in HOP**

**STEP 1:** Download secure app on iOS/Android

**STEP 2:** Review information about HOP and sign an electronic consent in the app to participate

**STEP 3:** Create a secure account

**STEP 4:** Explore your options for participating (DNA screening & Surveys)

**STEP 5:** If you choose to donate your DNA for genetic screening, request a HOP Kit and receive it in the mail.

HOP app is HIPAA compliant!
How are we Doing?
Enrollment as of 05/01/23 = 38,140

• Pre-COVID 3,827 (~12 months of recruitment)
  • Events and vending machines
• Post-COVID (since October 2020 ~30 months)
  • 34,313 participants enrolled
  • Social media, word-of-mouth, attendance at community events
  • 31,609 (92%) Consented to genetics screening and 29,880 (87%) requested a mailed kit
  • 23,415 Samples received in the lab (78% return rate)
  • 20,177 Tests results returned to date
  • 835 (4.1% - though anticipate closer to 5%) received genetic counseling for a positive result.

With over 40,000 participants enrolled in HOP since 2018 that brings us to over 1% of the adult population in Oregon.
Integrated Genomics Laboratory & the Healthy Oregon Project

PRESENTED BY: CHRIS HARRINGTON, PHD
ASSOC DIRECTOR - INTEGRATED GENOMICS LAB/DIRECTOR - GENE PROFILING SHARED RESOURCE

OCT 13, 2023
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Integrated Genomics Laboratory
https://www.ohsu.edu/integrated-genomics-laboratory

INTEGRATED GENOMICS
(Investigators can enter this workflow at any stage)

Coordinated pipeline of services which can be accessed at whatever point researcher requires
Integrated Genomics Laboratory (IGL) & the Healthy Oregon Project (HOP)

What HOP needed –
Inexpensive, reliable, high-throughput DNA extraction service for long term genetic screening project

Why reach out to IGL?

- Recent acquisition of high-throughput sample processing robot
- Expertise and experience of core staff
- Flexibility of core (compared to diagnostics lab)
- History of research support and collaboration between the IGL cores and Knight Cancer Institute researchers
IGL/HOP Collaboration | The Plan

Use IGL resources to develop standardized DNA extraction workflow for HOP samples
Knowledgeable, experienced staff
BSL2 Hood
High-throughput equipment

Challenges:
Protocol development
- Match to saliva collection kit
- Cheap & fast
Clinical testing approved laboratory for the extractions
Dedicated staff for routine throughput

DNA extraction robot
Liquid handling robot
Fluorescent plate reader
IGL/HOP Collaboration | The Setup Team

IGL

Trevor McFarland  Britt Daughtry  Sam Medica

HOP researchers & Knight Diagnostics Lab (KDL)

- Sarah McCabe, Manager, Genomics Lab/KDL
- Christopher Corless, Medical Director/KDL
- Paul Spellman, HOP PI/CEDAR & KCI
- Katie Johnson-Camacho, Sr. Human Subjects Research Specialist/CEDAR
- Gregory Goh, Molecular Technologist/KDL
- Travis Hayes, Sr. Specimen Processing Specialist/KDL
- Jane Thanner, Mgr/KDL Support Team/University Applications/ITG
- Other members of KDL

Aaron Larson – IGL Project Coordinator
(key for organizational support & communications)
IGL/HOP | Workflow Development

Our starting point –

- Platform: QIAGEN QIAsymphony robot
- Extraction kits: QIAsymphony DNA extraction kits
- Good partnership with QIAGEN technical and sales staff

Issues to address –

1. standardized sample intake, storage and transfers
2. sample preprocessing for QIAGEN protocol
3. saliva volumes needed for required yields
4. procedures to insure sample accuracy throughout multi-step process
5. information documentation and sharing
6. minimizing costs
IGL/HOP | Saliva DNA SOP

Saliva DNA Extraction Workflow (IGL)

- Recommended input = 10 mls saliva in mouthwash
- Turnaround times = 96 to 192 per week (routine; more possible)
- Minimum DNA concentration threshold for library prep = 5 ng/ul
  - but lower concentrations are working

Sequencing and gene variant analysis/KDL
IGL/HOP | CAP lab set-up

We needed to establish a College of American Pathologists (CAP) accredited laboratory to process saliva samples for genetic testing.

Our starting point –

No history of CAP/CLIA lab set-up or operations under these requirements

Partnered with members of the Knight Diagnostic Lab with primary support from Sarah McCabe

Required steps –

1. compliant laboratory set-up
2. documentation (lots of it!)
3. formalized staff training and competency reviews
4. College of American Pathologist (CAP) licensing
IGL/HOP | Throughput success !!!

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<thead>
<tr>
<th>Calendar Year</th>
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<td>2023 (thru June)</td>
<td>2784</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>23232</strong></td>
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Samples Processed (Including NTCs)
IGL/HOP | Hiccups & Ongoing Challenges

• Initial CAP surprise inspection
• Unexpected staff resignations  
  • only one full time HOP technician
• COVID pandemic

Ongoing Challenges

• Maintaining well-trained and adequate staff
• CAP lab regulatory maintenance with limited staff
• CAP requirements impact on rest of IGL activities/team
• High demand on IGL/HOP staff time during periodic lab inspections
• Adjusting to swings in HOP sample intake numbers
IGL/HOP | Benefits to healthcare mission, research community, and the IGL

- Reliable partner for HOP – over 20,000 DNA samples delivered with extremely low failure rates.
- IGL HOP staff became key contributors to set up of COVID testing lab at OHSU (beginning March, 2020).
- IGL staff better informed on issues of working with clinical specimens leading to more insightful support of core projects involving patient samples across campus.
- Aspects of CAP compliance requirements translated to better IGL staff training, improved equipment management protocols, and improvements in bench practices and SOPs in other core service areas.
**Patient Education Working Group**
Sue Williams
Rebecca Siego-Coyle

**Knight Diagnostics Lab**
Chris Corless
Sue Richards
Gregory Goh
Amiee Potter
Arpita Kulkarni
Sarah McCabe
Catherine Driscoll

**Integrated Genomics Lab**
Chris Harrington
Jacob Buitrago
Britt Daughtry
Tiana Weeks
SJ Kim
Syber Haverlack
Jinah Kim

**OHSU and University or Oregon Marketing**
Allen Tomlinson
Autumn Shafer
Darsen Campbell-Prissle

**Internal Advisory Board**
Lisa Coussens
Gordon Mills
Rosalie Sears
Kerri Winters-Stone
Aaron Grossberg
Gloria Coronado
Emily Ho
(Sadik Esener)

**Genetics**
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Kelly Hamman
Amelia Mulford
Brian O’Roak
Andrew Adey

**Providence**
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JB Rinaldi
Lindsey Dickey
Bill Wright
Aimee Shaykin
Walter Urba

**HOP Staff**
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Madeleine Mathis
Marit Simmons
Vanessa Serrato