



Cores in Support of Impactful Innovation: the Healthy Oregon Project

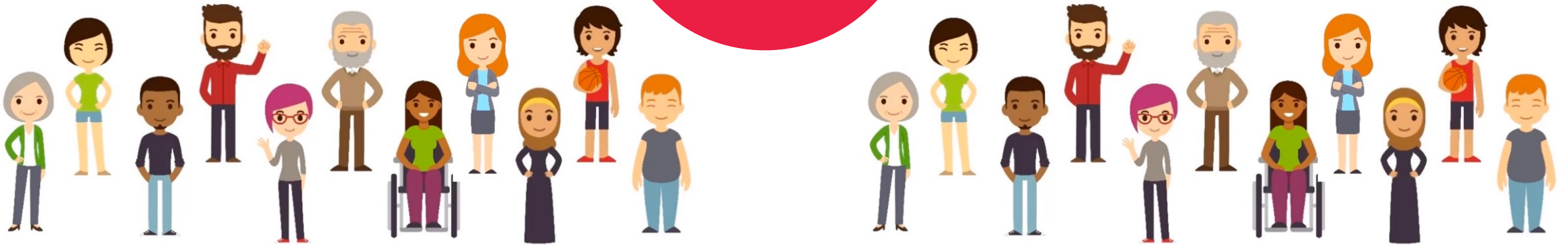
JACKILEN SHANNON, PHD, & CHRIS HARRINGTON, PHD

WESTERN ASSN OF CORE DIRECTORS

ANNUAL MEETING 2023



HEALTHY OREGON PROJECT



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.



HEALTHY
OREGON
PROJECT

40,000 Oregonians
Have Joined HOP Research!



Supporting Collaboration and Innovation by Design

Recruitment Assistance

HOP as resource to engage participants



Ancillary Studies

Collect additional data
Existing and new participants

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.
3. Costs and effectiveness, associated with genetic screening models.



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

ATM	MEN1	BAP1
MITF*	RAD15C	BARD1
MLH1	RAD15D	BMPR1A
MSH2	RB1	BRCA1
MSH6	RET	BRCA2
MUTYH	SMAD4	BRIP1
NBN	STK11	CDK4*
PALB2	TERF2IP	CDKN2A
PMS2***	TERT	CHEK2
POLD1*	TP53	POT1
APC	POLE*	PTEN
TSC1	TSC2	

*Only 2 probes covering a specific site:
CDK4: 12: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.



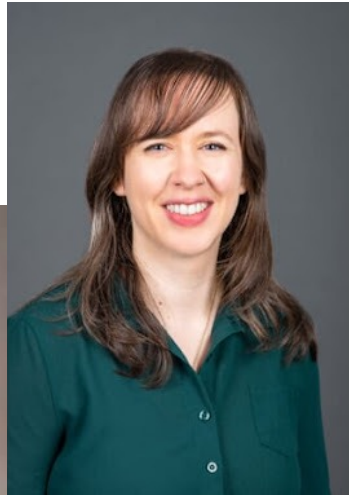
Receiving Positive Results

OHSU Genetic Counselor

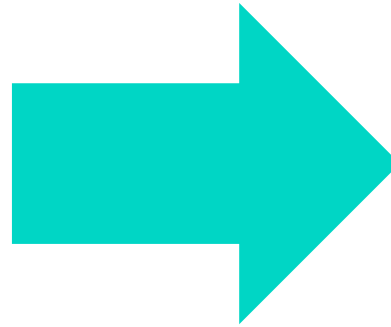
HOP Participant Navigator

Ryan Lutz

Kelly Hamman



Amelia Mulford



Consult for Results

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!

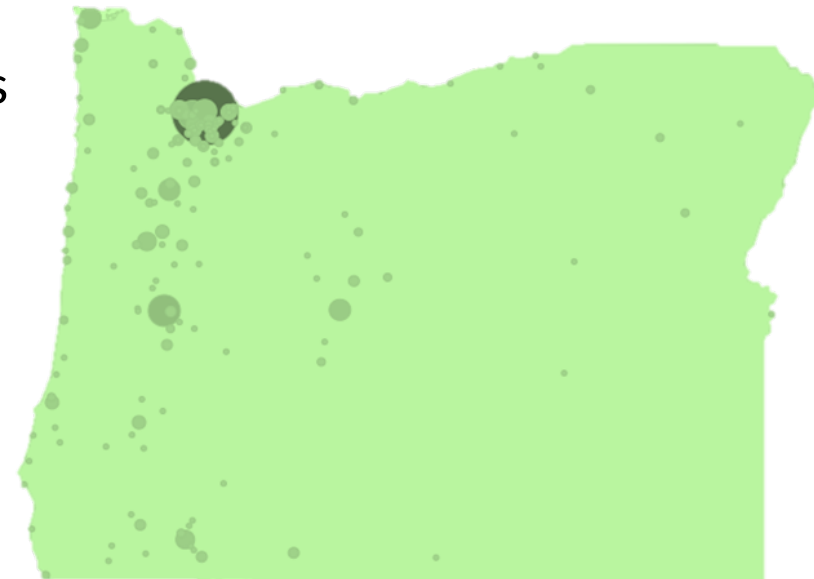


How are we Doing?

Enrollment as of 05/01/23= 38,140

- Pre-COVID 3,827 (~12months 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.





University Shared Resources

Integrated Genomics Laboratory & the Healthy Oregon Project

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PRESENTED BY: CHRIS HARRINGTON, PHD

ASSOC DIRECTOR - INTEGRATED GENOMICS LAB/DIRECTOR - GENE PROFILING SHARED RESOURCE



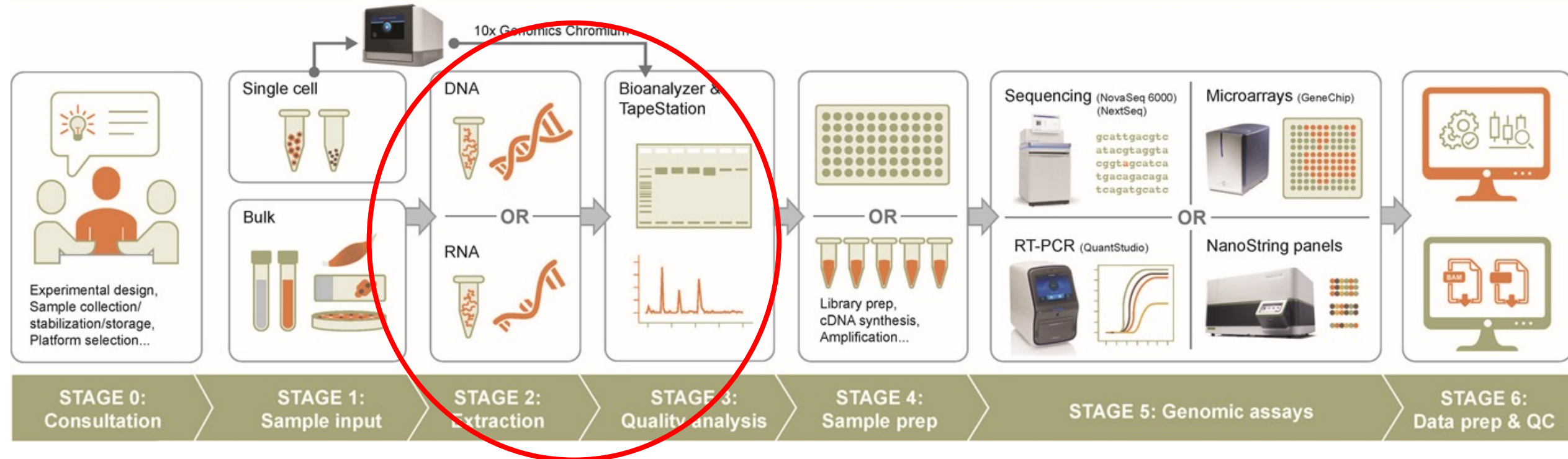
OCT 13, 2023

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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



**QIAGEN QIA Symphony
Isolation Robot**
Automated RNA/DNA
extraction protocols

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



DNA extraction robot



Liquid handling robot



Fluorescent plate reader

Challenges:

Protocol development

- Match to saliva collection kit
- Cheap & fast

Clinical testing approved laboratory for the extractions

Dedicated staff for routine throughput

IGL/HOP Collaboration | The Setup Team

IGL

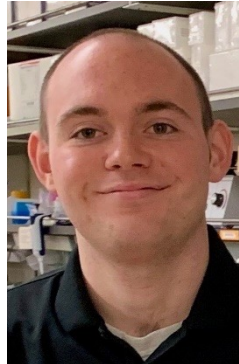
Trevor McFarland



Britt Daughtry



Sam Medica



Aaron Larson – IGL Project Coordinator
(key for organizational support & communications)

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

IGL/HOP | Workflow Development

Our starting point –

Platform: QIAGEN QIA Symphony robot

Extraction kits: QIA Symphony 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

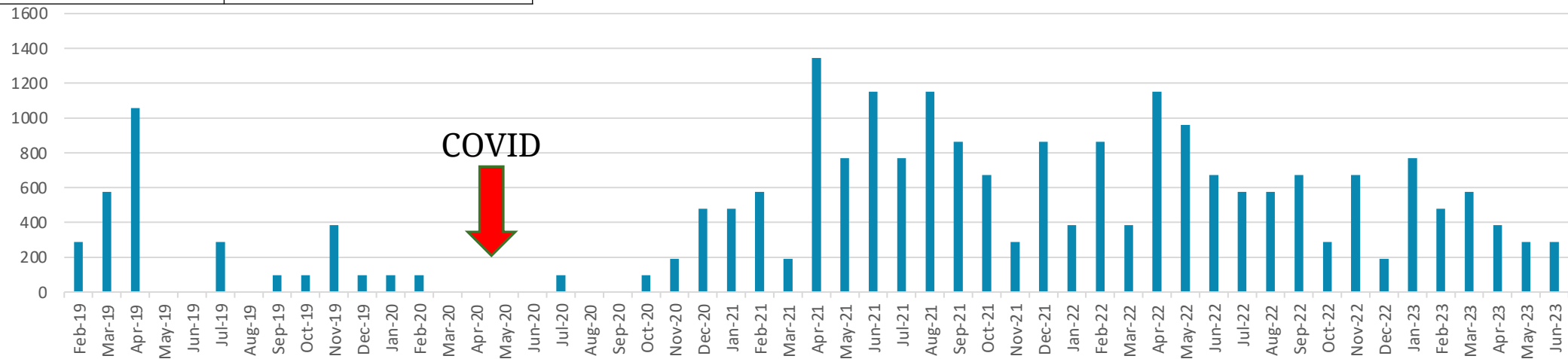
Required steps –

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 !!!

Calendar Year	Samples Processed
2019	2880
2020	1056
2021	9120
2022	7392
2023	2784 (thru June)
Total	23232

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

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Genetics

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Tiana Weeks

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Jinah Kim

Providence

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JB Rinaldi

Lindsey Dickey

Bill Wright

Aimee Shaykin

Walter Urba

OHSU and University of Oregon Marketing

Allen Tomlinson

Autumn Shafer

Darsen Campbell-Prissle

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Gordon Mills

Rosalie Sears

Kerri Winters-Stone

Aaron Grossberg

Gloria Coronado

Emily Ho

(Sadik Esener)

HOP Staff

Ryan Lutz

Madeleine Mathis

Marit Simmons

Vanessa Serrato

Thank You