Incorporating a Clinical Project into Your Core Lab

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IGL CAP Technical Supervisor | Sr. Core Scientist | Lab Manager
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What is CAP?

CAP (College of American Pathologists)

• Private, non-profit organization. Provides accreditation and certification services for clinical laboratories.

• CAP accreditation is voluntary. Laboratories choose to seek CAP accreditation to demonstrate their commitment to quality.

• Comprehensive evaluation of laboratory quality, detailed assessments of laboratory processes, quality management systems, and technical proficiency.
Why We Started – The Healthy Oregon Project

- CEDAR funding and NIH Moonshot Grant to Paul Spellman, Ph.D. and Jackie Shannon, Ph.D., R.D., M.P.H.

- **No cost** DNA screening for Oregonians.

- Analyze saliva sample by NGS for the pathogenic/likely pathogenic medically actionable variants in 32 genes associated with cancer and heart disease risk.

- Germline not somatic mutations.

- Provide a medical record to patient who has a positive result – **requires a clinical laboratory!**
Why We Started

• Knight Diagnostic Laboratory (KDL)
  • Fully operational clinical lab already CAP/CLIA certified and accredited. Sample accessioning group, automated library prep robot, NGS, and bioinformatics. No high throughput extraction robot.

• Integrated Genomics Laboratory (IGL)
  • Research Core with expertise high – throughput DNA extraction & normalization automation. No clinical experience or CAP accreditation.
Healthy Oregon Project Workflow

Figure 1. Pipeline for the enrollment of HOP participants and sample workflow

HOP participants sequenced as of April 15, 2022. Differences in numbers are reflective of the fluid pipeline and time it takes samples to process from consent in the HOP app through next-generation sequencing (NGS) and analysis. IGL, Integrated Genomics Laboratory, core laboratory; KDL, Knight Diagnostic Laboratories, clinical laboratory.
Dr. Harrington is a Research Associate Professor and Co-Director of the Integrated Genomics Laboratory at OHSU, specializing in RNA and DNA analysis technologies. She has worked on the HOP project since the proof of concept stage and has co-authored HOP publications.

In 2018, Britt joined the IGL team and initiated the implementation of the HOP IGL workflow. Britt’s role has been instrumental in ensuring the completion of CAP documentation, training programs, and laboratory operations, all in strict adherence to CAP specifications. During the pandemic, her CAP regulation expertise led her to become the Interim Technical Coordinator at the OHSU COVID Testing Lab.

In the Spring of 2022, Jake became a valuable addition to the IGL HOP team. His contributions have played a pivotal role in maintaining peak throughput and efficiency in HOP sample processing. With Jake’s keen attention to detail, strong work ethic, and innovative efficiency ideas, the IGL has achieved rapid turnaround times for sample processing.

Jinah, a proficient scientist, is taking on a supportive role within the HOP team. While currently in training, Jinah is poised to become an important figure in HOP IGL operations.
Population screening shows risk of inherited cancer and familial hypercholesterolemia in Oregon


Summary

The Oregon Health Project (OHP) is a nationwide cohort study that is building large research repository and enhancing the health of Oregonians through providing access to unique longitudinal samples to researchers for a disease-free cognitive, physical, and emotional health. The project collects samples related to inherited cancer and familial hypercholesterolemia. This type of national population screening data reflects the individual who may experience an isolated or familial medical appointment. Screening for these diseases is highly recommended in the United States by the American College of Physicians for individuals who may benefit from early intervention. This includes using a variety of high-throughput testing as an evidence-based screening tool that may assist in identifying these individuals at high risk for cancer and cardiovascular disease. Additionally, conducting annual and bi-annual comprehensive physical exams and checking for these disorders through a more frequent screening tool may be beneficial. Population-based screening and timely intervention can help prevent cancer and cardiovascular disease and improve overall health outcomes.

Introduction

Early detection of inherited genetic diseases through genetic testing or recognizing individuals who have a family history of these diseases can potentially increase survival rates and is predicted to lower healthcare costs for the affected individuals. However, without a strong family history of disease or other risk factors, an individual is unlikely to meet testing guidelines. Therefore, it may be difficult to identify those individuals at increased risk who may require surveillance due to their genetic profile. This study aims to identify individuals who meet the criteria for the type of disease being studied. Even with a positive family history or another risk factor, there may be barriers to early detection and determination of an individual’s risk due to costs associated with genetic testing or obtaining a proper referral. Genetic population-based screening can help identify these barriers and has successfully been used to gain this information in the past.

Several population screening models have been implemented across different countries, including the HOP (Oregon Project) and the Cancer Moonshot. The Oregon Project and the Alzheimer’s Disease Initiative have implemented programs that use population-based screening to identify individuals who are at risk for these diseases. These models include the use of genetic testing to identify individuals at high risk for disease, as well as education and support for individuals at increased risk. The HOP is an ongoing project that aims to build a large research repository and enhance the health of Oregonians. It is supported by an additional Oregon’s Cancer Early Detections Advanced Research Center. A self-funded federally funded National Cancer Institute and the Health and Human Services initiative clinical trial that allows for the use of this information has been initiated. The HOP is funded by a public-private partnership, which is a collaborative effort between the Oregon Health Authority and the Oregon Health and Science University.

The article was published in the American Journal of Human Genetics on 12th May 2023.
HOP Impact – On a Personal Level

• Friend found HOP through my social media post.
• Genetic counselor informed the mutation increases her lifetime risk of breast cancer up to 40%.
• Now sees a Breast Specialist and a Gynecological Oncologist.
• Obtains yearly breast MRIs and will seek yearly early detection methods for breast and ovarian cancer.
• “For all of this I am so grateful I learned about the Healthy Oregon Project”
Other Opportunities – Project for FDA Petition

- OHSU Hayflick lab gene expression clinical study for FDA petition.

- Pilot validation study and clinical sample processing workflow performed under CAP accredited laboratories – IGL and KDL.

- RNA extraction from blood and RNA normalization by the IGL → RT-qPCR testing by the KDL.

- The workload for CAP documentation was drastically reduced because HOP documentation sufficed in many instances or served as highly detailed templates.

- Added additional service fees for CAP Laboratory documentation, operations, consultations, and covering costs associated with accreditation (5% of total project cost).

Why They Are Glad They Chose Us.

Designing and testing of a project/experiment: “The IGL team offered multiple sessions to discuss experimental design, list of control samples and optimization. We even had multiple chances to run some test samples. IGL did not offer cookie-cutter advice. They (the IGL) provided tailored guidance and solutions and had a deep understanding of our project’s unique needs.”

Convenient sample delivery and fast delivery of results: “It was absolutely easy to hand samples over to IGL, thanks to meticulous coordination and location (we are in the same building). Also, the turnaround time for extraction was very short with efficient data delivery.”

Well-coordinated collaboration: “Our project involved total human blood RNA extraction by IGL and these samples needed to be delivered to KDL for the next step. The IGL made the transfer of samples to the KDL extremely easy and I did not need to do anything. All RNA sample data was shared without a single glitch.”

-Suh Young Jeong, Ph.D. – COASY Project Manager
Other Opportunities – COVID Testing to Diagnostic Lab

• COVID-19 pandemic starts → IGL HOP members fully shifted to creating and operating the OHSU COVID-19 Testing Laboratory.

• Technical and administrative skills acquired from HOP directly transferred to a CAP lab COVID-19 RNA extraction workflow.

• The construction, stocking and staffing of the lab was done in 14 days.

• This lab that CAP IGL members helped build is now the state-of-the-art, full-spectrum OHSU Clinical Molecular & Microbiology Lab – just down the hall from the IGL, and a collaborative partner.
The CAP Accreditation Process

**Year 1–Weeks 1-12**

1. Request application*
2. Review welcome kit
3. Complete application

**Year 2**

Receive CAP notification to reapply

4. Receive customized checklists
5. Schedule inspection date**

**Year 1–Weeks 35-52**

6. Host inspection day
7. Respond to deficiencies within 30 days
8. Support CAP review of responses
9. Receive certificate of accreditation

**Perform self-inspection and maintain continuous compliance**

10. Review of self-inspection
• Comprehensive sets of guidelines and standards.
• Designed to help laboratories ensure the accuracy, quality, and safety of their services.
• Depending on the work you are doing, you will be assigned customized checklists.
• The IGL CAP lab has the following checklists:
<table>
<thead>
<tr>
<th>CAP Checklists – What Do They Cover?</th>
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</thead>
<tbody>
<tr>
<td><strong>Laboratory General:</strong></td>
</tr>
<tr>
<td>• Quality management system</td>
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<tr>
<td>• Specimen collection and handling</td>
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<tr>
<td>• Specimen chain-of-custody</td>
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<tr>
<td>• Specimen transport and tracking</td>
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<tr>
<td>• Personnel qualification and</td>
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<tr>
<td>requirements</td>
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<tr>
<td>• Training and competency</td>
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<tr>
<td>• Physical facilities</td>
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<tr>
<td>• Laboratory safety</td>
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<tr>
<td><strong>All Common:</strong></td>
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<tr>
<td>• Policy and procedure manuals</td>
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<tr>
<td>• Reagents labeling, storage,</td>
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<tr>
<td>handling, disposal, etc.</td>
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<tr>
<td>• Instruments and equipment</td>
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<tr>
<td>maintenance</td>
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<tr>
<td>• Thermometers and temperature</td>
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<tr>
<td>dependent equipment and environments</td>
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<tr>
<td>• Pipette calibrations</td>
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<tr>
<td>• Test method validation</td>
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<tr>
<td>• Individualized quality control plans</td>
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<tr>
<td><strong>Molecular Pathology:</strong></td>
</tr>
<tr>
<td>• Molecular assay validation</td>
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<tr>
<td>• Turnaround time</td>
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<tr>
<td>• Specimen records</td>
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<tr>
<td>• Metrics for specimen quality and</td>
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<tr>
<td>quantity</td>
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<tr>
<td>• Specimen storage and retention</td>
</tr>
<tr>
<td>• Positive and negative controls</td>
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<td>• Assay performance monitoring</td>
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**CAP Requirements for IGL HOP Workflow**

- Receive samples from KDL via courier
- SOP for sample transfer/receiving/transport
- Policies for sample storage and environmental monitoring
- Policies for sample rejection criteria
- Error log for rejected samples
- Designated, secure storage area
- Temperature monitoring for storage areas (4°C, -20°C, and RT) checked daily
- Trained personnel with training and competency documents on file
- Chain of custody documentation
**CAP Requirements for IGL HOP Workflow**

- Receive samples from KDL via courier
- Concentrate saliva cells, lyse, barcode check and transfer to robot-compatible tubes
- Initial pilot validation study on file
- SOP for sample processing workflow
- Barcode/sample ID check file
- Certification documentation for biosafety cabinet and centrifuge PMs
- Safety policies and posted signs for biohazardous samples
- Inventory and specimen tracking documentation
- Chemical hygiene plan
- Maintenance logs for equipment cleaning
- Calibration documentations for pipets
- Separate, “clinical use only” consumables, stored in secure location.
**CAP Requirements for IGL HOP Workflow**

1. **Receive samples from KDL via courier**
   - Images showing samples in tubes.

2. **Concentrate saliva cells, lysed, barcode check and transfer to robot-compatible tubes**
   - Images showing concentration process.

3. **Extract DNA next day using QIAsymphony.**
   - Images showing QIAsymphony machine.

4. **Quantify & Normalize DNA with using Liquid handling robot and Plate Reader**
   - Images showing quantification and normalization process.

- Consumables lot recalls & actions taken
- Logs and reports for instrument crashes and errors
- Documentations for PMs and repairs
- Reagent lot tracking
- Reagent lot tests with “+” and “-” controls
- Failed standard curves and control testing stored on file
**CAP Requirements for IGL HOP Workflow**

- Receive samples from KDL via courier
- Concentrate saliva cells, lysed, barcode check and transfer to robot-compatible tubes
- Extract DNA next day using QIAsymphony.
- Transfer documentation and data to KDL via secure cloud service
- Quantify & Normalize DNA with using Liquid handling robot and Plate Reader

- Patient data transfer must be secure & HIPAA compliant
- Policies for retention of records and materials that must comply with laws and regulations
Receive samples from KDL via courier

Concentrate saliva cells, lysed, barcode check and transfer to robot-compatible tubes

Extract DNA next day using QIAsymphony.

Quantify & Normalize DNA with using Liquid handling robot and Plate Reader

Transfer documentation and data to KDL via Secure Cloud Service

Transfer Normalized DNA plate via courier to KDL

CAP Requirements for IGL HOP Workflow
The Inspection

• First inspection *should* be announced, on-site, and pre-arranged with the inspection team leader.

• Window of inspection will be ~6 months after you complete online application.

• CAP inspector will review the laboratory’s policies and procedures, observe personnel performing services, and review records.

• All checklist items relevant to your CAP lab are open for review.
The Inspection

All subsequent inspections*:
• Every 2-years
• You need to reapply
• Unannounced
• 1 hour notice given
• Within 90 days of inspection anniversary
• You can request blackout dates
• Self-inspections the year in between
CAP Deficiencies

- Inspectors want to find deficiencies, big or small.
- 30-days to officially respond to deficiencies.
- **Phase 1** deficiencies compromise the quality of the services without endangering the health and safety of patients, clients, or personnel.
  - Written response describing corrective action.
- **Phase 2** deficiencies may have a serious impact on the quality of services or may endanger the health and safety of patients, clients, or personnel.
  - Response of corrective action and supporting documentation.
- Potential consequences of failing to correct deficiencies are risk of not obtaining or losing CAP accreditation and/or probation.
CAP Deficiencies - Examples

• Failure to monitor room temperature. Phase 1.
  • Action: Installed Aeroscout room temperature monitors. Perform daily checks of temps, alert system set up if temps out of range, monthly environmental monitoring summary reports.

• Failure to lot validate diagnostic grade extraction kits. Phase 2.
  • Action: Implemented lot testing SOP for DNA extraction kits using pooled positive controls. QC metrics developed for determining satisfactory lots for extraction kits.
Lesson Learned & Advice!

• CAP accreditation improves your laboratory operations for research projects too.
• Find mentors and collaborators.
• Negotiate sharing instrument service contract expenses and personnel FTEs.
• Shared space/equipment used for clinical work is open to inspection.
• Understand if your lab will also need to be regulated by CLIA (Clinical Laboratory Improvement Amendments).
• Obtain copies of the CAP checklists to get a sense of what is required.
• Have the required documentation, operations, a validation study in the works.
• Perform a mock inspection.
Thank you!

Current & Past IGL Team Members:
• Chris Harrington, Ph.D.
• Trevor McFarland
• Samuel Medica
• Tiana Weeks
• Jacob Buitrago
• Syber Haverlack
• Jinah Kim, Ph.D.

KDL/CEEDAR Team Members:
• Sarah McCabe
• Christopher Corless, MD
• Katie Johnson-Camacho
• Madeleine Matheis
• Gregory Goh
• Travis Hayes
• Other members of KDL/CEEDAR

Qiagen Members:
• Karen Fortenberry
• Tony Stepan
Questions?

Britt Daughtry, Ph.D.
CAP Lab Technical Supervisor | Sr. Core Scientist | Lab Manager
13 October, 2023
Other CAP Checklists

- Anatomic Pathology
- Biorepository
- Chemistry and Toxicology
- Clinical Biochemical Genetics
- Cytogenetics
- Cytopathology
- Flow Cytometry
- Forensic Drug Testing
- Hematology and Coagulation
- Histocompatibility
- Immunology
- Microbiology
- Urinalysis
OBJECTIVES

- What is CAP?
- Why We Started a CAP Lab
- Healthy Oregon Project Workflow
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- HOP Impact
- Other Opportunities
- The CAP Accreditation Process
- CAP Checklists
- CAP Requirements for IGL HOP Workflow
- The Inspection
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- Lesson Learned & Advice