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Mapping the current state of cancer clinical omics

Catherine L. Schlechter

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MAPPING THE CURRENT STATE OF CANCER CLINICAL OMICS

By

Catherine L. Schlechter

A MASTER'S CAPSTONE PROJECT

**Presented to the Department of Medical Informatics & Clinical Epidemiology
and the Oregon Health & Science University**

School of Medicine

**in partial fulfillment of
the requirements for the degree of**

Master of Biomedical Informatics

May 2015

School of Medicine
Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's Capstone Project of

Catherine L. Schlechter

Mapping the Current State of Cancer Clinical Omics

Has been approved

Shannon McWeeney, PhD/Capstone Advisor

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Abstract

My capstone project was two-fold: (1) To create and administer a survey to bioinformatics leaders at 63 National Cancer Institute (NCI) Cancer Centers to assess the current use of Next Generation Sequencing (NGS) in the clinical cancer setting; and (2) To review and summarize highlights from the recent 2014/15 CI4CC Clinical Genomics Workshops, hosted by the non-profit consortia, Cancer Informatics for Cancer Centers (CI4CC), in conjunction with the NCI. This summary will help frame a white paper that will be published later this year.

Introduction

NGS technology is rapidly becoming a widely used tool in clinical oncology.¹ The ability to molecularly characterize tumor tissue on an individual level can reveal critical information about a patient's prognosis and ideal treatment options.²⁻⁴ In addition, the information can help match potential participants with clinical trials when approved treatments are not available.⁵ As the clinical demand for NGS testing grows, there has been a dramatic increase of laboratories are offering a variety of clinical-grade testing options from curated panels to whole exome and genome analysis.⁶ However, surveys of early adopters suggest the 'home brew' nature of informatics pipelines and lack of industry standards has led to inconsistent protocols and reporting methods.^{7,8}

The growing use of NGS technology in the oncology setting and need for industry standards was the focus of the recent 2014/15 joint NCI-CI4CC Clinical Genomics Workshops, hosted by the non-profit consortia, Cancer Informatics for Cancer Centers. The three-part conference series provided a focused forum for cancer informatics leaders to discuss and share their work. Using participating NCI cancer centers as an operational base, a survey was conducted to assess current use of NGS technology in the clinical cancer setting. In addition, a summary of topics covered during the meetings was generated including, but not limited to, current state of variant detection and interpretation, standardization of cancer-omics pipelines, integration of NGS into the electronic medical record (EMR), and current national and international cancer informatics collaborations.

Part 1: NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey

Introduction

In 2014, as part of the NCI-CI4CC efforts to map cancer clinical-omics on a national scale, a survey was administered to informatics leaders at NCI-designated cancer centers. The goal of the survey was to capture the current state of NGS use in the clinical cancer setting from a bioinformatics perspective.

Methods

The survey was developed through Survey Monkey and contained 11 questions (Appendix A). Questions spanned the length of the informatics pipeline from general methods of analysis to reporting of incidental findings.

Survey recipients included 63 (of 68) NCI-designated cancer centers that provided contact information for informatics leaders at their institutions. Recipients included 40 (of 41) comprehensive cancer centers, 18 (of 20) cancer centers, and 5 (of 7) basic laboratories.

Results

A total of 33 (52%) of cancer centers from across the United States responded to the survey. Eighteen (54%) of respondents represented comprehensive cancer centers, 11 (33%) cancer centers, and 4 (12%) basic laboratory cancer centers. For the purpose of this analysis, since basic laboratories by definition do not provide direct care to patients, their responses were not included in downstream analysis. In addition, one respondent indicated they were unsure of what services were offered, if any.

Of the 29 comprehensive and regular cancer centers who responded to the survey, 4 (14%) indicated they are not currently offer NGS services including 2 (50%) comprehensive cancer centers and 2 (50%) cancer centers. However, all four centers indicated they were planning to

implement the technology within 6 months to one year. (Appendix B, Figure 1) In addition, one center indicated they were unsure what, if any, NGS services were offered at their center.

Twenty-four (83%) of 29 cancer centers indicated they are currently utilizing NGS in the clinical cancer setting including 16 (67%) comprehensive cancer centers and 8 (33%) clinical cancer centers. A list of the 24 centers that indicated they are currently offering NGS services is listed in Appendix C.

Sixteen (67%) of these 24 centers that indicated they are offering NGS and went on to provide additional details about how the technology is being used at their facilities including 11 (69%) comprehensive cancer centers and 5 (31%) clinical cancer centers. All of these centers indicated they are offering multi-gene NGS panels. Six (38%) of these centers are also offering whole exome and/or whole genome sequencing. (Appendix B, Figure 2)

Most centers reported testing and analysis was being conducted at least in part within their institution. More specifically, 12/16 (75%) of NGS panels, 6/7 86% of whole exome sequencing, and 4/5 (80%) of whole genome sequencing tests are either entirely or partially conducted in-house. (Appendix B, Figures 3)

In addition, most centers reported analysis was being conducted using a combination of custom and commercial informatics tools. More specifically, 10/16 (63%) of NGS panels, 5/6 (83%) of whole exome sequencing, and 4/4 (100%) of whole genome sequencing utilize a combination of custom and commercial informatics tools. (Appendix B, Figure 4)

Fourteen of 16 centers reported their NGS services are CLIA certified. Two respondents were unsure if the testing offered through their centers was CLIA certified. (Appendix B, Figure 5)

Of the 14 centers that are offering CLIA certified NGS services, all those offering panels (n=14) are performing CLIA sequencing with validation. Three of these centers are also offering CLIA

certified WES, however, the model of testing was research NGS followed by Sanger confirmation.

Of the 6 centers that provided information about reporting incidental findings, 2 (33%) indicated they are reporting incidental findings, 2 (33%) indicated they are no, and 2 were unsure.

Thirteen (of 16 possible) centers provided information about incorporating results into the EMR and all state they either are or will soon be incorporating results into the EMR. Finally, 12 (of 16 possible) centers provided information about re-analysis of results. Five (42%) of these centers reported they are re-analyzing clinical cancer NGS data (either on pre-determined schedule or as requested) to reflect changing variant/annotation information.

Discussion

Among the respondents, 96% are currently or will be soon utilizing NGS in the clinical cancer centers. The dominant NGS platform is panel based with modest use of whole exome and whole genome sequencing.

Part 2: Summary of 2014/15 CI4CC Clinical Genomics Workshops

Introduction

The 2014/15 NCI-CI4CC Clinical Genomics Workshops, hosted by the non-profit consortia, Cancer Informatics for Cancer Centers was a three-part conference series that covered various topics associated with the growing use of NGS technology in the oncology setting. Participants included leaders in the field of next generation sequencing from both academia and industry. The following is a compilation of highlights presented at the meeting and grouped by topic including: Best Practice and Lessons Learned, Looking to the Future, Defining Actionable Results, Annotating and Presenting Results, and Overcoming the O-Gap.

VARIANT DETECTION

Best Practice and Lessons Learned

Contributing presentations from Washington University, Foundation Medicine, and Memorial Sloan Kettering Cancer Center.

NGS is quickly establishing itself as an increasingly important component of a comprehensive evaluation of the cancer patient. The transition from research to use in the clinical setting requires extensive investment including staff with broad expertise, namely in clinical laboratory testing, genomic technologies, and informatics. Before implementation, laboratories must conduct rigorous analytical validation to determine test accuracy and reproducibility. The more comprehensive the analysis, the more potential for targeted treatment options and innovative trial designs. However, to be successful in the clinical setting, the technology must also be a cost effective, timely, and reimbursable tool. There was uniform consensus that gene panels were still the most useful NGS platform for clinical cancer care. Concerns regarding FDA oversight and insurance reimbursement with regard to clinical NGS were also discussed.

Looking to the Future

Contributing presentations from Intel, University of California San Francisco, Moffit Cancer Center, and 7Bridges

The implementation of NGS in the clinical cancer setting highlights the ‘big data’ challenges associated with the technology, particularly for the analysis and storage of huge and ever increasing data sets. Multiple opportunities to optimize and accelerate the NGS analysis pipeline, particularly at the DNA sequencing and variant discovery levels, have been identified. Ongoing efforts are needed to develop and optimize algorithms and pipelines. It was noted that improvements were needed in computing at the chip and system level, as well as addressing the growing need to effortlessly communicate data seamlessly between local and cloud based systems. It was agreed that this requires substantial financial investment and collaborative efforts between multiple centers. The identification and inclusion of stakeholders, such as industry, researchers, clinicians, and patients, is critical.

VARIANT INTERPRETATION

Defining Actionable Results

Contributing presentations from MD Anderson Cancer Center and Actionable Genome Consortium

Actionable genetic alterations are defined as those that are potentially targetable with a proven or investigational therapy. Actionable results should ideally be considered independent of disease type, available clinical trials, and patient eligibility. Defining ‘*actionability*’ is critical to determining the utility of NGS technology in the clinical cancer setting. Ongoing efforts are needed to develop guidelines for assessing actionability. For example, AGC has proposed a class-based system that ranges from variants that should be tested as part of standard of care (i.e. class 1) to those with unknown biological or clinical significance (i.e. class 4). Examples of

evidence used for determining which class a variant belongs to include having been reported in NCCN/ASCO guidelines [ref/link], whether it is an FDA-approved indication, published literature showing a variant is predictive of prognosis or response, or is of value for diagnosis, and evidence from clinical trials. Challenges to assessing actionability occur in the context of equivocal results (ex. copy number changes) and subclonal findings. Our understanding of actionability is constantly changing based on available knowledge and multi-gene panels of 'actionable' genes should be dynamic and evolve as updates occur.

Annotating and Presenting Results

Contributing presentations from MD Anderson Cancer Center, Actionable Genome Consortium, and My Cancer Genome

Clinical annotation is critical as it can guide therapeutic response, phenotype or prognosis, and adverse event.

MD Anderson: Results of the analysis can be accessed through a Cancer Genome Mutation Browser or as an integrated report in the EHR. Annotation is used to maximize the clinicians understanding of actionability and include the following fields: Alteration Type (ex. splice site vs. indel), Functional Significance (ex. activating vs. inactivating), Annotation (free text description of literature review), Actionable Gene (ex. yes vs. no), and Actionable Variant (yes- literature based vs. yes- functionable genomics).

My Cancer Genome: Developed by the Vanderbilt-Ingram Cancer Center, My Cancer Genome is a web-based knowledge resource that's mission is "To curate and disseminate knowledge regarding the clinical significance of genomic alterations in cancer." Content is developed by 65 contributors from 21 institutions, in 10 different countries. The curated information about clinically relevant variants is made available through a website, mobile app, Vanderbilt's EHR, and as a laboratory reporting tool. Information provided for each variant includes: Location of

Gene, Levels of Evidence (ex. FDA approvals, guidelines, published trial results, case reports), Frequency of Alteration in Disease, and Response to Drug Sensitivity and Resistance.

DNA Nexus: Diverse computational methods can provide different results, both with respect to identification of genomic features, as well as the annotation regarding functional impact etc. Both individual and consortia examples were discussed to highlight the potential impact on interpretation. This has implications for how we present uncertainty and “trustworthiness” of results.

Actionable Genome Consortium (AGC): With representation from Industry (Illumina) and leaders from major cancer centers across the country, the Actionable Genome Consortium is focused on the development of best practices and standards for utilizing next generation sequencing in cancer care. The AGC is focused on a comprehensive characterization of the NGS life cycle from sample preparation to clinical reporting. There was tremendous discussion on how best to coordinate these efforts and how individual cancer centers can navigate this.

Overcoming the O-Gap

Contributing presentations from IOM, Friends of Cancer Research, Global Alliance for Genomics and Health (GA4GH), and Actionable Genome Consortium

The operationalization ('O') gap is the space in the innovation lifecycle between the pilot and operational stages of a project. With respect to cancer clinical omics, this is often the gap between research and clinical use (including clinical trials). It was noted that no single organization has access to all the resources required to enable precision medicine, thus a consortium approach is needed to address the size and complexity of problem. Multiple consortium and industry efforts are actively working to develop standards around NGS use in the clinical cancer setting.

Global Alliance for Genomics and Health (GA4GH) an international collaborative effort to “maximize the potential of genomic medicine through effective and responsible data sharing” (cite white paper here- see slide 25). Challenge is that data from millions of samples may be needed to achieve results and progress- i.e. showing patterns that would otherwise remain obscure. In 2014, GA4GH had 180 partners in 25 countries. Efforts are divided into four working groups focused on 4 areas of genomic medicine including: Clinical, Data, Regulatory and Ethics, and Security.

The Actionable Genome Consortium (AGC) provided updates on their development of best practices and guidelines. In addition, they discussed their approaches for promoting collaborative research focused on challenges in oncology genomics.

Discussion

The results of the survey conducted for this project highlight a number of themes that were also discussed at the 2014/15 NCI-CI4CC Clinical Genomics Workshops. The majority (86%) of respondents to this survey (excluding basic laboratories) are currently offering NGS services in the clinical oncology setting and the remaining 4 centers indicated they would be offering the service within the year. All centers are offering NGS gene panels with a smaller fraction offering whole exome and/or whole genome. The near universal use of this technology means these centers have already invested significantly in staff, technology, and education. Of those survey respondents currently using NGS, all were at least offering targeted gene panels. This seems to confirm the growing utility of the testing and is consistent with points made by various presenters during the workshops that gene panels are the most useful NGS platform for clinical cancer care.

However, a little over one third of reporting centers indicated they are also performing WES and WGS. These centers are at the forefront of variant discovery. While the more comprehensive

the analysis, the more potential for targeted treatment options, these centers will rely heavily on the ongoing efforts to develop guidelines for assessing actionability.

In addition, centers offering WES and WGS also face the added challenge of dealing with incidental findings and determining when and how these results will be communicated to relevant parties. Survey results showed a mixed response with only one third indicating they are reporting incidental findings. One respondent provided the additional feedback: “We report variants identified that are not definitively polymorphisms. In rare cases, we will note the association with gene alterations with potential underlying germ-line conditions, but only in the appropriate clinical context and only after discussion with ordering physician.” It’s clear from this comment and workshop discussions that dealing with incidental findings will be complex and will require a thoughtful approach that considers the patient, their circumstances, and the providers involved in their care.

One of the recurring themes at the workshops was concern regarding the lack of regulation and standardization of NGS protocols. One promising trend is that nearly all (88%) centers offering NGS services are doing so under a CLIA certificate which would suggest the centers are developing rigorous internal validation methods for determining test accuracy and reproducibility. However, results of the survey also suggest that between 75-80% of reporting centers are conducting NGS at least partially in-house and are typically using combinations of custom and commercial software. Additional work is needed to better understand if and to what degree differences in how analysis is conducted impact results and ultimately patient care.

The challenge of integrating NGS results into the EMR was also a recurring theme at the workshops. According to survey results, that challenge is actively being addressed with all responding centers indicating they either are or will be incorporating NGS results into the EMR. However, comments from some centers suggest there are differences in methods for

incorporating results: “Therapeutically relevant variants are reported in the EMR, but other variants not associated with clinical utility are not shared through the EMR “...“Yes and No actually, for patients where we use Foundation Medicine services, treatment recommendations based on their results are being entered into the patient medical record.” Gathering details on differences in EMR documentation of NGS results was beyond the scope of this survey, but would be an important exercise to better understand how centers are addressing this challenge.

Finally, the survey touched on one last topic of ‘re-analysis.’ Of the responding centers, less than half reported conducting re-analysis of NGS results. Comments from the survey suggest a variety of methods are currently being used from automatic re-analysis (i.e. when a new reference genome is released or new algorithms are developed) to re-analysis as requested. As the technology develops, guidelines and best-practices for how and when re-analysis occurs will be needed if patient care is to be based on the most accurate understanding of actionable results.

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Appendix A: NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey Questions

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

Hello,

In conjunction with NCI and the Cancer Informatics for Cancer Centers (CI4CC), we are working to map the clinical genomics landscape across the NCI-designated cancer centers. You have been identified based on your role in Bioinformatics/Informatics leadership for your cancer center to complete this short survey. Your participation is greatly appreciated.

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

Definitions (adapted from NCI dictionary):

Next-generation Sequencing (NGS)

A high-throughput method used to determine a portion of the nucleotide sequence of an individual's genome. This technique utilizes DNA sequencing technologies that are capable of processing multiple DNA sequences in parallel. Also called massively parallel sequencing and NGS.

Clinical cancer NGS

NGS technologies used for the treatment (or related service) of patients with cancer.

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

1. Is NGS currently being utilized at your institution (either as an in-house or send-out lab) for clinical care of patients with cancer?

- Yes, and I can provide details about NGS computational pipeline
- Yes, but I'm not the best person to provide details about NGS computational pipeline. (Please list a good contact at your institution in the text box below.)
- No
- Unsure (Please list a good contact at your institution in the text box below.)

Alternative contact information (Name and Email):

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

2. When do you expect your institute will begin using clinical cancer NGS?

- Within 6 months
- Within 1 year
- Within 5 years
- Unsure
- Our institution does not plan to use NGS for clinical cancer care at this time.

3. Are you the best person to contact about future plans to use NGS at your institution?

- Yes
- No (Please list a good contact at your institution in the text box below.)

Alternative contact information (Name and Email):

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

4. Sequence data for clinical cancer NGS is currently being analyzed by:

	Targeted Gene Panels	Whole Exome Sequencing	Whole Genome Sequencing
An in-house bioinformatics department or group or shared resource	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
An external commercial or academic center	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Not applicable (this test is not utilized at your institution for clinical care)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

5. Which category of bioinformatics tools are used for analysis of sequence data for clinical cancer NGS at your institution?

	Targeted Gene Panels	Whole Exome Sequencing	Whole Genome Sequencing
All custom (developed in-house)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
All commercial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
A combination of custom and commercial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Unsure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

6. Clinical cancer NGS results from your institution are CLIA certified:

- Yes
- No
- Unsure

Comment

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

7. What is your current model of CLIA certification?

	Gene Panels	Whole Exome Sequencing	Whole Genome Sequencing
CLIA sequencing and validation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Research sequencing followed by CLIA confirmation with Sanger sequencing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other (Please describe in text box below.)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Other

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

8. Do you report incidental findings to patients? (i.e. any findings beyond those that have a direct impact on cancer care management)

- Yes
- No
- Unsure

Comment

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

9. Do you have a specific strategy for which incidental findings you report to patients (such as binning, etc)?

- Yes
- No
- Unsure

Comment

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

10. Are clinical cancer NGS results incorporated into the electronic medical record?

- Yes
- No
- Unsure

Comments

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

11. Are you re-analyzing clinical cancer NGS data (either on pre-determine schedule or as requested) to reflect changing variant/annotation information?

- Yes
- No
- Unsure

Comment

NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey (Bioinformatics/Informatics)

Thank you very much for taking the time to complete this survey. We may contact you again if we have additional questions.

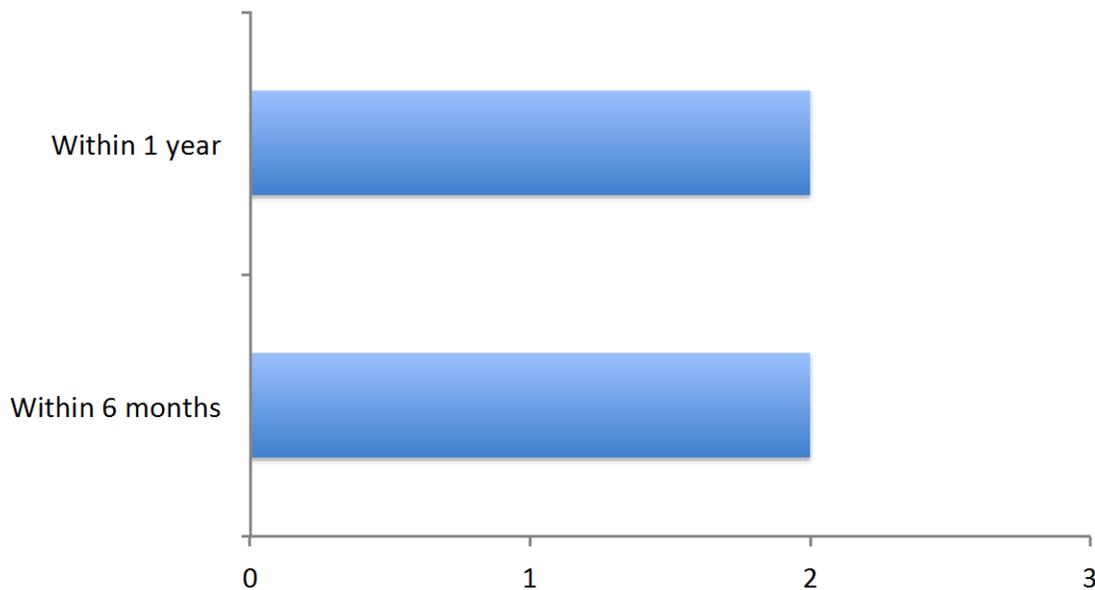
Appendix B: NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey Answers

Questions 1: A total of 33 (52%) of cancer centers from across the United States responded to the survey. Eighteen (54%) of respondents represented comprehensive cancer centers, 11 (33%) cancer centers, and 4 (12%) basic laboratory cancer centers.

Questions 2: Of the 29 comprehensive and regular cancer centers who responded to the survey, 4 (14%) indicated they are not currently offer NGS services including 2 (50%) comprehensive cancer centers and 2 (50%) cancer centers. However, all four centers indicated they were planning to implement the technology within 6 months to one year.

Appendix B, Figure 1:

Q2. Future Plans to Offer NGS (n = 4)

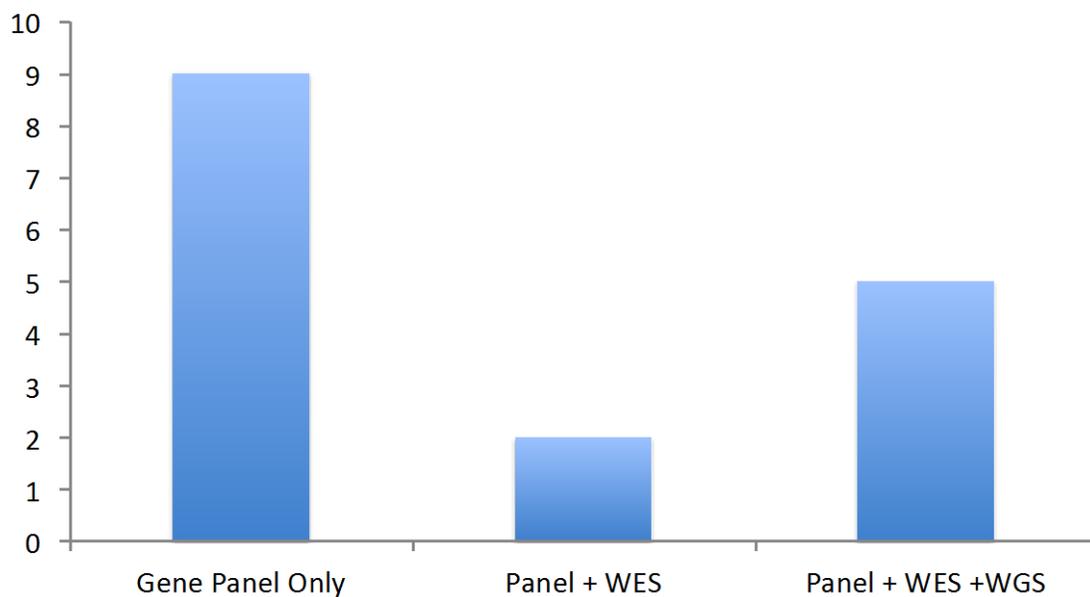


Question 3: Contact information provided as part of this question is not included in this document.

Question 4: Sixteen centers that indicated they are utilizing NGS went on to provide at least some additional details about how the technology is being used at their facilities. All reporting centers indicated they are offering multi-gene panels. Six of these centers are also offering whole exome and/or whole genome sequencing. Most centers reported testing and analysis was being conducted at least in-part within their institution.

Appendix B, Figure 2:

Q4a. What testing is being done? (n=16)

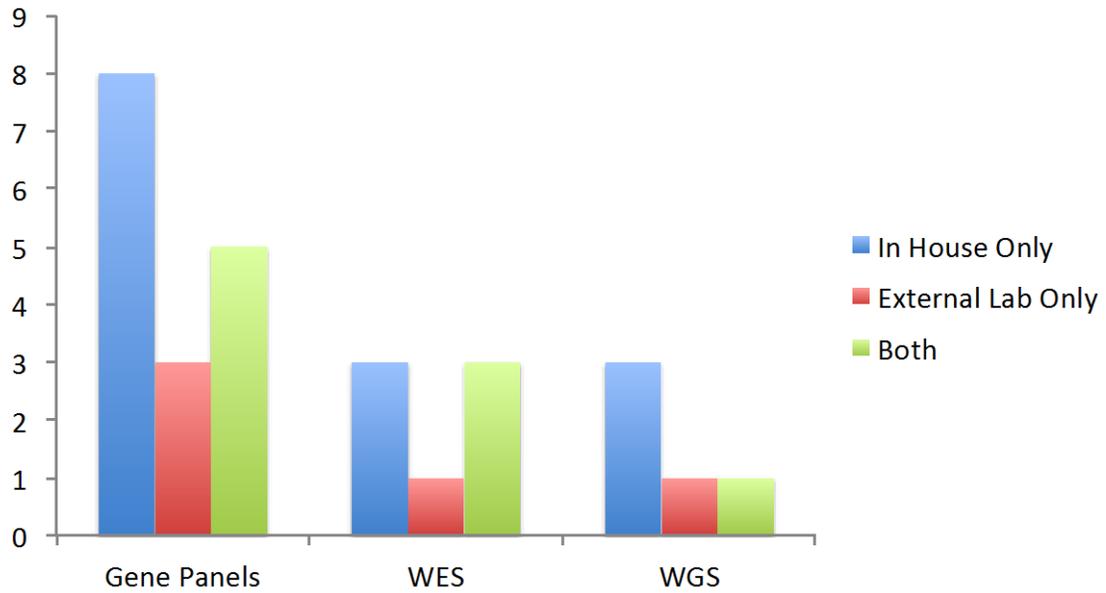


Most centers reported testing and analysis was being conducted at least in-part within their institution. More specifically, 12/16 (75%) of gene panel NGS, 6/7 86% of whole exome

sequencing, and 4/5 (80%) of whole genome sequencing tests are either entirely or partially conducted in-house.

Appendix B, Figure 3:

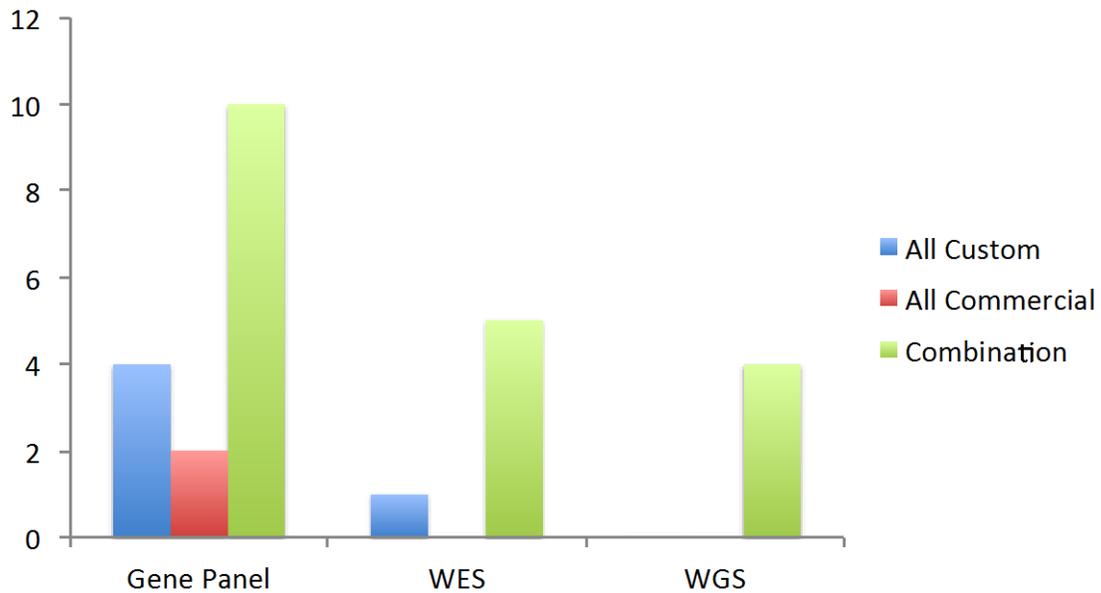
Q4b. Where is NGS testing being performed? (n = 16)



Question 5: In addition, most centers reported analysis was being conducted using a combination of custom and commercial informatics tools. More specifically, 10/16 (63%) of NGS panels, 5/6 (83%) of whole exome sequencing, and 4/4 (100%) of whole genome sequencing utilize a combination of custom and commercial informatics tools.

Appendix B, Figure 4

Q5. What informatics tools are being used? (n = 16)



Question 6: Fourteen of sixteen responding centers reported their NGS services are CLIA certified. Two respondents were unsure if the testing offered through their centers was CLIA certified.

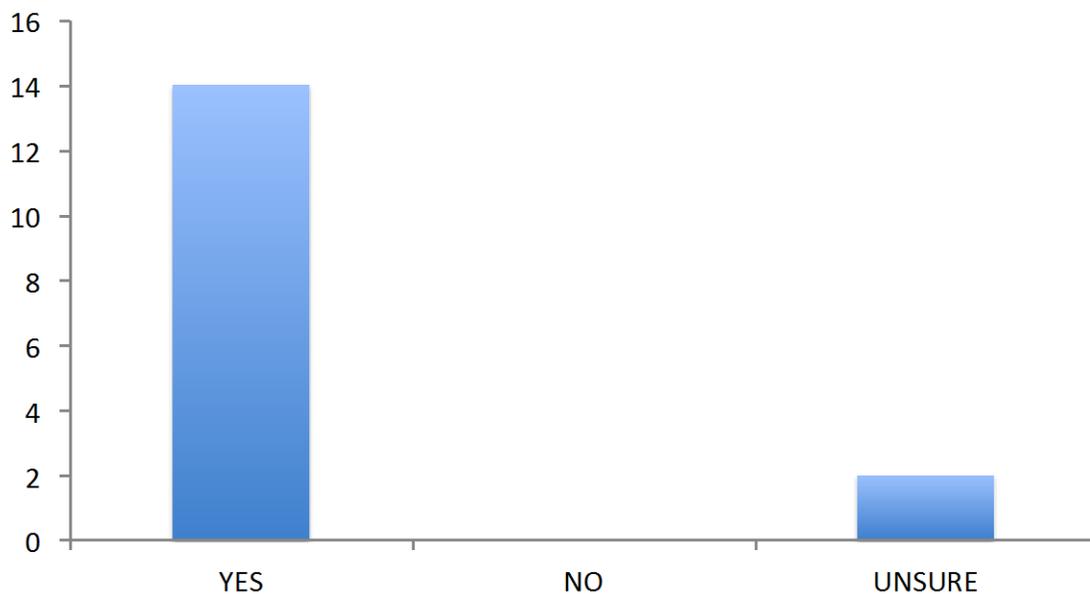
Additional comments included:

“Right now only the targeted panel being used is CLIA certified. Other CLIA certified labs are being used by some disease teams”

“We are currently developing Targeted gene panels and Exome sequencing in the CLIA/CAP certified lab”

Appendix B, Figure 5:

Q6. Are the NGS services offered CLIA certified? (n = 16)



Question 7: Of the 14 centers that are offering CLIA certified NGS services, all those offering panels (n=14) are performing CLIA sequencing with validation. Three of these centers are also offering CLIA certified WES, however, the model of testing was research NGS followed by Sanger confirmation.

Question 8: Of the 6 centers that provided information about reporting incidental findings, 2 (33%) indicated they are reporting incidental findings, 2 (33%) indicated they are no, and 2 were unsure.

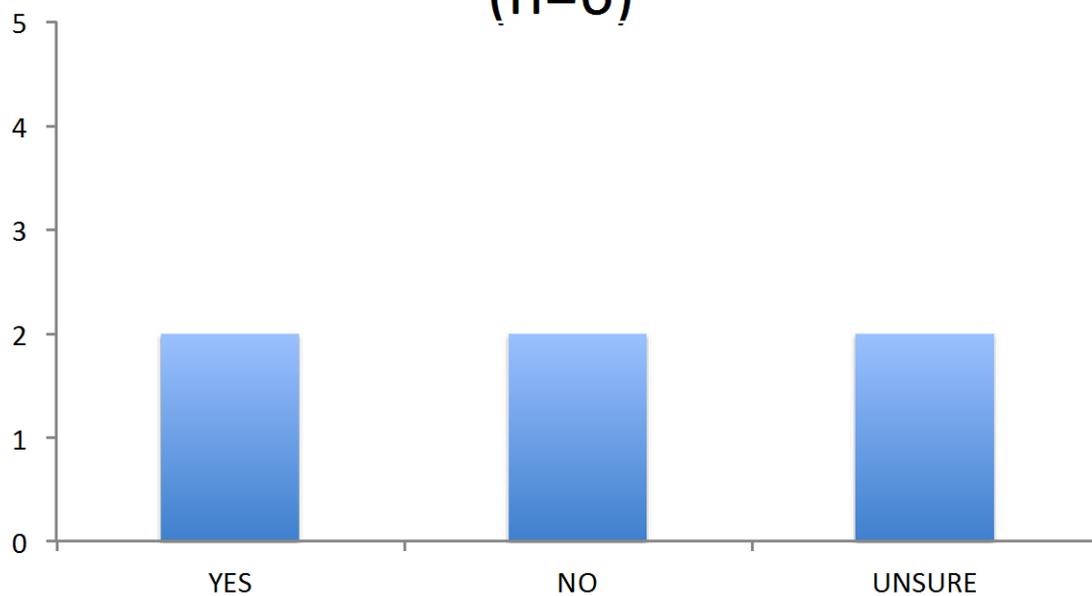
Additional comments included:

“We report variants identified that are not definitively polymorphisms. In rare cases, we will note the association with gene alterations with potential underlying germline conditions, but only in the appropriate clinical context and only after discussion with ordering physician”

Appendix B, Figure 6:

Q8. Are those offering WGS and/or WES reporting incidental findings?

(n=6)



Question 9: Of the two centers who answered this question, both were unsure if there was a specific strategy for reporting incidental findings.

Question 10: Thirteen (of 16 possible) centers provided information about incorporating results into the EMR and all state they either are or will soon be incorporating results into the EMR. (Includes 2 who are unsure about CLIA certification).

Additional comments included:

“Therapeutically relevant variants are reported in the EMR, but other variants not associated with clinical utility are not shared through the EMR. “

“they will be in the coming year”

“Yes and No actually, for patients where we use Foundation Medicine services, treatment recommendations based on their results are being entered into the patient medical record”

“Being done”

Question 11: Twelve out of 16 possible centers responded to this question, 5 of which indicated they are re-analyzing data to reflect changes in the variant or annotation information. (Appendix B, Figure 7)

Additional comments:

“VCU recently began its genomics initiative but this will become part of the downstream analysis when appropriate (i.e. new builds of the reference genomes)”

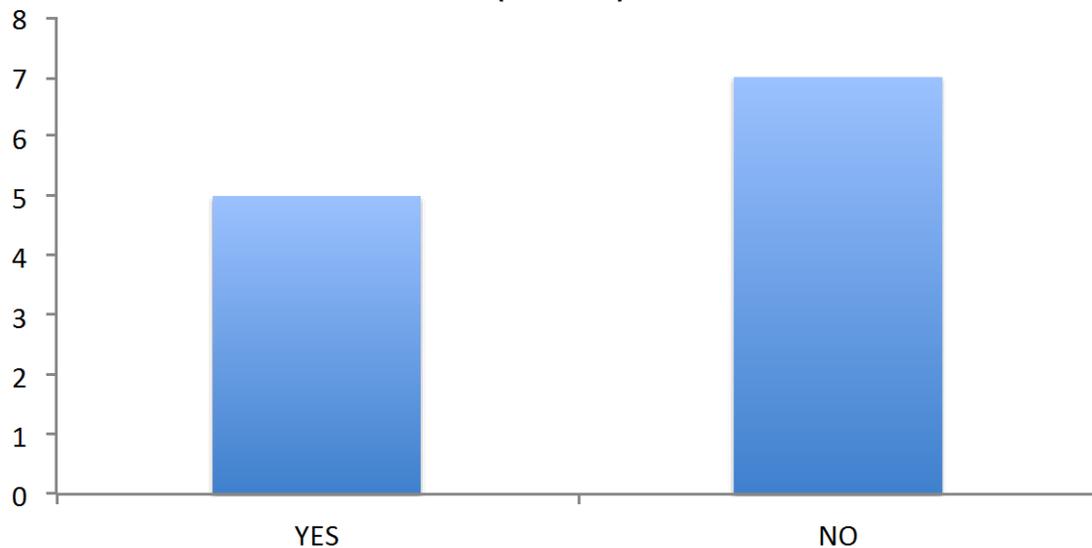
“Not at this time, although we are looking into this for future”

“as requested”

“We track changes in versions of algorithms and re-run”

Appendix B, Figure 7:

Q11. Are you re-analyzing clinical cancer NGS data (either on pre-determine schedule or as requested) to reflect changing variant/annotation information?
(n= 12)



Appendix C: NCI-CI4CC Cancer Clinical Omics US Mapping Effort Survey Respondents

Case Comprehensive Cancer Center
Cold Spring Harbor Laboratory Cancer Center
David H. Koch Institute for Integrative Cancer Research at MIT
Fox Chase Cancer Center
Fred Hutchinson Cancer Research Center
Georgetown Lombardi Comprehensive Cancer Center
Harold C. Simmons Cancer Center
Herbert Irving Comprehensive Cancer Center
Huntsman Cancer Institute
Kimmel Cancer Center
Markey Cancer Center
Masonic Cancer Center
Massey Cancer Center
Memorial Sloan-Kettering Cancer Center
OHSU Knight Cancer Institute
Robert H. Lurie Comprehensive Cancer Center
Sanford-Burnham Medical Research Institute
The Wistar Institute Cancer Center
UCSF Helen Diller Family Comprehensive Cancer Center
University of Colorado Cancer Center
University of New Mexico Cancer Research & Treatment Center
UW Paul P. Carbone Comprehensive Cancer Center University of Wisconsin
Vanderbilt-Ingram Cancer Center
Wake Forest Comprehensive Cancer Center