

Clinical Cancer Genetics Program

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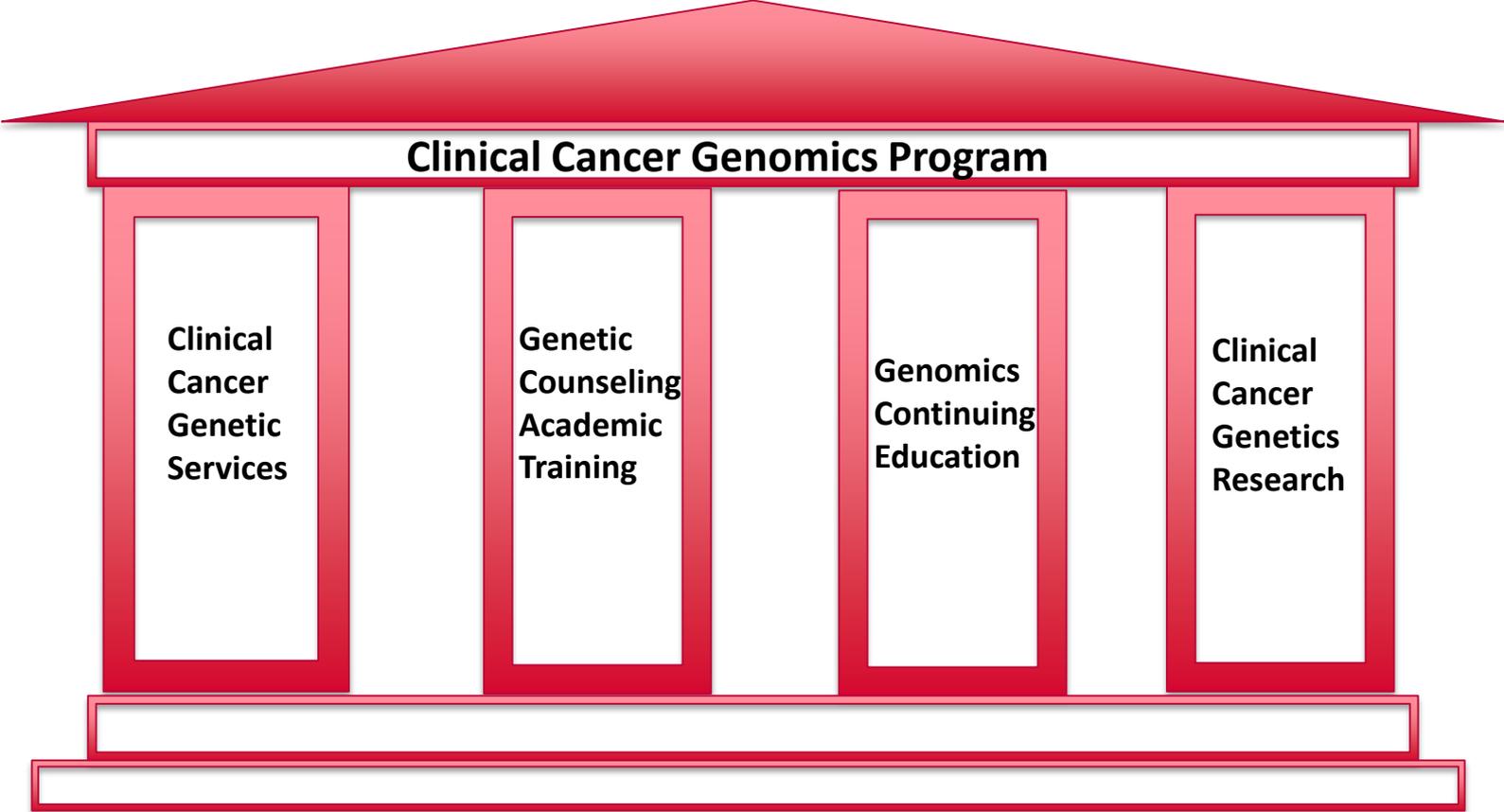


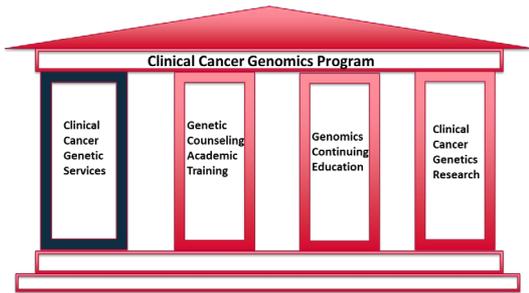
NATIONAL CANCER INSTITUTE
Center for Cancer Research

Background and Program Aims

- Concept proposal requested by CCR Clinical Director
 - Submitted November 2017
 - Funded April 2018
- Build on the existing clinical resources, infrastructure and initiatives already in place in the Genomic Healthcare Section of the Genetics Branch of the Center for Cancer Research
- Fill academic and continuing education gaps, and
- Provide the infrastructure for conducting research in clinical cancer genetics

Program Components

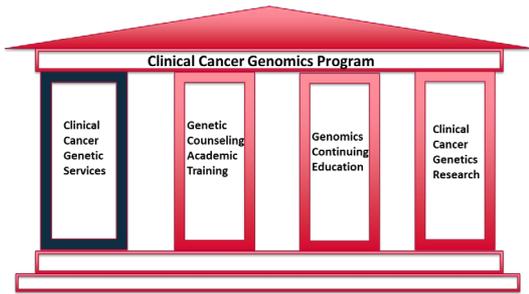




Clinical Cancer Genetic Services

Objectives:

- Expand capacity to provide a genetic clinical services for CCR and other NIH institutes as requested
- Provide support for ongoing NCI research studies that require genetic services or other genetic consultation i.e. during protocol development, germline incidental findings
- Provide long term follow-up services for individuals found to harbor a germline variant
- Provide clinical germline variant interpretations



Clinical Cancer Genetic Services

- Staffed with 3 genetic counselors and one cancer geneticist

Grace-Ann Fasaye, ScM, CGC



Alex Lebensohn, MS, CGC

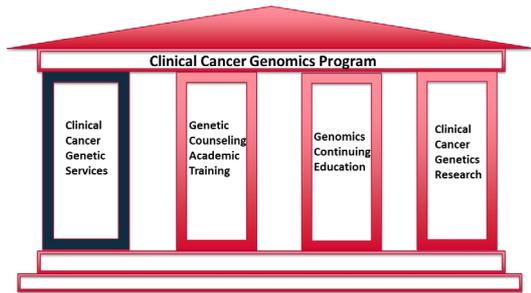


Chimene Kesserwan, MD, FCAP, FACMG



Yi Liu, MS

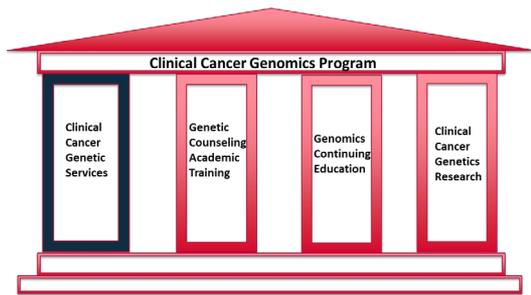




Clinical Cancer Genetic Services

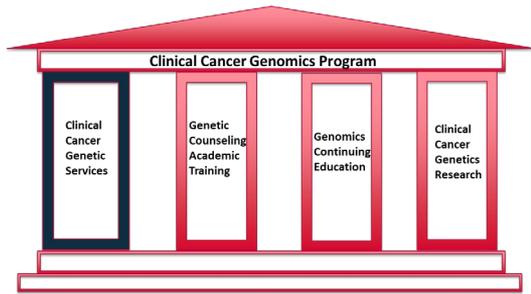
Requesting a Consult

- **DO NOT** enter consults in CRIS, those will be directed to NHGRI so there could be a delay in our response
- **NCI_GeneticConsult@mail.nih.gov** listed in the Global under NCI Genetic Consult Service
- Please include:
 - Patient name, MRN, reason for the consult, referring physician, study PI (or paying investigator if there is a test charge)



Clinical Cancer Genetic Services

- From 7/10/2019-7/9/2020 the service saw 280 consults from across all CCR branches
- Up from 194 consults in 2018-2019
- Includes implementing telemedicine without compromising consult availability or quality of patient/family genetic counseling
- Genetic counselors are embedded as part of the team in three services thus far: Prostate; Mesothelioma; and Inherited Gastric Cancer

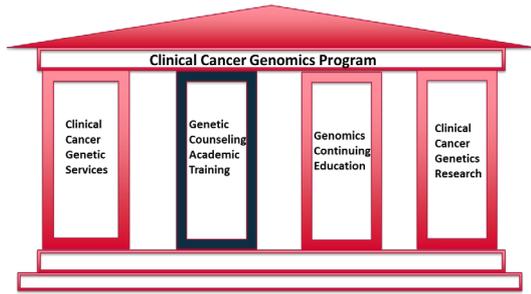


Clinical Cancer Genetic Services

- Centralized billing system
- Worked with Clinical Center DCRI to establish the CRIS Pedigree Tool
 - Will be working with them prospectively as we build online patient portal
- Expanding to include NHGRI clinical genetic fellows

Future Plans

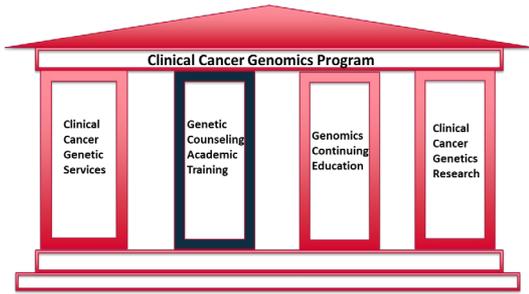
- Implementing the Laboratory of Pathology exome sequencing
 - Consent, pre/post genetic counseling, variant interpretation, pedigree collection



Genetic Counseling Academic Training

Objectives:

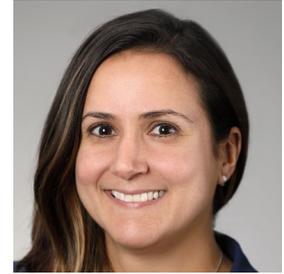
- Expand the existing training program for genetic counselors
 - Expand the cancer genetic content in the existing curriculum
 - Investigate outcomes of alternative mechanism(s) for training genetic counselors
 - Standardized patients/Simulation Center
 - Increase the number of genetic counselors trained annually



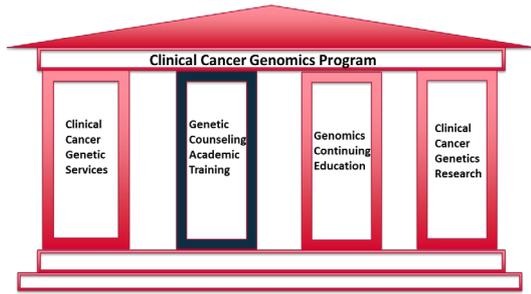
Genetic Counseling Academic Training

- Staffed by an Associate Program Director

Leila Jamal, ScM, PhD, CGC, start May 2020

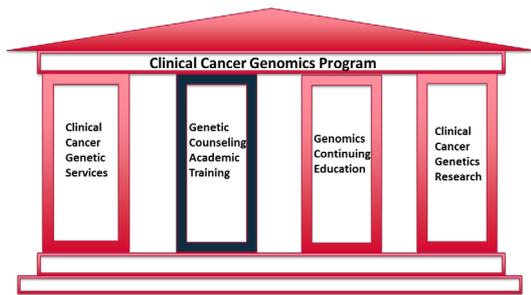


- Joint appointment with the Department of Bioethics
- Her research focuses on:
 - How patients and clinicians react to and use secondary finding information about germline cancer predisposition in their children
 - How patients react to and use inconclusive results from exome sequencing



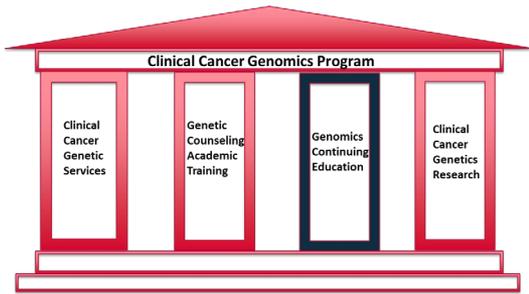
Genetic Counseling Academic Training

- Collaboration with NHGRI/MOU fully executed in May 2019
 - Program rebranded to the NIH Genetic Counseling Training Program
 - Increase student cohort from 4 to 6 per academic year starting August 2019
 - Accreditation substantive change request submitted and approved
 - Develop, evaluate, and disseminate novel training methods
 - Simulated patient rotation for first year launched 2020
 - Protocol submitted to evaluate the effectiveness, feasibility, and acceptability of this rotation



Genetic Counseling Academic Training

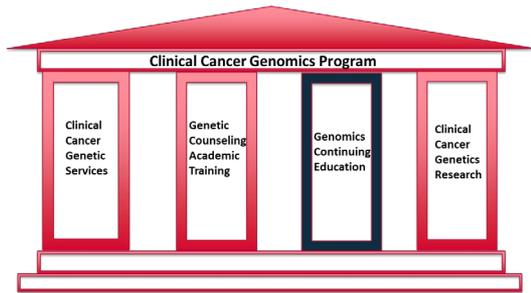
- Enhance the cancer genetics didactic and clinical training curricula for ALL students
 - Inferring the presence of germline variants from somatic test results
 - Hematologic malignancies
 - Pediatric cancer counseling
 - Environmental influences affecting germline cancer predisposition
 - Use and limitations of polygenic risk scores
 - Alternative/automated service delivery models for cancer risk assessment and counseling



Genomics Continuing Education

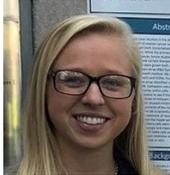
Objectives

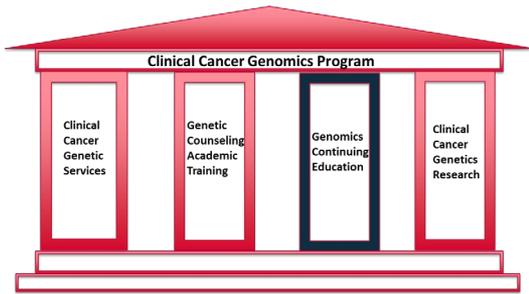
- Conduct cancer genetics education training programs
- Conduct a genomics for Faculty training program
 - Include ongoing support, annual refresher training, community of learning
 - Target intramural and extramural communities
 - Include all healthcare disciplines



Genomics Continuing Education

Intramural

- Urologic Oncology Branch
 - Genetics and Genomics of Genito-Urinary Cancers
 - Launched 10/9/2020, CE, Didactic/Journal Club/Case Presentations
- Thoracic Malignancies, approached about a similar model
- Post Bac-Anna Duemler, BS 
 - Association between *CDH1* orofacial cleft and cancer family history
 - *Genomics: Insights* article published (NHGRI and Smithsonian publication)



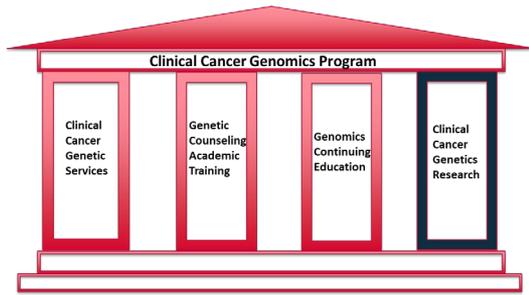
Genomics Continuing Education

Extramural

- Genetic counseling summer student
- Global Genetic and Genomic Community
- Oncology Nursing Society initiative
- Global Genomic Nursing Alliance educational meeting, July 2021

Future Plans

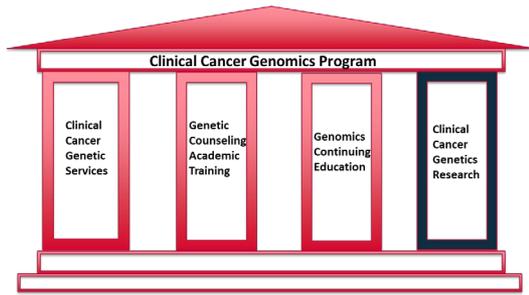
- Extramural education program in cancer genomics
- Community of learning



Clinical Cancer Genetics Research

Objectives:

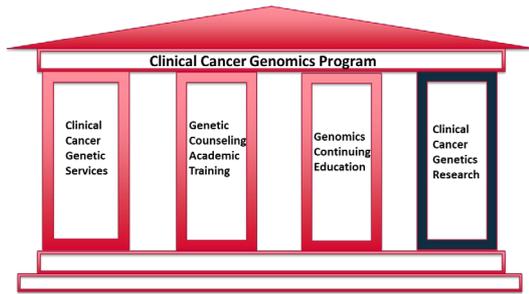
- Establish a platform for the expansion of clinical genetic and genomic research
- Establish mechanisms for translation of scientific discoveries into clinical practice



Clinical Cancer Genetics Research



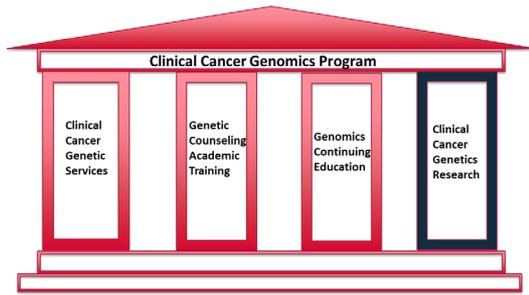
- Genomic Data Sharing
 - Staffed by Logan Manlove, MS
- Works with CBIIT on the development and maintenance of the GDS online portal (projects, data sharing plans, institutional certifications)
- Established an online mechanism for GSR Sensitivity Determinations
- Interface with all CCR intramural investigators (clinical, laboratory, and animal studies)
- There are >360 CCR studies registered in dbGaP



Clinical Cancer Genetics Research

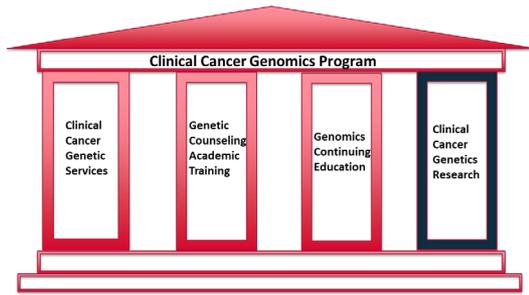
Regulation and Policy

- Protocol development
 - Genetic components
 - Data sharing applicability
- Incidental and secondary findings from research and clinical analysis
 - Notification, genetic education and counseling, CLIA confirmation if needed
 - Can include when research subject is deceased
- Incidental and secondary findings required reporting policy



Clinical Cancer Genetics Research

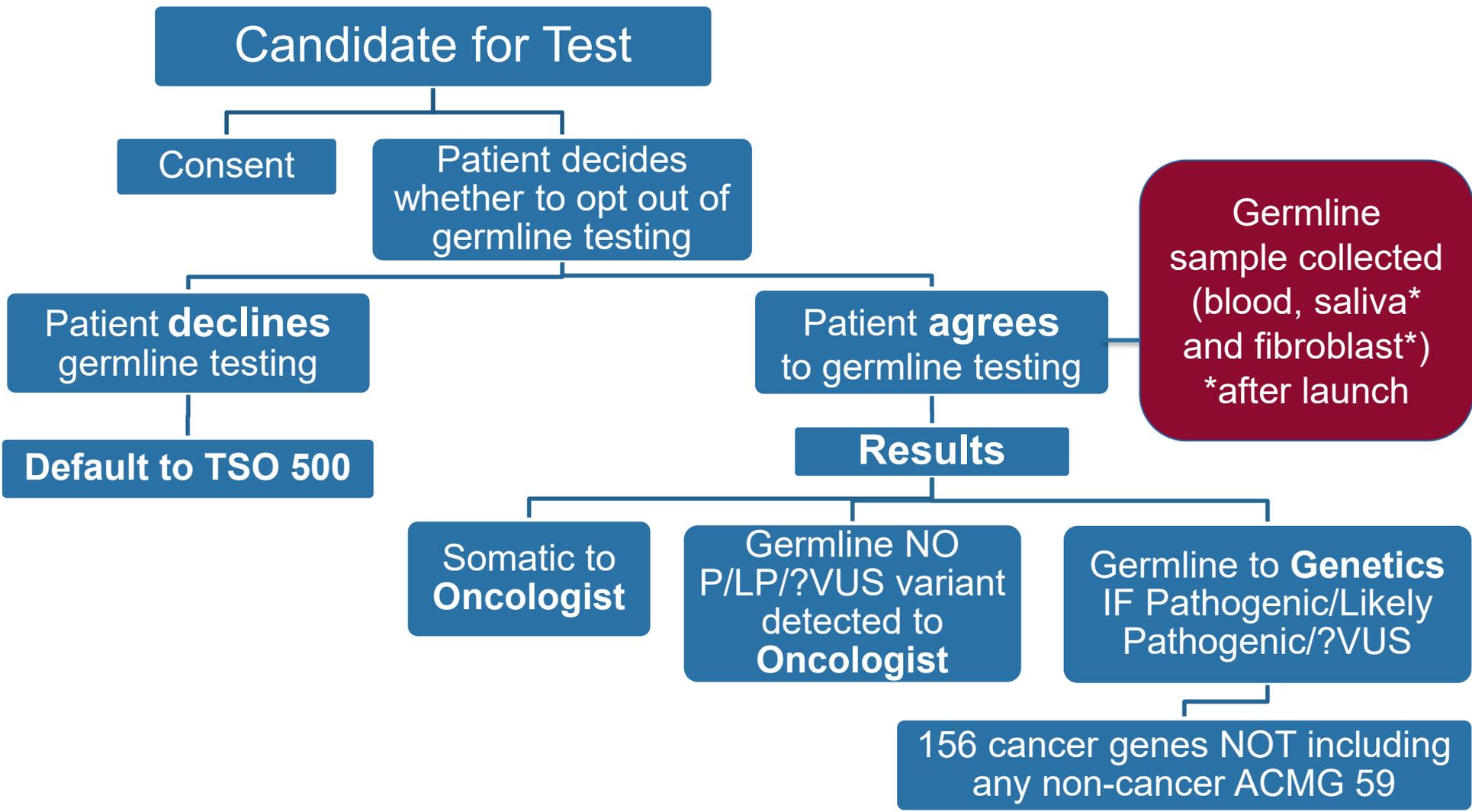
- Gastric Adenocarcinoma and Proximal Polyposis of the Stomach
 - Phenotyping assessment
- Pharmacogenomic Family Nurse Practitioner Education
- Genomic Implementation
 - National (GGNCI) and International (Global Genomic Nursing Alliance)
 - Competencies, Roadmap, Maturity Matrix, GGNPS refinement/translation
- OMICS Nursing Science and Education Network



Clinical Cancer Genetics Research

Future Plans

- Cascade Testing
- Genetic counseling workload assessment
- Variant assessments
- Whole exome sequencing initiative with Laboratory of Pathology
 - Launches January 2021



Considerations/Discussions

- Launch January 2021/Volume estimate 10/wk, increasing over time
- Consent at the point of care (POC)
 - Genetic counseling staff will start but long-term capacity for POC consent as volume increases over time is an issue
 - Train staff clinicians, senior fellows to perform pre/test counseling/consent
 - Supplement with online short consent education program for patients/family
 - Consent form still needs HMID approval (~1 month) then HMID formatting
 - Online remote consent formatting (1 day)
- NIH 527-1 completed at the time of consent/Pedigree preferred
- Order placement, may not be in the realm of the research nurses*
- Germline sample
 - Blood only currently
 - Saliva capacity is actively being worked on
 - Fibroblast capacity (for pts with heme malignancies, post transplant) after

launch

Considerations/Discussion, continued

- Providers will have the option to order disease-specific panels
- Incidental/Secondary Findings
 - The full ACMG 59 is not being reported in phase 1
 - Only ACMG cancer genes plus *TGFBR1* and *TGFBR2* (Loeys-Dietz)
 - Genomics Research Results Working Group
 - Intramural policy
 - **ACMG Incidental/Secondary Findings list has been revised**
 - At ASHG reported last step is approval by the ACMG Board
 - Germline results
 - Pathogenic, likely pathogenic and variants of uncertain significance (VUS)
 - Likely pathogenic and VUS can be up and downgraded
 - LP will review every 6 months
 - Changes in variant classification will result in an updated germline report

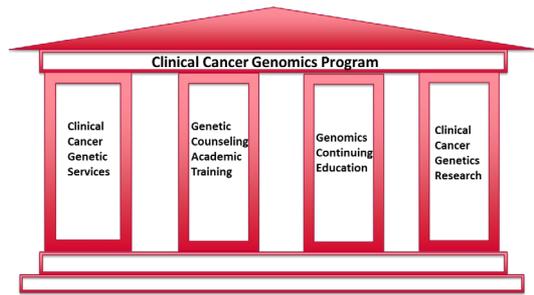
Considerations/Discussions, continued

- Incidental/Secondary Findings continued
 - Rate of germline findings in adults
 - MSKCC experience* only reporting Pathogenic/Likely Pathogenic
 - Reporting 76 cancer susceptibility genes
 - 17.5% (182/1040)
 - 9.7% (101/1040) did not meet clinical guidelines for germline testing
 - Rate of germline findings in pediatrics
 - St. Jude experience** reporting Pathogenic/Likely Pathogenic
 - Reporting 156 cancer susceptibility genes
 - 11.8% (289/2450) survivors
 - Rate of evidence for germline actionable variants in somatic only sequencing
 - UPENN experience *** doing germline testing based on somatic findings
 - 5% (81/2308) had somatic finding warranting germline testing
 - 58% 27/48 confirmed in the germline

*Mandelker et al. 2017, PMID: 28873162

**Wilson et al. 2019, PMID: 31736278

***Clark et al. 2019 PMID: 31511844



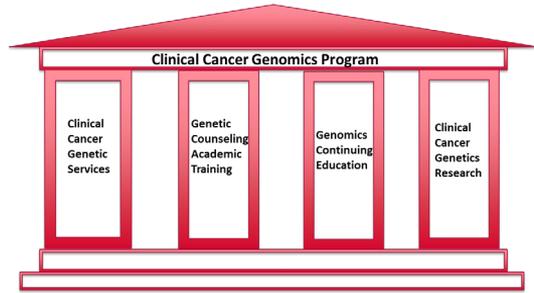
Intersection of the CCGP Pillars

■ Consults

- Comprehensive family history may identify a genetic differential diagnosis not otherwise appreciated
- Assessment of the adequacy of prior genetic testing
- A default to somatic only testing DOES NOT eliminate the likelihood that test results could identify evidence of germline variant
- Germline/somatic WES germline incidental findings

■ Post Initial Consult Further Evaluation

- Variant of Uncertain Significance (VUS) workup



It Takes a Village



Center for Cancer Research

Bill Dahut, MD, Mel Bronez

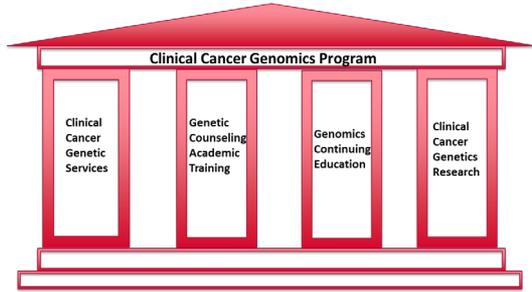
Genetics Branch

Paul Meltzer, MD, PhD

Melissa Shue, Kandie Webb, Nancy Sossavi, Bev Stalker

National Human Genome Research Institute

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Questions/Discussion



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