CGA-IGC Newsletter
Quarterly release: Q2

2018 CGA Annual Meeting Update

The 2018 CGA Annual Meeting in San Diego, CA is only 6 months from now and registration will open in a few weeks. Veteran CGA members know that the meeting always delivers high impact speakers and topics, but new members or those considering attending their first CGA meeting may not be aware. We wanted to give everyone a sneak peak of plans for the meeting. Also, please remember to pass this on to colleagues or trainees who may be considering signing up!

Please note the meeting will start on Sunday, October 14 at 1:00 PM this year with a focus on the hamartomatous polyposis syndromes. Joy Larsen Haidle, CGC will give the Anne Krush lectureship on updates on juvenile polyposis syndrome, and other lectures will include Peutz-Jeghers syndrome and a discussion on Cowden syndrome and potential pharmaceutical treatments. The next session will be the opening half of the Presidential Plenary session with oral presentations of the top research abstracts. Following this, one of the annual traditions will continue with Dr. James Church leading a discussion based on challenging cases. The research poster presentations will then close out the session.

On Monday, October 15 begins with a focus on multiple aspects of pancreatic cancer. Dr. Gloria Peterson will give the Jass lectureship on the prevalence of germline mutations in pancreatic cancer patients, and other lectures will focus on treatment and surveillance options. We then shift to lectures on tumor testing, which promise to be extremely helpful navigating this brave new world. Dr. David Leiberman will give the Herrera lectureship on a Familial Colorectal Cancer Guideline. The next session switches gears to focus on risk assessment from both the patient and populations levels. The day is then capped off with two highlights from every meeting - the “Jeopardy” event followed by the Lifetime Achievement award.

The last day of the meeting has plenty to offer with great morning concurrent sessions. The Diagnostics tract will focus on MyCode (Geisinger) penetrance data, upfront tumor sequencing and pre-implantation genetic diagnosis. The Management tract will include case-based discussions of high yield cases with national experts in hereditary cancers and management. The morning will conclude with a fourth exciting Yet-to-be-Named Lectureship given by Dr. Randy Burt, as well as the second half of the Presidential Plenary abstract session.

In addition to the general sessions, both “Breakfast with the Experts” and “Curbside Consults” will be available in morning sessions. These are excellent chances to learn more about a particular topic that keeps coming up in your practice or to see what the CGA experts have to offer about your difficult cases.

<<Section II>>

2018 CGA Annual Meeting – Lifetime Achievement Recipient

Content TBD

<<Section III>>

Educational Resources Update

Monthly Journal Scan
We know how difficult it is to keep up on the multi-disciplinary literature relevant to hereditary GI cancers. We have launched a new effort this year to systematically scan all high-impact journals from the fields of **Genetics, Gastroenterology, Oncology, Gastrointestinal Surgery, Pathology, General Medicine and Science** so our members can access these publications in one place. Please visit our Journal Scan webpage for monthly updates.

Webinar Series
We will be broadcasting a webinar in **June 2018** hosted by Dr. Michael Hall entitled **"Universal Mismatch Repair Screening for Lynch Syndrome: Where Are We Now?"** Dr. Hall will discuss this rapidly evolving topic and be available for a live discussion and question & answer session! The live webinar will be free for all CGA members to participate. The recording will be also be available if you miss the live session. CEU credits will be available for a fee. Stay tuned for details.

Dr. Hall is an Associate Professor of Medicine at Fox Chase Cancer Center in the gastrointestinal oncology and cancer prevention and control programs. He is a trained health services researcher and clinical cancer geneticist. He received his undergraduate and medical degrees from Columbia University in New York City. He went on to complete an internal medicine residency at Harvard's Brigham and Women's hospital and a fellowship in Hematology/Oncology at the University of Chicago where he established a clinical and research focus in GI cancers and genetic risk and earned a master's degree in health services research. His current research includes the study of patient attitudes and preferences

toward hereditary risk assessment and testing, novel methods to communicate of high risk information within families, and collaborative research in gene discovery and large testing database analyses. He is the recipient of individual and collaborative research funding from the Chemotherapy Foundation, the Greenwall Foundation, and the National Cancer Institute. Most recently, along with Dr. Sarah Bass from the Temple University School of Public Health, he received a 5 year 1.2 million dollar Health Equity grant from the American Cancer Society to study and improve the communication of hereditary cancer risks discovered from tumor testing to African Americans with cancer.

Podcast Series

The CGA education committee will be publishing a podcast series this year on the **"Multi-Disciplinary, Patient-Centered Management of Lynch Syndrome Patients."** We will be interviewing experts in Gastroenterology, Gynecology, Oncology and Urology about the approach to cancer risk reduction and management in Lynch Patients. This podcast series will be available for free for CGA members. Stay tuned for details!

<<Section IV>>

Highlight of Articles from CGA Members

Assessment of Tumor Sequencing as a Replacement for Lynch Syndrome Screening and Current Molecular Tests for Patients With Colorectal Cancer.
Hampel H, Pearlman R, Beightol M, Zhao W, Jones D, Frankel WL, Goodfellow PJ, Yilmaz A, Miller K, Bacher J, Jacobson A, Paskett E, Shields PG, Goldberg RM, de la Chapelle A, Shirts BH, Pritchard CC; Ohio Colorectal Cancer Prevention Initiative Study Group.
JAMA Oncol. 2018 Mar 29. doi: 10.1001/jamaoncol.2018.0104. [Epub ahead of print]
PMID: 29596542
Review: With increasing use of tumor sequencing, we sought to determine whether or not up front tumor sequencing on all colorectal cancer patients could be used as a single test to replace all other universal tumor screening for Lynch syndrome tests and tumor tests for KRAS, NRAS and BRAF that are recommended for all stage IV colorectal cancer patients for treatment purposes. We collaborated with the University of Washington who provided Oncoplex tumor sequencing on 419 population-based colorectal cancer patients who were receiving all the other standard of care tests as part of their participation in the Ohio Colorectal Cancer Prevention Initiative and an additional 46 patients who were known to have Lynch syndrome to ensure that tumor sequencing could identify all germline mutation in the MMR genes. The outcome was that upfront tumor sequencing was more sensitive and equally specific as MSI and IHC for detecting Lynch syndrome. In addition, it accurately identified the KRAS, NRAS and BRAF mutations. There were some additional benefits to upfront tumor sequencing including the ability to identify germline mutations in the DPYD gene which causes toxicity to 5-FU based chemotherapy which could be helpful for treating these patients and the identification of 8 additional patients with germline mutations in other hereditary cancer genes. Since this is a more expensive test to be proposing doing on all colorectal cancer patients, a cost-effectiveness study will need to be performed to determine if eliminating up to 6 other tests in a subset of patients might already make this approach cost-effective. Otherwise, it may need to wait until the costs of tumor sequencing panels come down as they have with germline panels.

Interaction between polymorphisms in aspirin metabolic pathways, regular aspirin use and colorectal cancer risk: A case-control study in unselected white European populations.

Sheth H, Northwood E, Ulrich CM, Scherer D, Elliott F, Barrett JH, Forman D, Wolf CR, Smith G, Jackson MS, Santibanez-Koref M, Haile R, Casey G, Jenkins M, Win AK, Hopper JL, Marchand LL, Lindor NM, Thibodeau SN, Potter JD, Burn J, Bishop DT.

PLoS One. 2018 Feb 9;13(2):e0192223. doi: 10.1371/journal.pone.0192223. eCollection 2018.

PMID: 29425227

Review: Observational studies and randomized controlled trials have shown chemopreventive effect of regular aspirin use to reduce the risk of colorectal cancer (CRC). However, this effect varies between individuals. To follow-up on prior literature that indicated that single nucleotide polymorphisms (SNPs) may contribute to this variation, this study leveraged two large population-based datasets to perform a meta-analysis on a combined study sample of 3325 cases and 2262 controls. It tested for gene x environment (GxE) interactions across 42 SNPs in 15 candidate genes with evidence in the literature for having an association with CRC risk putatively modified by aspirin use. This study replicated a prior finding that indicated an association between SNP rs6983267 in *CCAT2* and reduced CRC risk [Tenesa *et al.* Nature Genet 2008]. However, no GxE interactions reached statistical significance after multiple test correction. Overall, this study did not provide evidence for variable chemopreventive effect of aspirin in subset of individuals stratified by genotype of SNPs in genes involved in aspirin pathways.

Comprehensive Analysis of Hypermutation in Human Cancer.

Campbell BB, Light N, Fabrizio D, Zatzman M, Fuligni F, de Borja R, Davidson S, Edwards M, Elvin JA, Hodel KP, Zahurancik WJ, Suo Z, Lipman T, Wimmer K, Kratz CP, Bowers DC, Laetsch TW, Dunn GP, Johanns TM, Grimmer MR, Smirnov IV, Larouche V, Samuel D, Bronsema A, Osborn M, Stearns D, Raman P, Cole KA, Storm PB, Yalon M, Opocher E, Mason G, Thomas GA, Sabel M, George B, Ziegler DS, Lindhorst S, Issai VM, Constantini S, Toledano H, Elhasid R, Farah R, Dvir R, Dirks P, Huang A, Galati MA, Chung J, Ramaswamy V, Irwin MS, Aronson M, Durno C, Taylor MD, Rechavi G, Maris JM, Bouffet E, Hawkins C, Costello JF, Meyn MS, Pursell ZF, Malkin D, Tabori U, Shlien A.

Cell. 2017 Nov 16;171(5):1042-1056.e10. doi: 10.1016/j.cell.2017.09.048. Epub 2017 Oct 19.

PMID: 29056344

Review: A large-scale analysis of hypermutation in 81,337 pediatric and adult cancer tumours, analyzed the driver mutations, signature analysis and mutation order to give insight into tumour evolution and identify clinically actionable mutation signatures. Highlights from the article showed; (1) Hypermutation was detected in tumor types not previously associated with high mutation burden. Replication repair deficiency was a major contributing factor. Mutation burden analysis reveals new drivers of hypermutation in POLE and POLD1, (2) Timing of replication repair deficiency determines mutation signature composition, (3) Germline replication repair deficiency identified from tumor-only sequencing, (4) Unbiased clustering, based on mutational context, revealed clinically relevant subgroups regardless of the tumors' tissue of origin, highlighting similarities in evolutionary dynamics leading to hypermutation. Mutagens, such as UV light, were implicated in unexpected cancers, including sarcomas and lung tumors, and (5) Mutation burden and signatures have value for screening, surveillance, and therapy.

<<Section IV>>

CGA-IGC Calendar of Events

April

1. Quarterly newsletter released

2. Journal Scan update released

May

1. Abstract submission site opens on **May 1**
    - Please watch for further details in upcoming emails

2. Registration for annual meeting opens on **May 1**
    - Please watch for further details in upcoming emails

3. Collaborative Fund application process opens on **May 14**

4. Twitter Journal Club with Dr. Jewel Samadder discussing sulindac and erlotinib in familial adenomatous polyposis and effect on duodenal adenomas (https://www.ncbi.nlm.nih.gov/pubmed/27002448 - open access) and colorectal neoplasia (https://www.ncbi.nlm.nih.gov/pubmed/29423501 - open access) on **May 21 at 8 PM Eastern**

5. Journal Scan update released

June

1. Webinar video with Dr. Michael Hall discussing: "Universal Mismatch Repair Screening for Lynch syndrome: Where Are We Now?"

2. Journal Scan update released

July

1. Next edition of the quarterly newsletter

2. Abstract submission closes on **July 6**

3. Collaborative Fund submission closes on **July 27**

4. Journal Scan update released