The Cancer Genomics Research Laboratory and Division of Cancer Epidemiology and Genetics (DCEG):

A Great Partnership

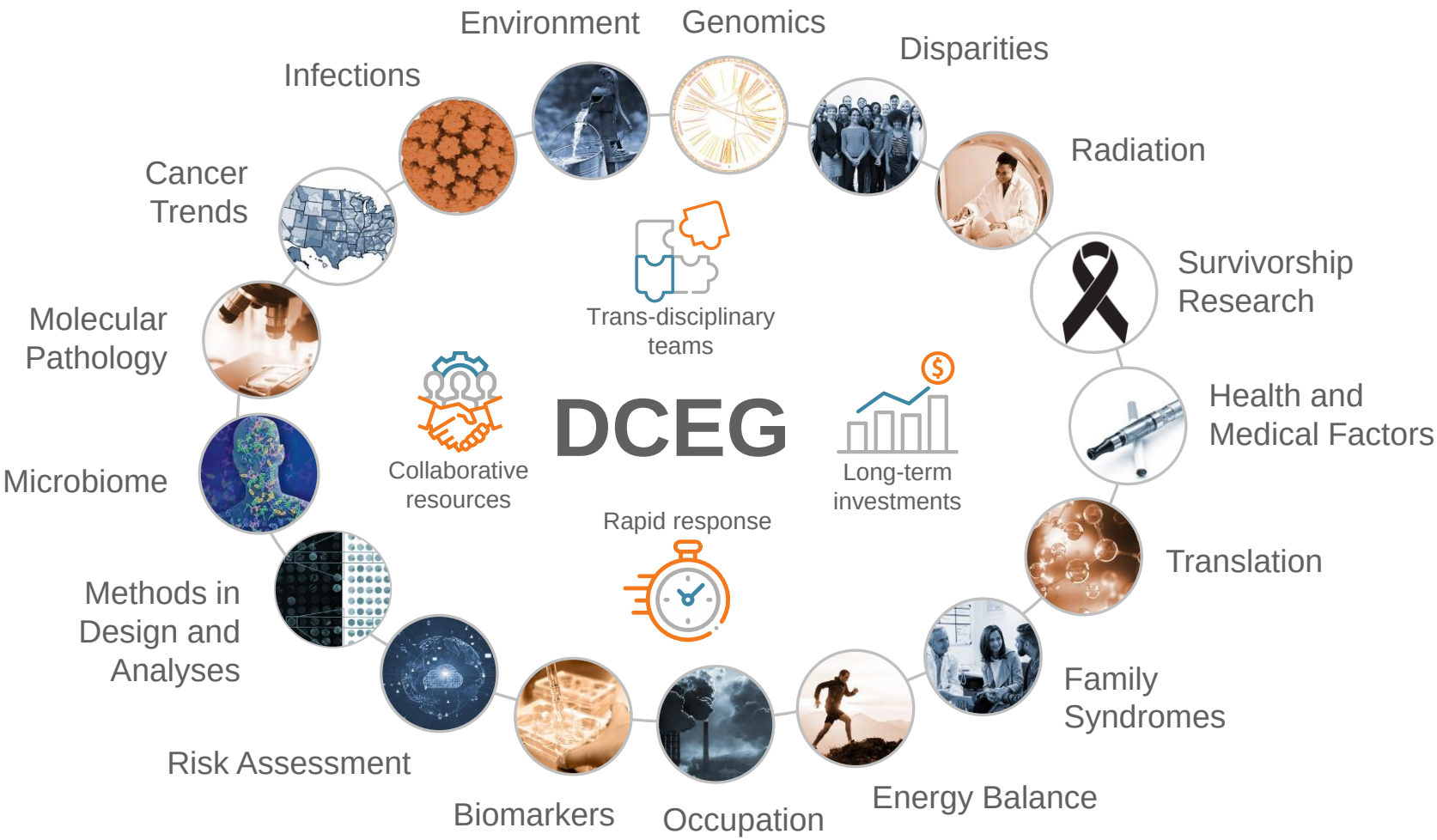
Stephen J. Chanock, M.D., Director

Division of Cancer Epidemiology & Genetics

NIH NATIONAL CANCER INSTITUTE Division of Cancer Epidemiology & Genetics

Frederick National Laboratory for Cancer Research

CGR Cancer Genomics Research


Environment
Genomics
Disparities
Infections
Radiation
Cancer Trends
Survivorship Research
Molecular Pathology
Trans-disciplinary teams
Health and Medical Factors
Collaborative resources
DCEG
Long-term investments
Microbiome
Translation
Rapid response
Methods in Design and Analyses
Family Syndromes
Risk Assessment
Energy Balance
Biomarkers
Occupation

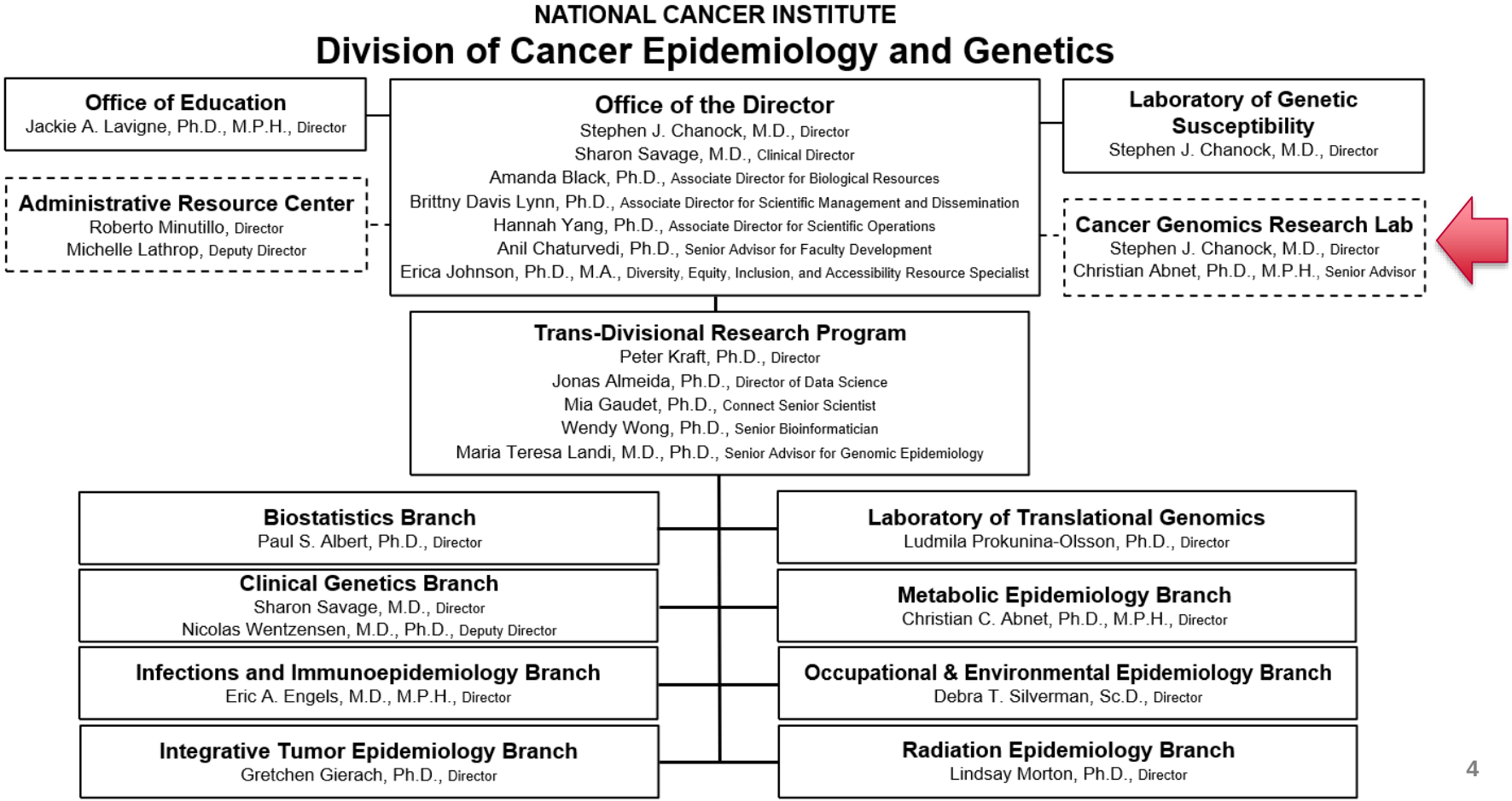
2001 to 2020: Genetic Odyssey

CGR moves to CRL @ Shady Grove in summer 2020

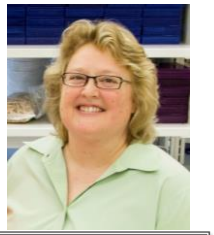
CGR at NCI Shady Grove Campus

Colocalization drives Innovation

Seamless integration within DCEG



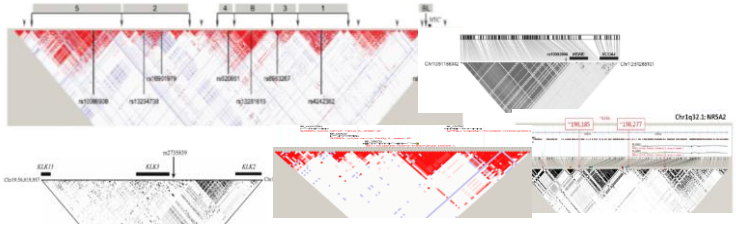
CGR Organization

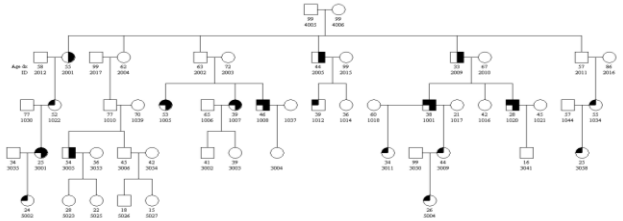


Dr. Yeager shifted to advisory role in 2022
Program Director, Biomedical Science at Hood College

- Belynda Hicks, CGR Director
  - Meredith Yeager, CGR Sr. Principal Scientist
    - Amy Hutchinson, Operations
      - Michael Beerman, LIMS (4) Staff
      - Adri O'Neil, Quality Mgmt (2) Staff
      - Project Management (4) Staff
      - Budget/Admin (2) Staff
      - Biospecimen Coordinator (DCEG/OD Embed)
    - Aaron Rozeboom, MDPL
      - Petra Lenz, Pathologist
      - Leslie Johnston, Histology (4) Staff
      - Scott Lawrence, Digital Pathology (2) Staff
    - Lakshmi Viswanathan, DESL
      - Remy Hilsabeck, Logistics/Staging (5) Staff
      - Aliquoting/Extraction (7) Staff
    - Kristie Jones, Genomics
      - Herb Higson, Genome Discovery (5) Staff
      - Kedest Teshome, Targeted Techniques (4) Staff
      - HPV Genomics (5) Staff
      - Tianna Zhao, Functional (2) Staff
      - Scientist (LTG Embed)
    - Casey Dagnall, Dev/Opt/Implement (5) Staff
    - Nathan Cole, IT/ Data Mgmt (3) Staff
    - Komal Jain, Scientific Support and Operations
      - Difei Wang, Research Analysis (6) Staff
      - Branch Embedded Bioinformaticians (6) Staff
      - Software Engineer
    - Jia Liu, Bioinformatics Production
      - GWAS Analysis (2) Staff
      - Sequencing Analysis (3) Staff
      - Microbiome Analysis (2) Staff

CGR…*by the numbers* (as of July 2023)

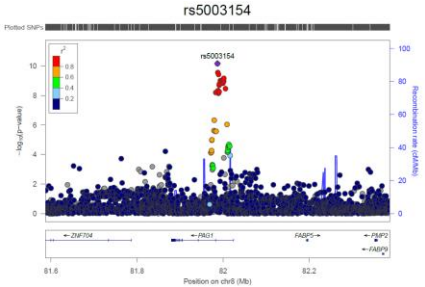


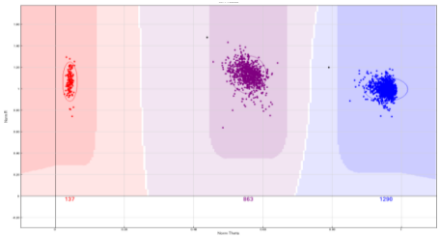


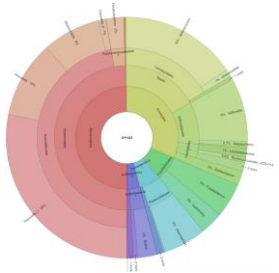
Variant Detection
766,852 GWAS Infinium/iSelect 1,395,525 Targeted Genotyping 52,892 Targeted Sequencing 32,442 Germline Exome 7,588 Somatic Exome 2,711 PacBio Sequencing 734 Whole Genome Sequencing

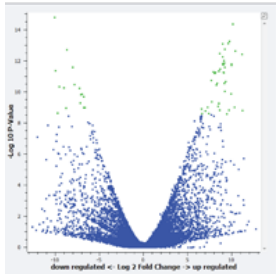
Functional Assessment
29,773 Methylation Arrays 30,952 Telomere length 5,226 mRNA Sequencing 1,832 miRNA Sequencing 568 Functional Sequencing

Non-human
27,237 HPV Sequencing 54,128 HPV typing 24,582 16S rRNA sequencing 489 Metagenomic Sequencing

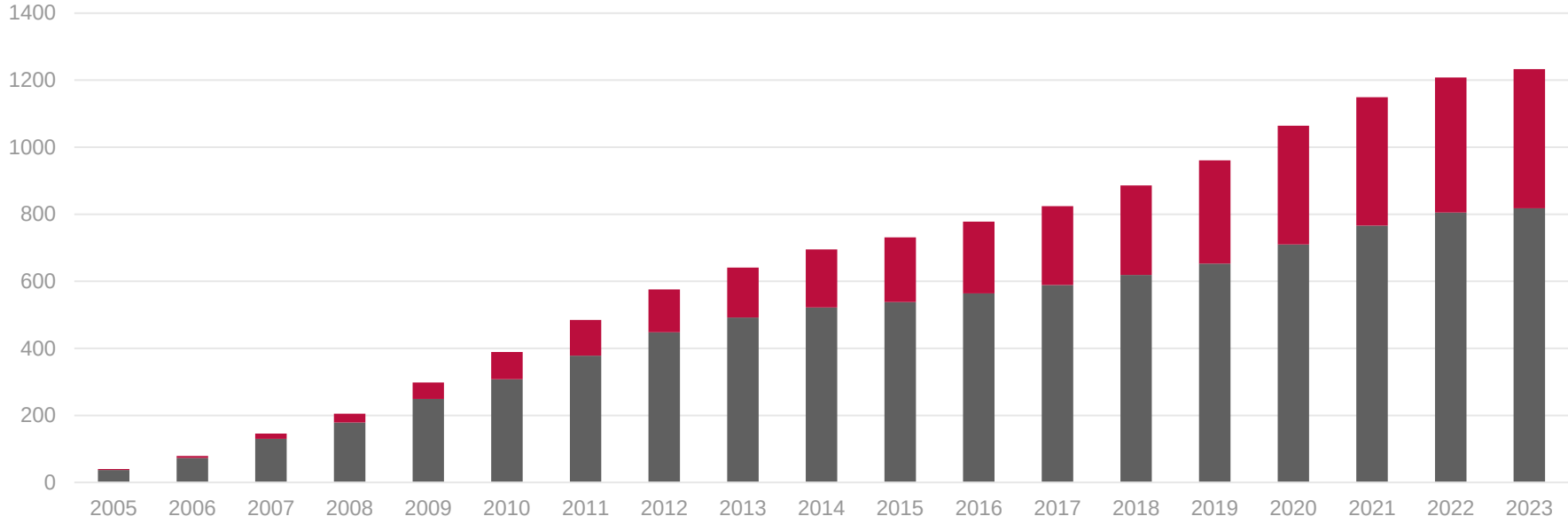








CGR Coauthored Publications 2005 – present)



- High Impact (IF>10): ~400 +

~150 pre-2005

Subcontract Coordination with Center for Cancer Genomics (CCG)

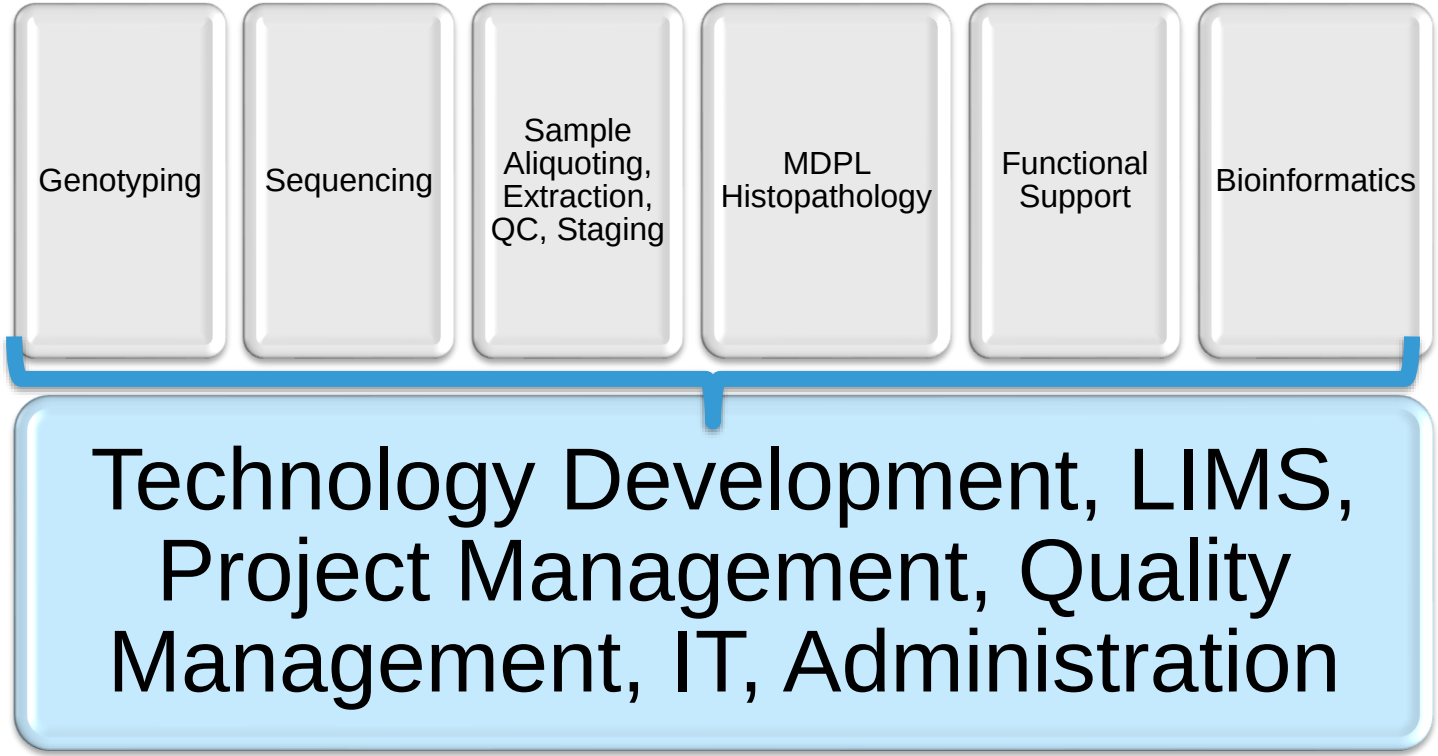
Leverage CCG Subcontract to supplement key research in DCEG

Study	Nationwide		Broad - WGS		
	Tumor	Normal	Tumor	Normal	Germline
Sherlock Lung	1770	1371	1532	617	934
Chernobyl Thyroid	618	541	451	378	251
Hong Kong Breast	186	186	96	92	49
EAGLE Italian Lung	1171	163	150	19	40
Italian Kidney	218	97	95	22	7
Chernobyl Trios	.	.	.	.	340
Italian Melanoma	.	.	.	.	213
PLCO Colorectal	138	4	.	.	.

NIH NATIONAL CANCER INSTITUTE
Center for Cancer Genomics

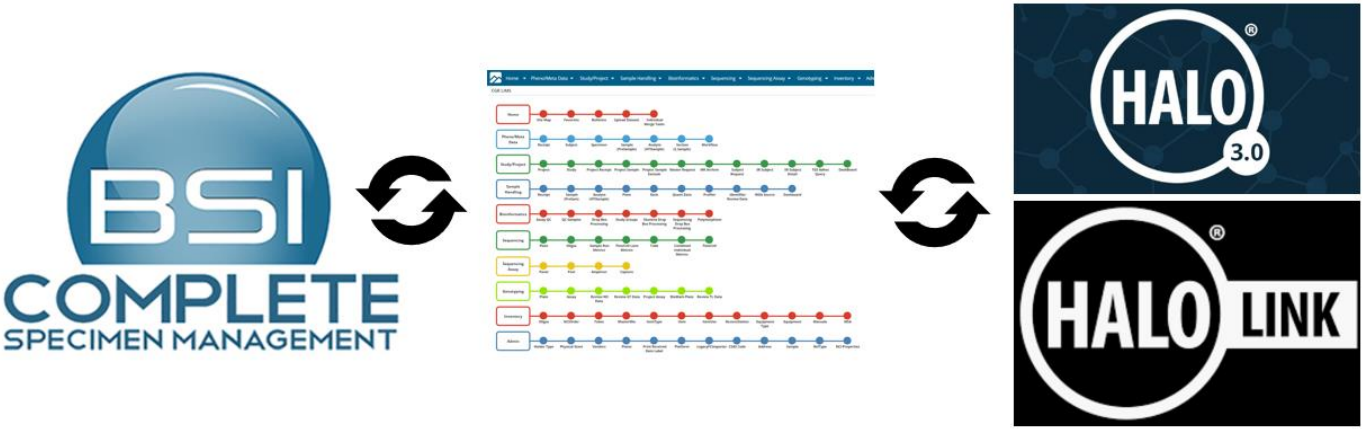
Many thanks to L Staudt et al

CGR
Integrally involved in DCEG from planning to publication



Management of all work through CGR LIMS

- CGR LIMS (LabVantage Sapphire) came online in 2003 and tracks all processes
- CGR LIMS shares via API sample inventory and image metadata between BSI and HALO

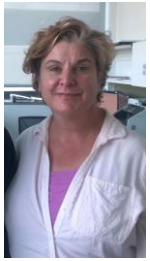


- Investment from DCEG key to support (4 staff for CGR LIMS) and allows LIMS to grow alongside technology and support organization
- CGR LIMS critical to quality management, inventory management, SOPs
- CGR LIMS Team recipient of 2023 FNL Outstanding Achievement Award

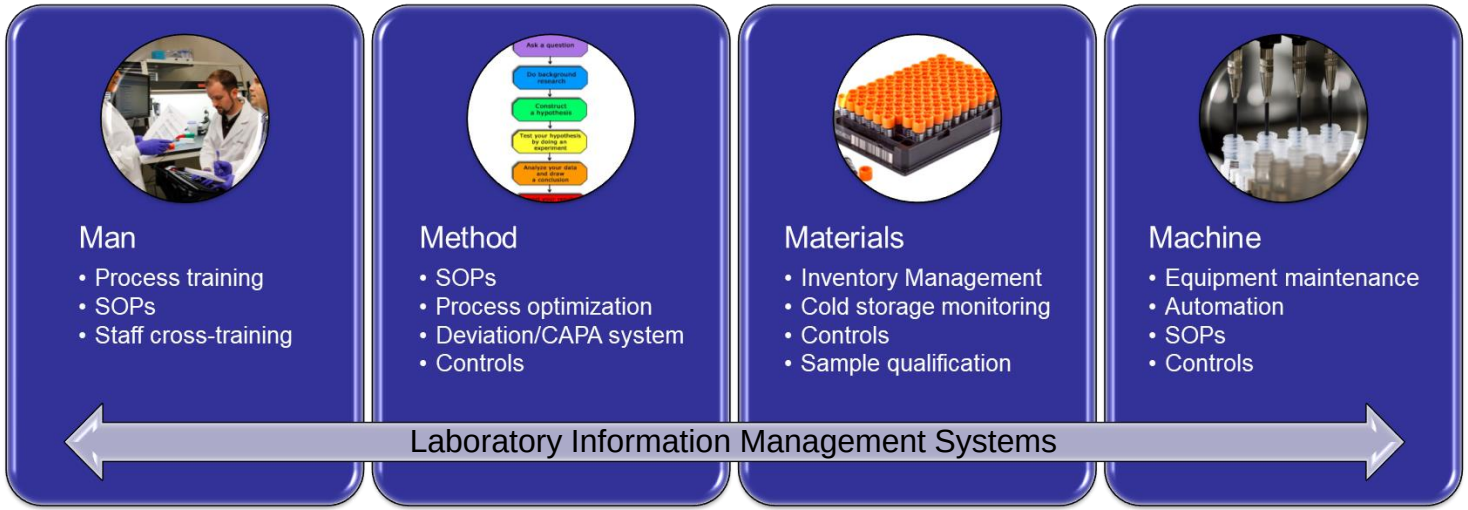
Coordination with NCI – Frederick Biorepository

- Central Repository houses over 15M biospecimens
- DCEG has over 12.5 M biospecimens (50+ types)
- BSI:CGR-LIMS real-time updates critical for traceability

CGR Dedication to Quality Management- ‘4Ms’

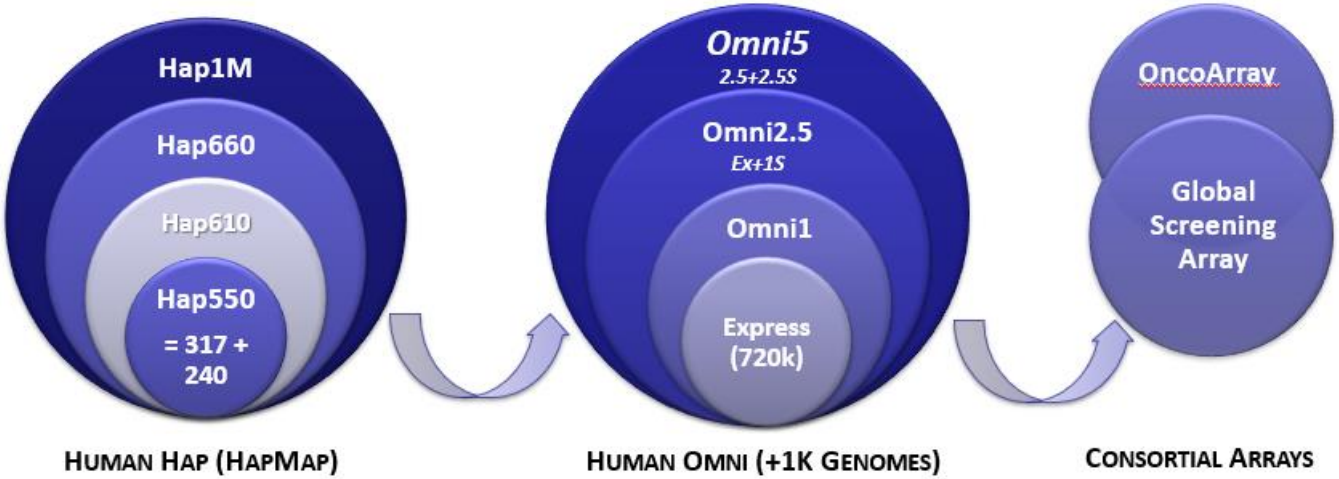


- High throughput **and** high quality not easy to obtain and maintain
- Continual improvement via active SOP system and Deviation/CAPA
- Documentation (Teams, LIMS, FogBugz, Github, Jupyter)
- Benchmarking and Controls for all new wet lab and analytical pipelines

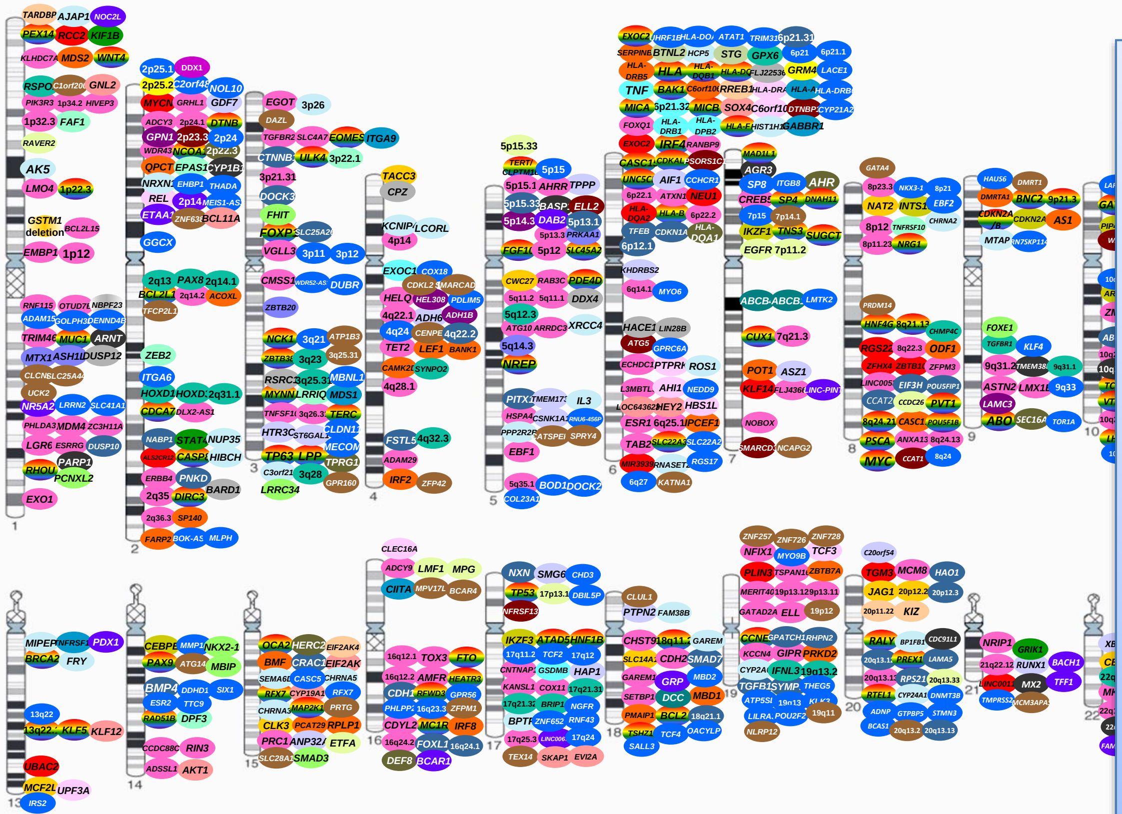


CGR Genotyping Chips (*Illumina*)

- CGR and DCEG leading GWAS studies since 2006
- Robust pipelines, automation key to high quality and throughput
- Larger consortia efforts key to detect smaller effect variants



Underlying Genetic Architecture of Cancer Susceptibility: March 2023



>1400 GWAS Signals
70% <u>include CGR data</u>

For > 30 “cancers”
Rare to Common

Ancestral
~85% whites
~14% East Asia
~1 % African Ancestry

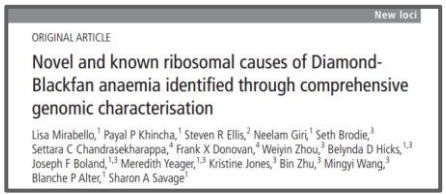
~15% Pleiotropy
(shared between cancers)

~10% Pleiotropy with other chronic diseases

36 Basal Cell
17 Bladder
312 Breast
13 Cervical
81 CLL
120 Colorectal
15 Cutaneous Sq
22 Endometrial
29 Esophageal
6 Ewing Sarcoma
3 Gallbladder
11 Gastric
37 Glioma
24 Hodgkins
13 Kidney
7 Liver
98 Lung
22 Melanoma
94 Multiple
23 Multiple Myeloma
14 Nasopharyngeal
18 Neuroblastoma
15 Non-Hodgkin
10 Oral
2 Osteosarcoma
38 Ovary
28 Pancreas
16 Pediatric ALL
431 Prostate
60 Testicular
17 Thyroid
3 Wilms

Leveraging Sequencing Technology: From chemistry to analytical pipelines

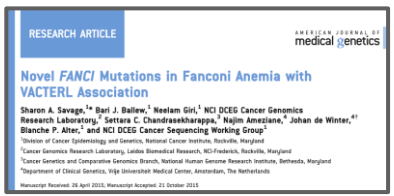
- Exome sequencing for family studies
- Population based exome studies
- Early adoption of long read PacBio applications


New loci

ORIGINAL ARTICLE

Novel and known ribosomal causes of Diamond-Blackfan anaemia identified through comprehensive genomic characterisation

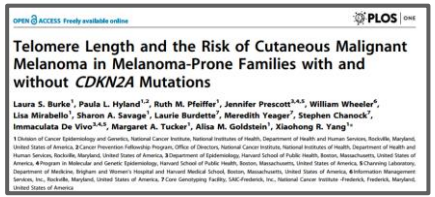
Lisa Mirabello,[1] Payal P Khincha,[1] Steven R Ellis,[2] Neelam Giri,[1] Seth Brodie,[3] Settara C Chandrasekharappa,[4] Frank X Donovan,[4] Weiyin Zhou,[3] Belynda D Hicks,[1,3] Joseph F Boland,[1,3] Meredith Yeager,[1,3] Kristine Jones,[3] Bin Zhu,[3] Mingyi Wang,[3] Blanche P Alter,[1] Sharon A Savage[1]


RESEARCH ARTICLE

AMERICAN JOURNAL OF medical genetics

Novel *FANCI* Mutations in Fanconi Anemia with VACTERL Association

Sharon A. Savage,[1*] Bari J. Ballew,[1] Neelam Giri,[1] NCI DCEG Cancer Genomics Research Laboratory,[2] Settara C. Chandrasekharappa,[3] Najim Ameziane,[4] Johan de Winter,[4†] Blanche P. Alter,[1] and NCI DCEG Cancer Sequencing Working Group[1]


OPEN ACCESS Freely available online

PLOS ONE

Telomere Length and the Risk of Cutaneous Malignant Melanoma in Melanoma-Prone Families with and without *CDKN2A* Mutations

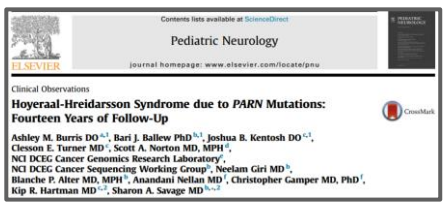
Laura S. Burke[1], Paula L. Hyland[1,2], Neil M. Pfeiffer[1], Jennifer Prescott[3,4,5], William Wheeler[6], Lisa Mirabello[1], Sharon A. Savage[1], Laurie Burdette[7], Meredith Yeager[7], Stephen Chanock[7], Immaculata De Vivo[3,4,5], Margaret A. Tucker[2], Alisa M. Goldstein[1], Xiaohong R. Yang[1*]


Hum Genet (2015) 134:775–787

ORIGINAL INVESTIGATION

Juvenile myelomonocytic leukemia due to a germline *CBL* Y371C mutation: 35-year follow-up of a large family

Anand Pathak[1] · Alexander Pemov[1] · Mary L. McMaster[2] · Ramita Dewan[3] · Sarangan Ravichandran[3] · Evgenia Pak[4] · Amalia Dutra[4] · Hyo Jung Lee[5] · Aurelie Vogt[6] · Xijun Zhang[6] · Meredith Yeager[6] · Stacie Anderson[6] · Martha Kirby[6] · NCI DCEG Cancer Genomics Research Laboratory · NCI DCEG Cancer Sequencing Working Group · Neil Caporaso[2] · Mark H. Greene[1] · Lynn R. Goldin[2] · Douglas R. Stewart[1]


Contents lists available at ScienceDirect

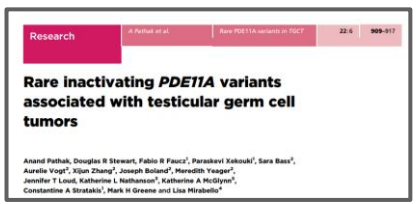
Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Clinical Observations

Hoyeraal-Hreidarsson Syndrome due to *PARN* Mutations: Fourteen Years of Follow-Up

Ashley M. Burris DO[a,1], Bari J. Ballew PhD[b,1], Joshua B. Kentosh DO[c,1], Clesson E. Turner MD[c], Scott A. Norton MD, MPH[d], NCI DCEG Cancer Genomics Research Laboratory[e], NCI DCEG Cancer Sequencing Working Group[b], Neelam Giri MD[b], Blanche P. Alter MD, MPH[b], Anandani Nellan MD[f], Christopher Gamper MD, PhD[f], Kip R. Hartman MD[c,2], Sharon A. Savage MD[b,*,2]


Research

A Pathak et al. Rare PDE11A variants in TGCT 22:6 909-917

Rare inactivating *PDE11A* variants associated with testicular germ cell tumors

Anand Pathak, Douglas R Stewart, Fabio R Fauca', Paraskevi Xekouki', Sara Bass', Aurelia Vogt', Xijun Zhang', Joseph Boland', Meredith Yeager', Jennifer T Loud, Katherine L Nathanson', Katherine A McGlynn', Constantine A Stratakis', Mark H Greene and Lisa Mirabello'

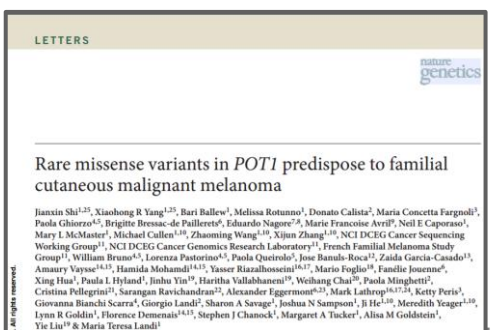

From www.thelancet.org by guest on June 27, 2017. For personal use only.

Plenary Paper

RED CELLS, IRON, AND ERYTHROPOIESIS

Whole-exome sequencing and functional studies identify *RPS29* as a novel gene mutated in multicase Diamond-Blackfan anemia families

Lisa Mirabello,[1] Elizabeth R. Macari,[2] Lea Jessop,[1] Steven R. Ellis,[3] Timothy Myers,[1] Neelam Giri,[1] Alison M. Taylor,[2] Katherine E. McGrath,[2] Jessica M. Humphries,[2] Bari J. Ballew,[1] Meredith Yeager,[4] Joseph F. Boland,[4] Ji He,[4] Belynda D. Hicks,[4] Laurie Burdett,[4] Blanche P. Alter,[1] Leonard Zon,[5,6] and Sharon A. Savage[1]


LETTERS

nature genetics

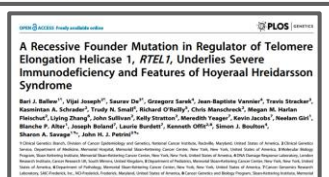
Rare missense variants in *POT1* predispose to familial cutaneous malignant melanoma

Jianxin Shi[1,25], Xiaohong R Yang[1,25], Bari Ballew[1], Melissa Rotunno[1], Donato Calista[2], Maria Concetta Fargnoli[3], Paola Ghiorzo[4,5], Brigitte Bressac-de Paillerets[6], Eduardo Nagore[7,8], Marie Francoise Avril[9], Neil E Caporaso[1], Mary L McMaster[1], Michael Cullen[1,10], Zhaoming Wang[1,10], Xijun Zhang[1,10], NCI DCEG Cancer Sequencing Working Group[11], NCI DCEG Cancer Genomics Research Laboratory[11], French Familial Melanoma Study Group[11], William Bruno[4,5], Lorenza Pastorino[4,5], Paola Queirolo[3], Jose Banuls-Roca[12], Zaida Garcia-Casado[13], Amaury Vaysse[14,15], Hamida Mohamdi[14,15], Yasser Riazalhosseini[16,17], Mario Foglio[18], Fanélie Jouenne[6], Xing Hua[1], Paula L Hyland[1], Jinhu Yin[19], Haritha Vallabhaneni[19], Weihang Chai[20], Paola Minghetti[2], Cristina Pellegrini[21], Sarangan Ravichandran[22], Alexander Eggermont[8,23], Mark Lathrop[16,17,24], Ketty Peris[3], Giovanna Bianchi Scarra[4], Giorgio Landi[2], Sharon A Savage[1], Joshua N Sampson[1], Ji He[1,10], Meredith Yeager[1,10], Lynn R Goldin[1], Florence Demenais[14,15], Stephen J Chanock[1], Margaret A Tucker[1], Alisa M Goldstein[1], Yie Liu[19] & Maria Teresa Landi[1]


BRIEF COMMUNICATION

Germline *TP53* Variants and Susceptibility to Osteosarcoma

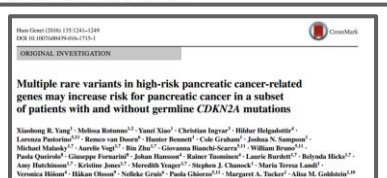
Lisa Mirabello, Meredith Yeager, Phuong L. Mai, Julie M. Gastier-Foster, Richard Gorlick, Chand Khanna, Ana Patiño-Garcia, Luis Sierrasesúmaga, Fernando Lecanda, Irene L. Andrulis, Jay S. Wunder, Nalan Gokgoz, Donald A. Barkauskas, Xijun Zhang, Aurelie Vogt, Kristine Jones, Joseph F. Boland, Stephen J. Chanock, Sharon A. Savage


OPEN ACCESS Freely available online

PLOS GENETICS

A Recessive Founder Mutation in Regulator of Telomere Elongation Helicase 1, *RTEL1*, Underlies Severe Immunodeficiency and Features of Hoyeraal Hreidarsson Syndrome

Bari J. Ballew[1*], Vijai Joseph[2*], Saurav De[3], Grzegorz Sarek[4], Jean-Baptiste Vannier[4], Travis Stracker[5], Kasmintan A. Schrader[6], Trudy N. Small[6], Richard O'Reilly[6], Chris Manschreck[6], Megan M. Harlan Fleischut[6], Liying Zhang[7], John Sullivan[8], Kelly Stratton[9], Meredith Yeager[7], Kevin Jacobs[7], Neelam Giri[1], Blanche P. Alter[1], Joseph Boland[7], Laurie Burdett[7], Kenneth Offit[2,6], Simon J. Boulton[4], Sharon A. Savage[1*], John H. J. Petrini[5*]


Hum Genet (2016) 135:1241–1249

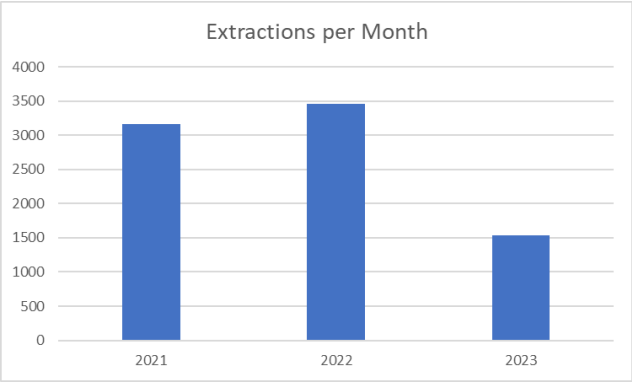
ORIGINAL INVESTIGATION

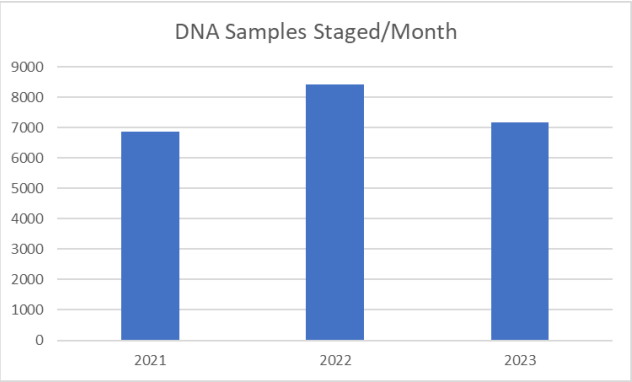
Multiple rare variants in high-risk pancreatic cancer-related genes may increase risk for pancreatic cancer in a subset of patients with and without germline *CDKN2A* mutations

Xiaohong R. Yang[1] · Melissa Rotunno[1,2] · Yanxi Xiao[1] · Christian Ingvar[3] · Hildur Helgadottir[4] · Lorenza Pastorino[5,6] · Remco van Doorn[7] · Hunter Bennett[1] · Cole Graham[1] · Joshua N. Sampson[1] · Michael Malasky[1,2] · Aurelie Vogt[1,2] · Bin Zhu[1,2] · Giovanna Bianchi-Scarra[5,6] · William Bruno[5,6] · Paola Queirolo[8] · Giuseppe Fornaciari[9] · Johan Hansson[10] · Rainer Tuominen[10] · Laurie Burdett[1,2] · Belynda Hicks[1,2] · Amy Hutchinson[1,2] · Kristine Jones[1,2] · Meredith Yeager[1,2] · Stephen J. Chanock[1] · Maria Teresa Landi[1] · Veronica Höiom[4] · Håkan Olsson[4] · Nelleke Gruis[7] · Paola Ghiorzo[5,11] · Margaret A. Tucker[2] · Alisa M. Goldstein[1,10]

High Throughput Sample Management

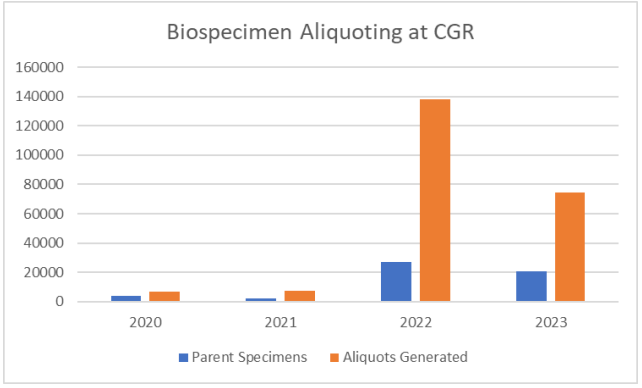
- CGR build out of dedicated sample logistics unit
- High throughput germline sample extraction methods
- Support for extractions from FFPE tissues
- Standardized QC, sample staging protocols





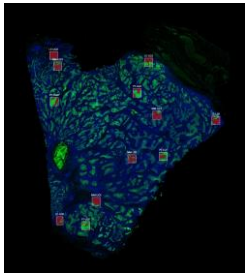
Leveraging CGR Aliquoting Capabilities for new FNLCR/NCI Efforts

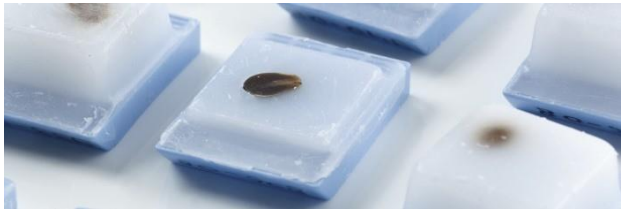
- Automated and manual aliquoting available
- Thaw time configured for study aims
- Samples maintained at +4C or less
- Fully integrated mechanical chillers
- BSI used to track all child vials, shipments, and residual returns
- Enhanced BSL2+ safety capabilities

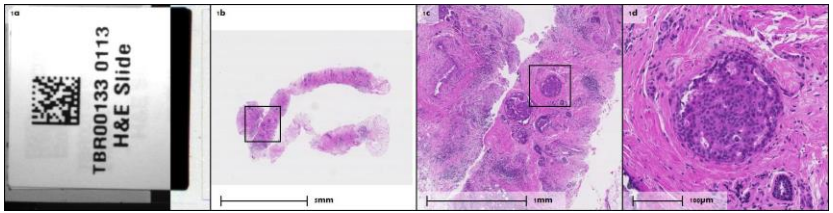


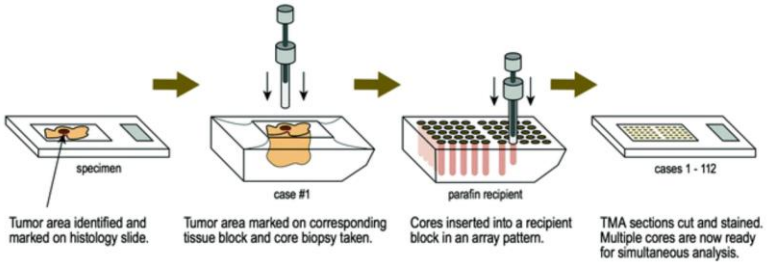
Expansion: Molecular and Digital Pathology
Enabling somatic studies

- Pathologist review, scoring, annotation support
- Tissue sectioning, tumor/cell enrichment through macro/microdissection
- H&E, chromogenic IHC, multiplex IF
- Tissue microarray construction
- Support for spatial biology approaches









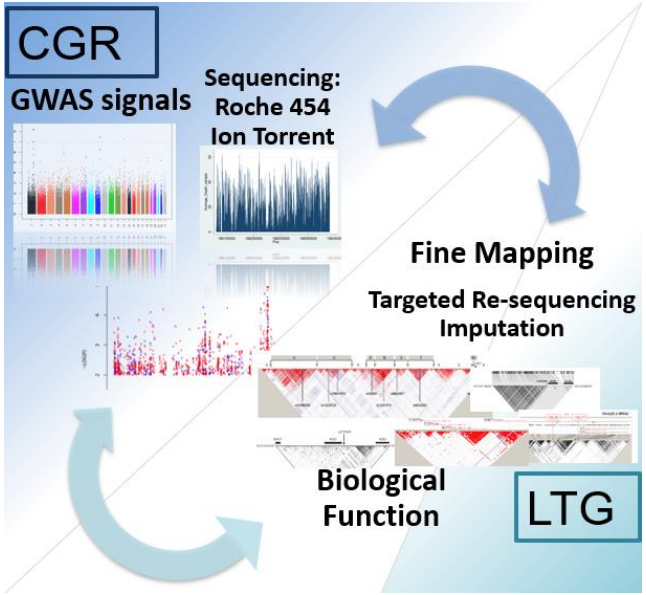
Digital Pathology at CGR: Creating an NCI Resource

- Established at DCEG by CGR/MDPL in 2018
- Expanded to an NCI-wide resource in 2020
- Enables large scale digital pathology image management and analysis
- Allows NCI and DCEG scientists to combine datasets across multiple cohorts
- Supports AI-enabled trained algorithms
- PLCO Image repository
- Effort recognized by 2023 NCI Directors OD Award

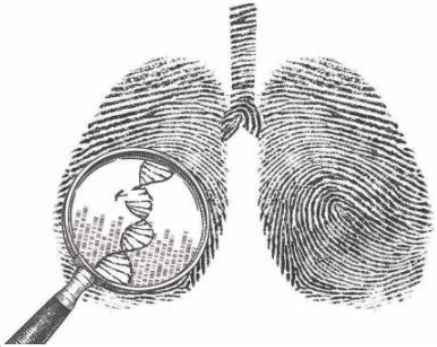
NIH NATIONAL CANCER INSTITUTE

Close Engagement with LTG/LGS drives discovery

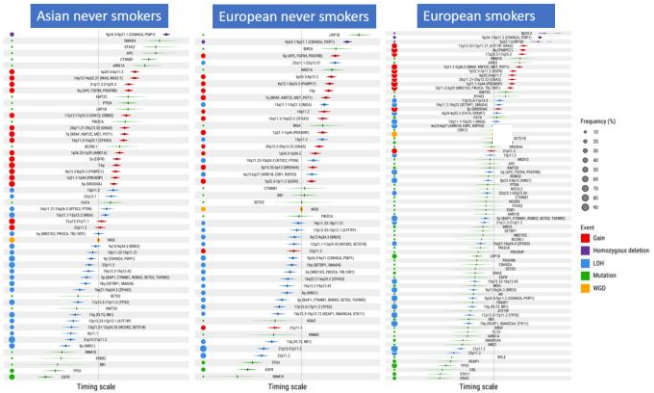
- Support functional validation or characterization of findings derived from GWAS/sequencing
  - CGR contributed to 100 papers from LTG/LGS
- Understand how genetic variations cause cancer susceptibility and outcome
- Evaluate the functional consequence of the genomic/epigenetic alterations
- Determine the pathogenesis of cancer using genomic, functional, and cell-based assays
- Support training of students/fellows



Sherlock-*Lung* **(NCI Directors Award Recipient 2023)**



- Ongoing mutational signature analyses in >2000 non-smoking lung adenocarcinoma
- Integrated analysis of WGS, histology and radiology data
- CGR manages work at NCH, Broad, generates RNA, methylation data, supports digital pathology efforts



ARTICLES
https://doi.org/10.1038/s41588-021-00920-0
nature genetics

Genomic and evolutionary classification of lung cancer in never smokers

Tongwu Zhang[1], Philippe Joubert[2], Naser Ansari-Pour[3], Wei Zhao[1], Phuc H. Hoang[1], Rachel Lokanga[4], Aaron L. Moye[5], Jennifer Rosenbaum[6], Abel Gonzalez-Perez[7], Francisco Martínez-Jiménez[7], Andrea Castro[8], Lucia Anna Muscarella[9], Paul Hofman[10], Dario Consonni[11], Angela C. Pesatori[11,12], Michael Kebede[1], Mengying Li[1], Bonnie E. Gould Rothberg[13,14], Iliana Peneva[15,16], Matthew B. Schabath[17], Maria Luana Poeta[18], Manuela Costantini[19], Daniela Hirsch[4], Kerstin Heselmeyer-Haddad[4], Amy Hutchinson[1,20], Mary Olanich[1,20], Scott M. Lawrence[1,20], Petra Lenz[1,20], Maire Duggan[21], Praphulla M. S. Bhawsar[1], Jian Sang[1], Jung Kim[1], Laura Mendoza[1], Natalie Saini[22], Leszek J. Klimczak[23], S. M. Ashiqul Islam[24], Burcak Otlu[24], Azhar Khandekar[24], Nathan Cole[1,20], Douglas R. Stewart[1], Jiyeon Choi[1], Kevin M. Brown[1], Neil E. Caporaso[1], Samuel H. Wilson[22], Yves Pommier[25], Qing Lan[1], Nathaniel Rothman[1], Jonas S. Almeida[1], Hannah Carter[26], Thomas Ried[4], Carla F. Kim[5,26], Nuria Lopez-Bigas[2,27], Montserrat Garcia-Closas[1], Jianxin Shi[1], Yohan Bossé[2,28], Bin Zhu[1], Dmitry A. Gordenin[22], Ludmil B. Alexandrov[24], Stephen J. Chanock[1], David C. Wedge[3,29] and Maria Teresa Landi[1]✉

Tracing Lung Cancer Risk Factors Through Mutational Signatures in Never-Smokers

The Sherlock-Lung Study

Maria Teresa Landi✉, Naoise C. Synnott, Jennifer Rosenbaum, Tongwu Zhang, Bin Zhu, Jianxin Shi, Wei Zhao, Michael Kebede, Jian Sang, Jiyeon Choi, Laura Mendoza, Marwil Pacheco, Belynda Hicks, Neil E. Caporaso, Mustapha Abubakar, Dmitry A. Gordenin, David C. Wedge, Ludmil B. Alexandrov, Nathaniel Rothman, Qing Lan, Montserrat Garcia-Closas, and Stephen J. Chanock

✉ Correspondence to Dr. Maria Teresa Landi, Integrative Tumor Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Room 7E106, 9609 Medical Drive, Rockville, MD 20892 (e-mail: landim@mail.nih.gov).

Initially submitted April 3, 2020; accepted for publication October 16, 2020.

Confluence: Mapping Breast Cancer Susceptibility in the Cloud

- Breast Cancer Association Consortium (BCAC)
- Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)
- African-Ancestry Breast Cancer Genetic Study (AABCGS)
- Asia Breast Cancer Consortium (ABCC)
- Latin America Genomics Breast Cancer Consortium (LAGENO-BC)

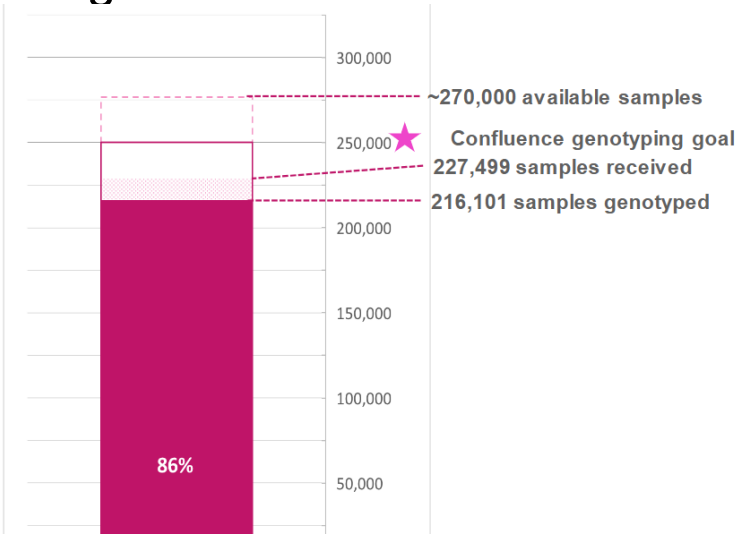
Target: 350,000 cases and >350,000 controls

Confluence
Uncovering breast cancer genetics

Confluence

Uncovering breast cancer genetics

- CGR Scientists worked with a large consortia to design custom content to accelerate breast cancer research on the Illumina Global Screening and Global Diversity Arrays
- Collaborative genotyping and support @ Cambridge University (D Easton)
- CGR• 118,588 samples received
  • 109,226 samples scanned
- CGR instrumental in developing
  Cloud-based resource for study



Critical Role of CGR in Follow-up Studies of Chornobyl Accident

- Comprehensive Genomic Characterization of Radiation-Related-Thyroid Cancer in Ukraine (Morton et al *Science* 2021)
- Hosting of Chornobyl Tissue Bank- An international resource

- Family Study of Possible Transgenerational Effects of Adults Exposed to Radiation following the Chernobyl Accident – (Yeager* et al *Science* 2021)

Study of Possible Transgenerational Effect due to Protracted Radiation Following Chernobyl:

- No increase in DeNovo Mutations in relation to dose exposure
  - Adequate power to detect elevated rates in adult children (survivor bias)
- No evidence of radiation-induced single base mutation or epigenetic signature
- Extended gonadal doses
- Alter the balance between new gonadal DNMs and

  DNA repair


RESEARCH

RADIATION RISKS

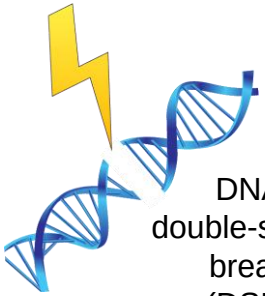
Lack of transgenerational effects of ionizing radiation exposure from the Chernobyl accident

Yeager et al. *Science* 2021

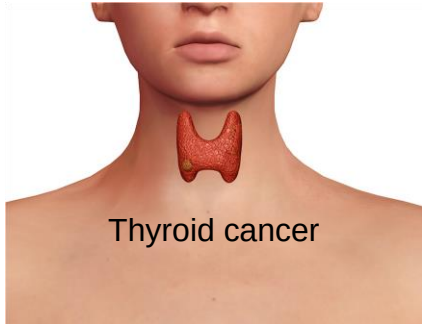
Distinct Opportunity to Investigate the Intersection of Discrete Radiation Exposure, Epidemiology & Landscape Genomic Analysis

April 26, 1986

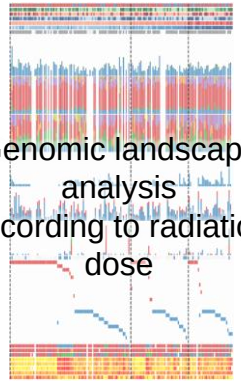
Morton et al. *Science* 2021



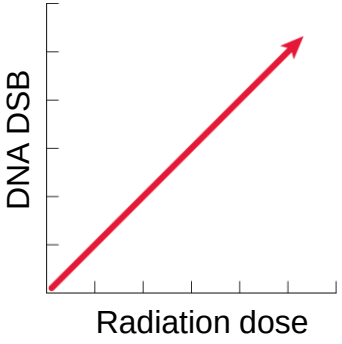
DNA double-strand break (DSB)

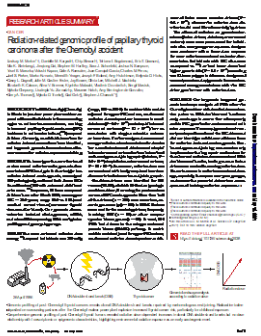


Thyroid cancer



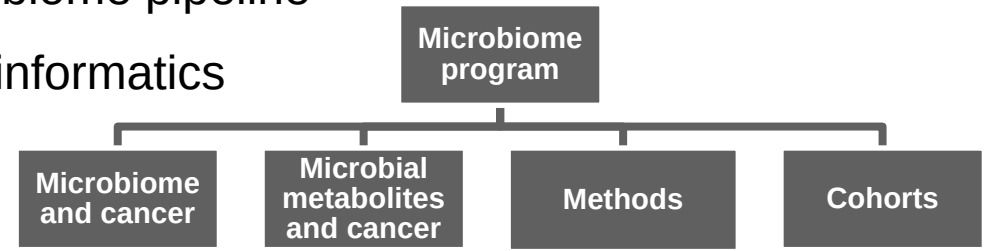
Genomic landscape analysis according to radiation dose





Microbiome Studies at DCEG/CGR

- Close collaboration with focus on methodological work
- Establish best cost-effective methods for collecting fecal and oral samples for prospective studies
- Estimate sample size requirements for shotgun sequencing studies
- Develop quality control standards to evaluate reproducibility
- Investigate long-term stability of the microbiome in freezer
- Standardize methods across microbiome pipeline
  - DNA extraction, sequencing, bioinformatics



H. pylori Genome Project (*Hp*GP)

- Characterize the spectrum of genomic and epigenomic variations of H. pylori strains isolated from patients with various stages of the carcinogenesis process
- Identify molecular features that may contribute to pathologic effects
- Establish a repository of multidimensional data and well-characterized strains for utilization by the scientific community
- CGR Staff presenting recent results at the European Helicobacter and Microbiota Study Group - EHMSG 2023

N=1,011 SMRT/PacBio genomes/epigenomes

- Non-atrophic gastritis: 606
- Advanced intestinal metaplasia: 172
- Gastric cancer: 233

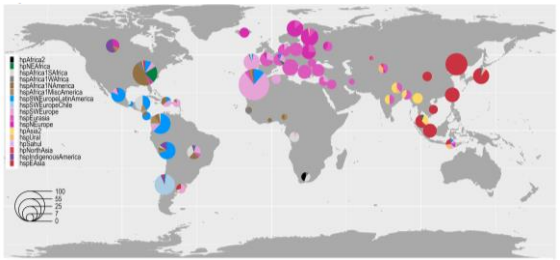
nature reviews disease primers
https://doi.org/10.1038/s41572-023-00431-8

Primer

Check for updates

Helicobacter pylori infection

Peter Malfertheiner[1,2], M. Constanza Camargo[3], Emad El-Omar[4], Jyh-Ming Liou[5], Richard Peek[6], Christian Schulz[1,7], Stella I. Smith[8] & Sebastian Suerbaum[7,9,10]



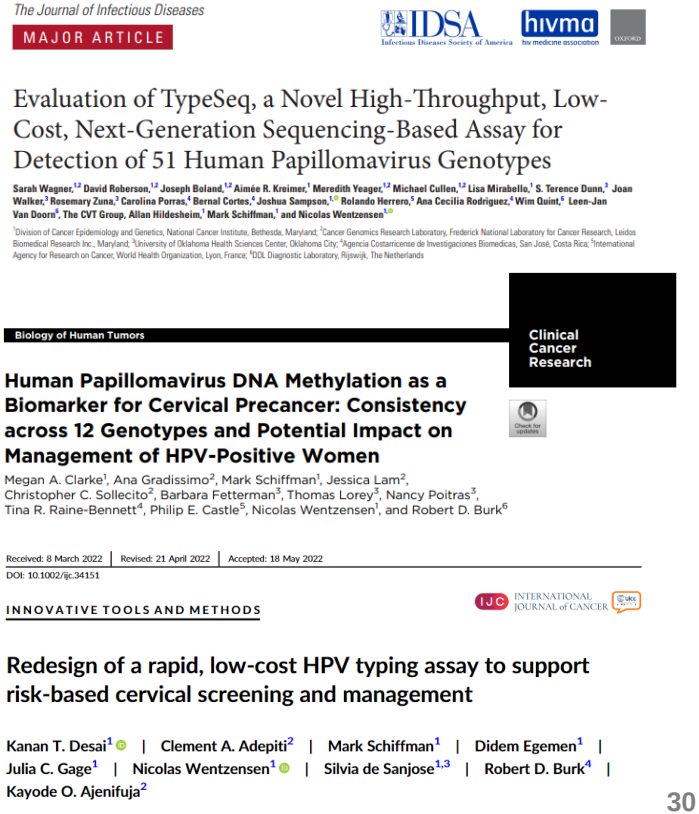
Nature 2023 in Review

Human Genetics & COVID-19 in DCEG/CGR

- NCI COVID-19 in Cancer Patients Study (NCCAPS): Prospective Study of COVID-19 in Cancer Patients
- COVIDcode Study: NIH Clinical Center IRB approved study of 2,500 cases
  - Collaboration between investigators in NHGRI, NCI, and NIAID
- COVNET: a large-scale study of the germline genetics of COVID-19 susceptibility and manifestations
  - ~30,000 GWAS & 5,000 Whole Genome Sequencing (WGS) of COVID-19 cases

Leveraging CGR Expertise in HPV Assay Development

- High throughput, low-cost 50+ HPV Typing
  - TypeSeq1, TypeSeq2
  - Critical for epi studies, vaccine trials
- Methylation
  - Key biomarker for progression from infection to precancer
- Screenfire optimization for HPV high risk screening in LMIC environments
  - Temp stable reagents
  - Low-cost instrumentation
  - Screening for high-risk types only



The Journal of Infectious Diseases

MAJOR ARTICLE

Evaluation of TypeSeq, a Novel High-Throughput, Low-Cost, Next-Generation Sequencing-Based Assay for Detection of 51 Human Papillomavirus Genotypes

Sarah Wagner,[1,2] David Roberson,[1,2] Joseph Boland,[1,2] Aimée R. Kreimer,[1] Meredith Yeager,[1,2] Michael Cullen,[1,2] Lisa Mirabello,[1] S. Terence Dunn,[3] Joan Walker,[3] Rosemary Zuna,[3] Carolina Porras,[4] Bernal Cortes,[4] Joshua Sampson,[1,7] Rolando Herrero,[5] Ana Cecilia Rodriguez,[4] Wim Quint,[6] Leen-Jan Van Doorn[6], The CVT Group, Allan Hildesheim,[1] Mark Schiffman,[1] and Nicolas Wentzensen[1,8]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland; [2]Cancer Genomics Research Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research Inc., Maryland; [3]University of Oklahoma Health Sciences Center, Oklahoma City; [4]Agencia Costarricense de Investigaciones Biomedicas, San José, Costa Rica; [5]International Agency for Research on Cancer, World Health Organization, Lyon, France; [6]DDL Diagnostic Laboratory, Rijswijk, The Netherlands

Biology of Human Tumors

Clinical Cancer Research

Human Papillomavirus DNA Methylation as a Biomarker for Cervical Precancer: Consistency across 12 Genotypes and Potential Impact on Management of HPV-Positive Women

Megan A. Clarke[1], Ana Gradissimo[2], Mark Schiffman[1], Jessica Lam[2], Christopher C. Sollecito[2], Barbara Fetterman[3], Thomas Lorey[3], Nancy Poitras[3], Tina R. Raine-Bennett[4], Philip E. Castle[5], Nicolas Wentzensen[1], and Robert D. Burk[6]

Received: 8 March 2022 | Revised: 21 April 2022 | Accepted: 18 May 2022

DOI: 10.1002/ijc.34151

INNOVATIVE TOOLS AND METHODS

IJC INTERNATIONAL JOURNAL of CANCER

Redesign of a rapid, low-cost HPV typing assay to support risk-based cervical screening and management

Kanan T. Desai[1] | Clement A. Adepiti[2] | Mark Schiffman[1] | Didem Egemen[1] | Julia C. Gage[1] | Nicolas Wentzensen[1] | Silvia de Sanjose[1,3] | Robert D. Burk[4] | Kayode O. Ajenifuja[2]

DCEG and NCI investment in HPV Research

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research Paper

A study of type-specific HPV natural history and implications for contemporary cervical cancer screening programs

Maria Demarco[a,b,1,*], Noorie Hyun[a,c,1], Olivia Carter-Pokras[b], Tina R. Raine-Bennett[d], Li Cheung[a], Xiaojian Chen[a], Anne Hammer[e,f], Nicole Campos[g], Walter Kinney[h], Julia C. Gage[a], Brian Befano[i], Rebecca B. Perkins[j], Xin He[b], Cher Dallal[b], Jie Chen[b], Nancy Poitras[k], Marie-Helene Mayrand[l,m], Francois Coutlee[n], Robert D. Burk[o], Thomas Lorey[k], Philip E. Castle[o], Nicolas Wentzensen[a], Mark Schiffman[a]

Papillomavirus Research 1 (2015) 3–11

Contents lists available at ScienceDirect

Papillomavirus Research

journal homepage: www.elsevier.com/locate/pvr

Deep sequencing of HPV16 genomes: A new high-throughput tool for exploring the carcinogenicity and natural history of HPV16 infection

Michael Cullen [a,b], Joseph F. Boland [a,b,e], Mark Schiffman [a], Xijun Zhang [a,b], Nicolas Wentzensen [a], Qi Yang [a,b], Zigui Chen [f], Kai Yu [a], Jason Mitchell [a,b], David Roberson [a,b], Sara Bass [a,b], Laurie Burdette [a,b], Moara Machado [c], Sarangan Ravichandran [d], Brian Luke [d], Mitchell J. Machiela [a], Mark Andersen [e], Matt Osentoski [e], Michael Laptewicz [e], Sholom Wacholder [a], Ashlie Feldman [a,b], Tina Raine-Bennett [g], Thomas Lorey [g], Philip E. Castle [f,h], Meredith Yeager [a,b], Robert D. Burk [i,j,l], Lisa Mirabello [a,g,k,l]

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[b] Cancer Genomics Research Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc., Frederick, MD, USA
[c] Departmento de Biologia Geral, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil
[d] Frederick National Laboratory for Cancer Research, Simulation, Analysis and Mathematical Modeling Group Advanced Biomedical Computing Cen
Frederick, MD, USA
[e] Thermo Fisher Scientific (Formerly Life Technologies), Carlsbad, CA, USA
[f] Department of Epidemiology and Population Health, At Albert Einstein College of Medicine, Bronx, NY, USA
[g] Regional Laboratory and Women's Health Research Institute, Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA
[h] Global Coalition Against Cervical Cancer, Arlington, VA, USA
[i] Division of Gynecologic Oncology, Department of Obstetrics & Gynecology and Women's Health, at Albert Einstein College of Medicine, Bronx, NY, USA

JNCI J Natl Cancer Inst (2022) 114(6): djac034

https://doi.org/10.1093/jnci/djac034
First published online February 17, 2022
Article

Cervical Precancers and Cancers Attributed to HPV Types by Race and Ethnicity: Implications for Vaccination, Screening, and Management

Jacqueline Mix, PhD [1], Mona Saraiya, MD,[1,*] Benjamin D. Hallowell, PhD,[1] Brian Befano, MS,[2] Li C. Cheung, PhD [3], Elizabeth R. Unger, MD, PhD [4], Julia W. Gargano, PhD,[5] Lauri E. Markowitz, MD,[5] Philip E. Castle, PhD [3,6], Tina Raine-Bennett, MD,[7] Joan Walker, MD [8], Rosemary Zuna, MD,[8] Mark Schiffman, MD,[3] Nicolas Wentzensen, MD, PhD [3], Julia C. Gage, PhD [3]

ORIGINAL ARTICLE

Genetic variation within the human papillomavirus type 16 genome is associated with oropharyngeal cancer prognosis

K. A. Lang Kuhs[1,2*], D. L. Faden[3,4], L. Chen[5], D. K. Smith[6], M. Pinheiro[7], C. B. Wood[8,9], S. Davis[8], M. Yeager[7,10], J. F. Boland[7,10], M. Cullen[7,10], M. Steinberg[7,10], S. Bass[7,10], X. Wang[11], P. Liu[12], M. Mehrad[13], T. Tucker[1], J. S. Lewis, Jr[8,13], R. L. Ferris[14,15] & L. Mirabello[7]

[1]Department of Epidemiology, College of Public Health, University of Kentucky, Lexington; [2]Department of Medicine, Vanderbilt University Medical Cancer, Nashville; [3]Department of Otolaryngology, Massachusetts Eye and Ear, Massachusetts General Hospital, Harvard Medical School, Boston; [4]Broad Institute of MIT and Harvard, Cambridge; [5]Division of Cancer Biostatistics, Department of Internal Medicine and Biostatistics and Bioinformatics Shared Resource Facility, Markey Cancer Center, University of Kentucky, Lexington; [6]Department of Biostatistics, Vanderbilt University Medical Center, Nashville; [7]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville; [8]Department of Otolaryngology – Head and Neck Surgery, Vanderbilt University Medical Center, Nashville; [9]Department of Otolaryngology – Head and Neck Surgery, University of Tennessee Health Science Center, Memphis; [10]Cancer Genomics Research Laboratory, Leidos Biomedical Research, Inc., Frederick; [11]Department of Pharmacology and Regenerative Medicine, The University of Illinois at Chicago, Chicago; [12]Department of Radiation Oncology, Washington University School of Medicine, St. Louis; [13]Department of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville; [14]University of Pittsburgh Medical Center Hillman Cancer Center, Pittsburgh; [15]Department of Otolaryngology-Head and Neck Surgery, University of Pittsburgh Medical Center, Pittsburgh, USA

Available online 16 March 2022

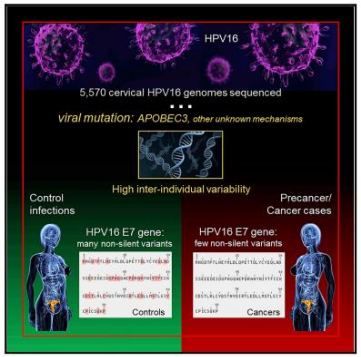
viruses

MDPI

Article

Phylogenomic Analysis of Human Papillomavirus Type 31 and Cervical Carcinogenesis: A Study of 2093 Viral Genomes

Maisa Pinheiro [1], Ariana Harari [2], Mark Schiffman [1], Gary M. Clifford [3], Zigui Chen [4], Meredith Yeager [1,5], Michael Cullen [1,5], Joseph F. Boland [1,5], Tina Raine-Bennett [6], Mia Steinberg [1,5], Sara Bass [1,5], Yanzi Xiao [1], Vanessa Tenet [3], Kai Yu [1], Bin Zhu [1], Laurie Burdett [1,5], Sevilay Turan [1,5], Thomas Lorey [7], Philip E. Castle [1,8], Nicolas Wentzensen [1], Robert D. Burk [2,9,*,†] and Lisa Mirabello [1,*,†]



Cell

Article

HPV16 E7 Genetic Conservation Is Critical to Carcinogenesis

Lisa Mirabello,[1,14,*] Meredith Yeager,[1,2] Kai Yu,[1] Gary M. Clifford,[3] Yanzi Xiao,[1] Bin Zhu,[1] Michael Cullen,[1,2] Joseph F. Boland,[1,2] Nicolas Wentzensen,[1] Chase W. Nelson,[4] Tina Raine-Bennett,[5] Zigui Chen,[6] Sara Bass,[1,2] Lei Song,[1,2] Qi Yang,[1,2] Mia Steinberg,[1,2] Laurie Burdett,[1,2] Michael Dean,[1] David Roberson,[1,2] Jason Mitchell,[1,2] Thomas Lorey,[7] Silvia Franceschi,[3] Philip E. Castle,[8] Joan Walker,[9] Rosemary Zuna,[9] Aimée R. Kreimer,[1] Daniel C. Beachler,[1,10] Allan Hildesheim,[1] Paula Gonzalez,[11] Carolina Porras,[11] Robert D. Burk,[6,12,13] and Mark Schiffman[1,13]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, MD, USA
[2]Cancer Genomics Research Laboratory, Leidos Biomedical Research, Inc., Frederick, MD, USA
[3]Infections and Cancer Epidemiology Group, International Agency for Research on Cancer 150, Cours Albert Thomas, 69372 Lyon Cedex 08, France
[4]Sackler Institute for Comparative Genomics, American Museum of Natural History, New York City, NY, USA
[5]Women's Health Research Institute, Division of Research, Kaiser Permanente Northern California, Oakland, CA, USA
[6]Department of Microbiology, The Chinese University of Hong Kong, Shatin, Hong Kong
[7]Regional Laboratory, Kaiser Permanente Northern California, Oakland, CA, USA
[8]Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA
[9]University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[10]HealthCore Inc., Safety and Epidemiology, Wilmington, DE, USA
[11]Agencia Costarricense de Investigaciones Biomédicas (ACIB), former Proyecto Epidemiológico Guanacaste, Fundación INCIENSA, Guanacaste, Costa Rica
[12]Departments of Pediatrics, Microbiology and Immunology, and Obstetrics & Gynecology and Women's Health, Albert Einstein College of Medicine, Bronx, NY, USA
[13]These authors contributed equally
[14]Lead Contact
*Correspondence: mirabellol@mail.nih.gov
http://dx.doi.org/10.1016/j.cell.2017.08.001

Establishing Resource within CGR for HPV Typing

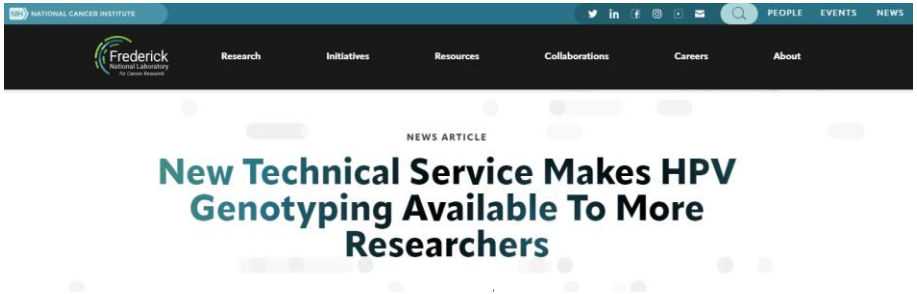
- Leveraging existing resources and expertise
  - High throughput sample management, extraction, analysis
  - Established project management, LIMS tracking, quality management
- Laboratory staff embedded within existing structure to run HPV genomic typing assays
- Allows for 75-100K tests per year with minimal additions
- Future capacity available after completion of vaccine trials
  - ESCUDDO, PRIMAVERA, PRISMA

Transferring Technology to the Community

- Transfer HPV typing to Costa Rica to support NCI vaccine trials (escuddo, primavera, prisma)
- Engagement with FNLCR Technical Services Program

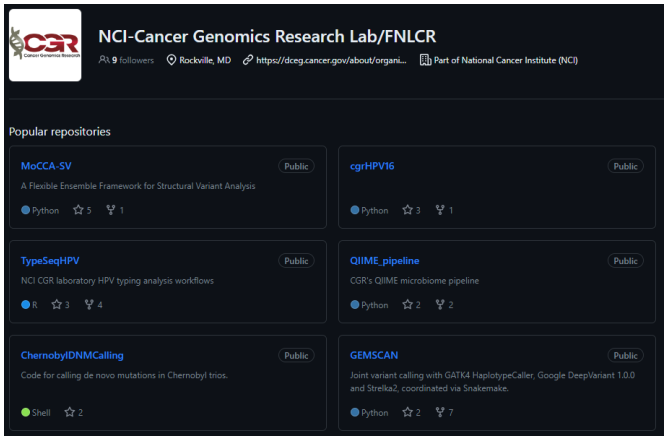
proyecto escuddo
ESTUDIO COMPARATIVO DE UNA Y DOS DOSIS VACUNA CONTRA EL PAPILOMA HUMANO

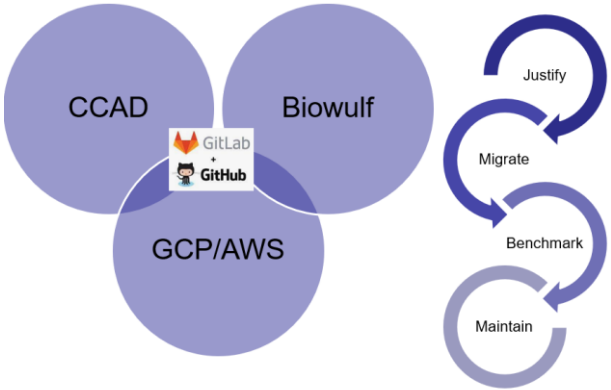
prisma
Prevención del cáncer de cérvix con **una sola dosis de vacuna contra VPH** en mujeres adultas jóvenes.



CGR and DCEG drive and support FAIR principles

Project Submission Title	Grant/ Intramural/Contract #	Principal Investigator	Genomic DSP	IC	BSI	Submission Status	Actions
A Genome-wide Association Study (GWAS) of Risk for Osteosarcoma (v1)	1ZIACP010142-18	Mirabello, Lisa	✓	✓	✓	✓	
A genome-wide association study of prostate cancer in West African men (v1)	1ZIACP010180-15	Cook, Michael	✓	✓	✓	✓	
A novel recurrent mutation in MITF predisposes to familial and sporadic melanoma (v1)	1ZIACP010201-07	Brown, Kevin	✓	✓	✓	✓	
Analyzing Familial Bladder Cancer Families with Whole Exome Sequencing To Uncover Germline Allelic V (v1)	1ZIACP004410-40	Stewart, Doug	●	●	✗	✗	
Associations of breast cancer, urinary estrogens and prostaglandin E with the IgA-stained and -un...	1ZIACP010214-07	Goedert, James	✓	N/A	✓	✓	
CGEMS Breast Cancer GWAS (v1)	1ZIACP010187-12	Chanock, Stephen	✓	✓	✓	✓	
CGEMS Pancreatic Cancer (PanScan) (v1)	1ZIACP010193-10	Stolzenberg-Solomon, Rachael	✓	✓	✓	✓	
CGEMS Prostate Cancer (v1)	1ZIACP010187-12	Chanock, Stephen	✓	✓	✓	✓	





Downstream Analysis & Embedded Support

- Pipeline optimization and migration (Biowulf, Cloud/Strides, NIDAP) to enable reuse, reproducibility and improvement by NCI community
  - Deposition of code in GitHub
- Support for investigator driven analyses for functional and biological insights
- Development of support for new applications for single cell, spatial biology and AI based applications
- Dedicated bioinformatics staff (6) embedded in DCEG branches
- Active coordination with DCEG Bioinformatics Virtual Core (W Wong director)

CGR-DCEG Credo

"This is not a 'core'. This is the Department of Human Genetics of DCEG and is critical to its important mission."

David Botstein during 2011 Evaluation

NIH NATIONAL CANCER INSTITUTE Division of Cancer Epidemiology & Genetics

Frederick National Laboratory for Cancer Research

CGR Cancer Genomics Research

Acknowledgements

Cancer Genomics Research Laboratory

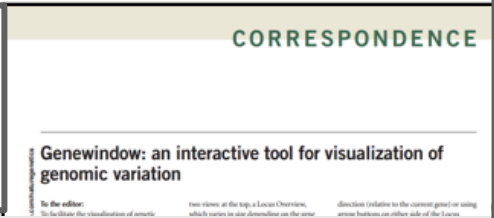
D528–D532 Nucleic Acids Research, 2004, Vol. 32, Database issue
DOI: 10.1093/nar/gkh005

SNP500Cancer: a public resource for sequence validation and assay development for genetic variation in candidate genes

Bernice R. Packer[a], Meredith Yeager, Brian Staats, Robert Welch, Andrew Crenshaw, Maureen Kiley, Andrew Eckert, Michael Beerman, Edward Miller, Andrew Bergen[1], Nathaniel Rothman[1], Robert Strausberg[2] and Stephen J. Chanock[3]

Intramural Research Support Program, SAIC-Frederick, NCI-FCRDC, Frederick, MD, USA, [1]Division of Cancer Epidemiology and Genetics, [2]Office of Cancer Genomics, National Cancer Institute, Bethesda, MD, USA and [3]Section on Genomic Variation, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Gaithersburg, MD, USA

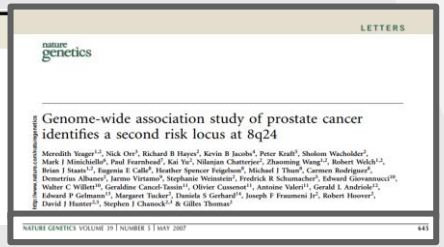
Received July 8, 2003; Revised and Accepted August 7, 2003



CORRESPONDENCE

Genewindow: an interactive tool for visualization of genomic variation

To the editor:



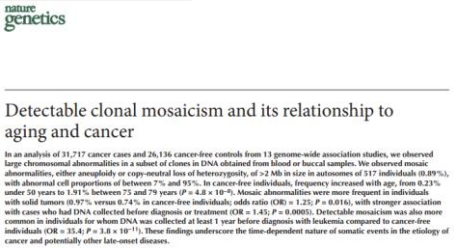
LETTERS

nature genetics

Genome-wide association study of prostate cancer identifies a second risk locus at 8q24

Meredith Yeager[1,2], Nick Orr[3], Richard B Hayes[2], Kevin B Jacobs[4], Peter Kraft[5], Sholom Wacholder[2], Mark J Minichiello[6], Paul Fearnhead[7], Kai Yu[2], Nilanjan Chatterjee[2], Zhaoming Wang[1,2], Robert Welch[1,2], Brian J Staats[1,2], Eugenia E Calle[8], Heather Spencer Feigelson[8], Michael J Thun[8], Carmen Rodriguez[8], Demetrius Albanes[9], Jarmo Virtamo[9], Stephanie Weinstein[9], Fredrick R Schumacher[5], Edward Giovannucci[10], Walter C Willett[10], Geraldine Cancel-Tassin[11], Olivier Cussenot[11], Antoine Valeri[12], Gerald L Andriole[13], Edward P Gelmann[14], Margaret Tucker[2], Daniela S Gerhard[15], Joseph F Fraumeni Jr[2], Robert Hoover[2], David J Hunter[4,5], Stephen J Chanock[2,3] & Gilles Thomas[3]

NATURE GENETICS VOLUME 39 | NUMBER 5 | MAY 2007 643



nature genetics

Detectable clonal mosaicism and its relationship to aging and cancer

In an analysis of 31,717 cancer cases and 26,136 cancer-free controls from 13 genome-wide association studies, we observed large chromosomal abnormalities in a subset of clones in DNA obtained from blood or buccal samples. We observed mosaic abnormalities, either aneuploidy or copy-neutral loss of heterozygosity, of >2 Mb in size in autosomes of 517 individuals (0.89%), with abnormal cell proportions of between 7% and 95%. In cancer-free individuals, frequency increased with age, from 0.23% under 50 years to 1.91% between 75 and 79 years ($P = 4.8 \times 10^{-9}$). Mosaic abnormalities were more frequent in individuals with solid tumors (0.97% versus 0.74% in cancer-free individuals; odds ratio (OR) = 1.25; $P = 0.016$), with stronger association with cases who had DNA collected before diagnosis or treatment (OR = 1.45; $P = 0.0005$). Detectable mosaicism was also more common in individuals for whom DNA was collected at least 1 year before diagnosis with leukemia compared to cancer-free individuals (OR = 35.4; $P = 3.8 \times 10^{-11}$). These findings underscore the time-dependent nature of somatic events in the etiology of cancer and potentially other late-onset diseases.

2001: Core Genotyping Facility Established

2001-2004: Candidate gene studies, TaqMan, SNP500

2005-2007: Genewindow, CGEMS for first GWAS, Pregenotyping QC

2008 - 2010: LTG established, Roche454 for fine mapping, mosaicism

2011-2013: Illumina, Ion PGM, Proton sequencing, add DESL, rename to CGR

CGR Milestones

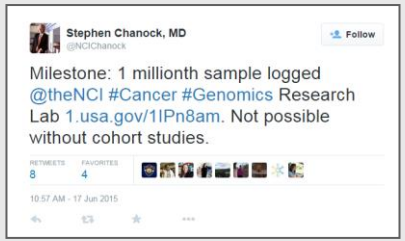
2014: Research group for HPV genomics, functional applications, Chernobyl studies

2015-2017: telomere length, 16S microbial sequencing, population scale WES, 1M sample mark

2018: MDPL established, HALO digital pathology, TypeSeq1 published

2019-2021: Automated sample store, CGR moves to CRL, digital spatial pathology

2022-current: Validation of TypeSeq2, PLCO Atlas, Confluence, 2M sample mark



Stephen Chanock, MD
@NCIChanock
Follow

Milestone: 1 millionth sample logged @theNCI #Cancer #Genomics Research Lab 1.usa.gov/1IPn8am. Not possible without cohort studies.

RETWEETS 8 FAVORITES 4

10:57 AM - 17 Jun 2015

The Journal of Infectious Diseases
MAJOR ARTICLE

IDSA hivma

Evaluation of TypeSeq, a Novel High-Throughput, Low-Cost, Next-Generation Sequencing-Based Assay for Detection of 51 Human Papillomavirus Genotypes

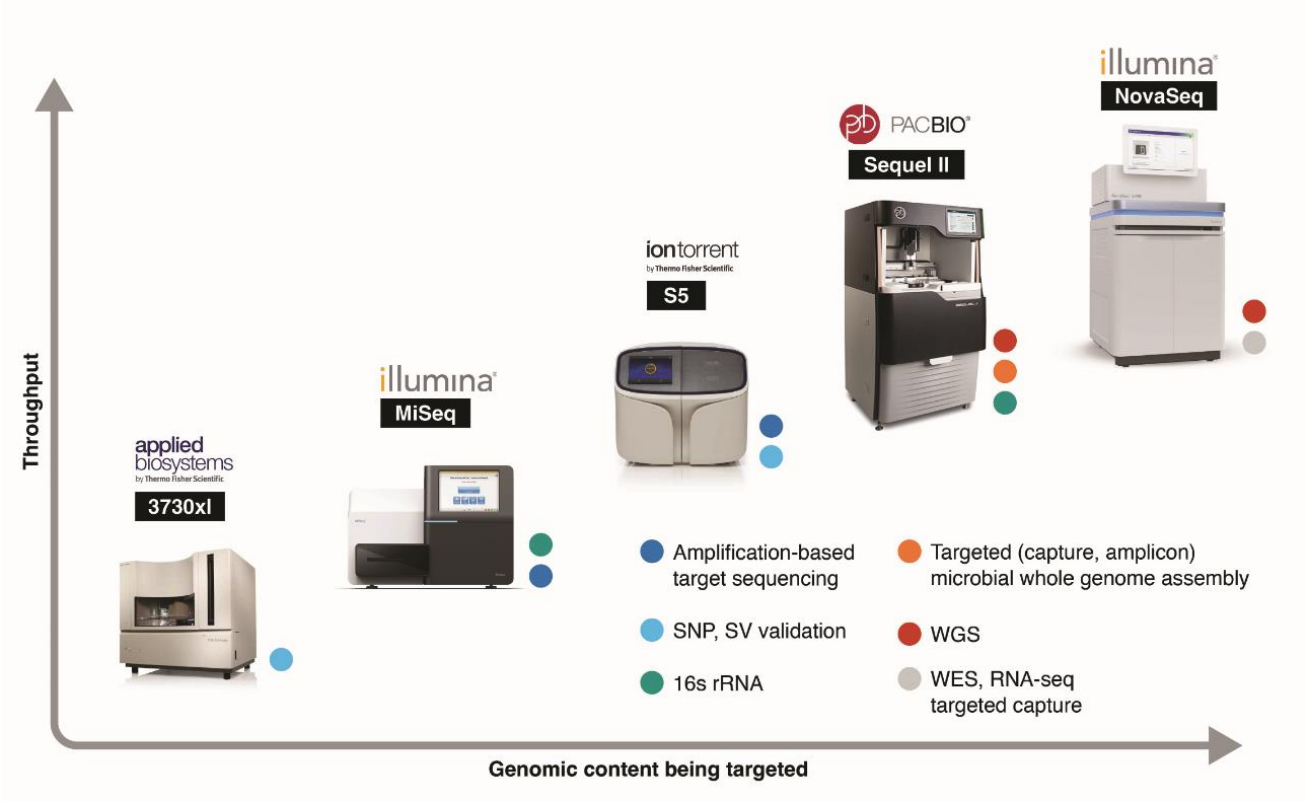
PLCO ATLAS

Visualize and interact with genome-wide association study results

Primary Analysis Support

Genotyping/GWAS	•Project-based QC reports •Study-level support (imputation, meta-analysis, association analysis) •Publication support
Sequencing	•QC, SNP/indel/SV variant calling, annotation •Delivery of richly annotated .vcf files •Germline, de novo and somatic pipelines •Bulk and targeted (Nanostring) RNA Sequencing
Methylation	•Analysis for array data •Project-based QC reports •Normalization via minfi
Microbiome	•Mothur and QIIME2 pipelines; delivery of OTU tables, alpha and beta diversity matrices •Support for metagenomics
Other Support	•Mosaicism/CNV •Data transfer support (Globus, Cloud, sftp) •Data posting to dbGaP, SRA, GEO, GDC •TGS, Atlas, Github

Current CGR Sequencing Capabilities

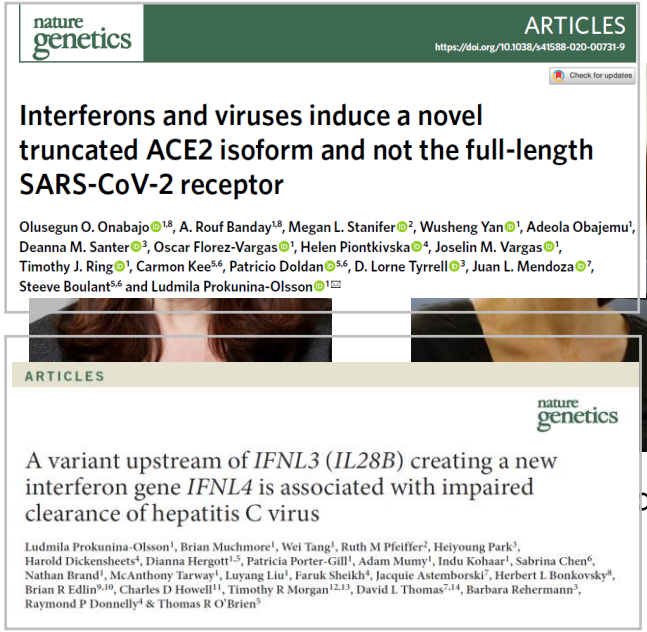


Sequencing History at CGR (Active)
ABI 3730xl DNA Analyzer
Roche 454 Genome Sequencer FLX
Illumina Hi-Scan
Illumina HiSeq 2000
Illumina MiSeq
Ion Torrent Personal Genome Machine
Illumina HiSeq 2500
Illumina NextSeq 500
Ion Proton System
PacBio Sequel
Illumina HiSeq 4000
Ion S5 Sequencer
Illumina iSeq 100
Illumina NovaSeq 6000
PacBio Sequel IIe
What's Next...to be determined

Summary of Laboratory Applications Available at CGR

Logistics and Quality Management	Sample Aliquoting, Extraction and QC	Molecular and Digital Pathology Support	Genotyping	Sequencing
• International shipping support • Provision of sample collection kits and barcode labels • Reagent and supplies inventory management • SOP development and maintenance • Equipment maintenance • Staff training program • Deviation and CAPA/continual improvement support	• Extraction of DNA and RNA from germline blood, saliva • Dual extraction from FFPE tissue samples • Extraction for microbiome studies (fecal, oral, tissue) • Pathology assessment of nuclear cell count/tissue area to guide extraction activities • Qualitative and quantitative assessment of RNA/DNA via multiple methods • High throughput temperature controlled biospecimen aliquoting • High throughput sample normalization and sample rearray • High throughput assay plating based on mass and/or volume	• Pathology review for Dx confirmation, tissue quality, tumor annotation • Support for H&E staining and pathology review • Tissue fixation/embedding/re-embedding for archival specimens • Sectioning of blocks for all downstream applications • Hand macrodissection and laser capture microdissection • Chromogenic IHC and multiplex immunofluorescence assay support • Tissue microarray construction • Digital whole slide scanning and high-capacity image management • Digital pathology support for data analysis • Digital spatial pathology support via GeoMX	• TaqMan targeted genotyping • Targeted CNV relative telomere length by qPCR • Illumina GWAS (all array types supported) • Methylation analysis via Illumina EPIC array • HPV methylation • HPV genotyping	• Sanger sequencing (multiple applications) • Targeted human sequencing via AmpliSeq (Ion Torrent), Illumina, PacBio • Human whole exome, whole genome sequencing • Microbial targeted 16s RNA and metagenomic sequencing • Microbial denovo assembly with long read PacBio sequencing • wtRNA sequencing • miRNA sequencing • Targeted RNA expression by Nanostring • 10X single cell RNA and ATAC-Seq • Whole genome HPV sequencing

Collaborations with LTG



nature genetics

ARTICLES

https://doi.org/10.1038/s41588-020-00731-9

Check for updates

Interferons and viruses induce a novel truncated ACE2 isoform and not the full-length SARS-CoV-2 receptor

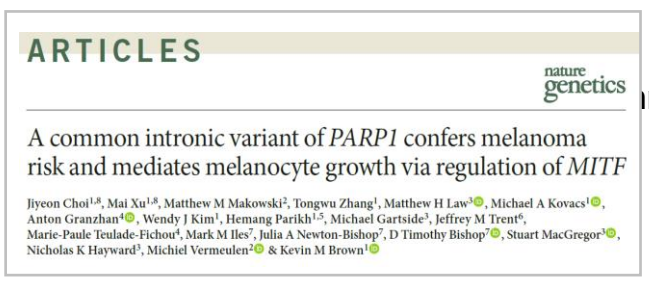
Olusegun O. Onabajo[1,8], A. Rouf Banday[1,8], Megan L. Stanifer[2], Wusheng Yan[1], Adeola Obajemu[1], Deanna M. Santer[3], Oscar Florez-Vargas[1], Helen Piontkivska[4], Joselin M. Vargas[1], Timothy J. Ring[1], Carmon Kee[5,6], Patricio Doldan[5,6], D. Lorne Tyrrell[3], Juan L. Mendoza[7], Steeve Boulant[5,6] and Ludmila Prokunina-Olsson[1]✉

ARTICLES

nature genetics

A variant upstream of *IFNL3* (*IL28B*) creating a new interferon gene *IFNL4* is associated with impaired clearance of hepatitis C virus

Ludmila Prokunina-Olsson[1], Brian Muchmore[1], Wei Tang[1], Ruth M Pfeiffer[2], Heiyoung Park[3], Harold Dickensheets[4], Dianna Hergott[1,5], Patricia Porter-Gill[1], Adam Mumy[1], Indu Kohaar[1], Sabrina Chen[6], Nathan Brand[1], McAnthony Tarway[1], Luyang Liu[1], Faruk Sheikh[4], Jacquie Astemborski[7], Herbert L Bonkovsky[8], Brian R Edlin[9,10], Charles D Howell[11], Timothy R Morgan[12,13], David L Thomas[7,14], Barbara Rehermann[3], Raymond P Donnelly[4] & Thomas R O'Brien[5]

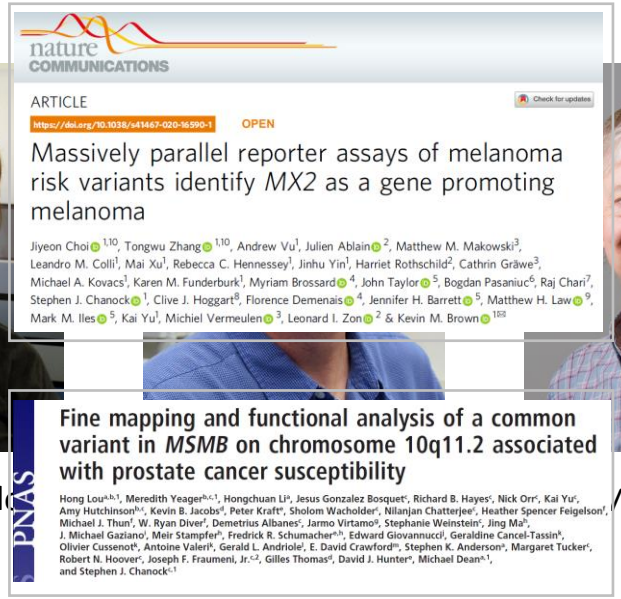


ARTICLES

nature genetics

A common intronic variant of *PARP1* confers melanoma risk and mediates melanocyte growth via regulation of *MITF*

Jiyeon Choi[1,8], Mai Xu[1,8], Matthew M Makowski[2], Tongwu Zhang[1], Matthew H Law[3], Michael A Kovacs[1], Anton Granzhan[4], Wendy J Kim[1], Hemang Parikh[1,5], Michael Gartside[3], Jeffrey M Trent[6], Marie-Paule Teulade-Fichou[4], Mark M Iles[7], Julia A Newton-Bishop[7], D Timothy Bishop[7], Stuart MacGregor[3], Nicholas K Hayward[3], Michiel Vermeulen[2] & Kevin M Brown[1]



nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-16590-1 OPEN

Check for updates

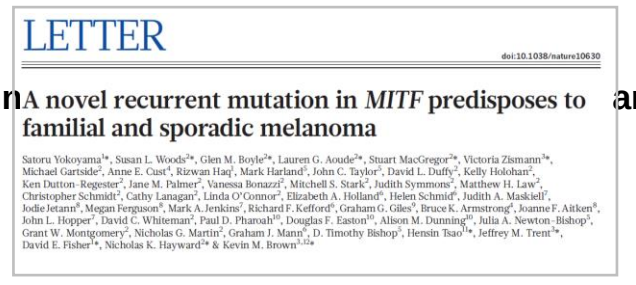
Massively parallel reporter assays of melanoma risk variants identify *MX2* as a gene promoting melanoma

Jiyeon Choi[1,10], Tongwu Zhang[1,10], Andrew Vu[1], Julien Ablain[2], Matthew M. Makowski[3], Leandro M. Colli[1], Mai Xu[1], Rebecca C. Hennessey[1], Jinhu Yin[1], Harriet Rothschild[2], Cathrin Gräwe[3], Michael A. Kovacs[1], Karen M. Funderburk[1], Myriam Brossard[4], John Taylor[5], Bogdan Pasaniuc[6], Raj Chari[7], Stephen J. Chanock[1], Clive J. Hoggart[8], Florence Demenais[4], Jennifer H. Barrett[5], Matthew H. Law[9], Mark M. Iles[5], Kai Yu[1], Michiel Vermeulen[3], Leonard I. Zon[2] & Kevin M. Brown[1]✉

PNAS

Fine mapping and functional analysis of a common variant in *MSMB* on chromosome 10q11.2 associated with prostate cancer susceptibility

Hong Lou[a,b,1], Meredith Yeager[b,c,1], Hongchuan Li[a], Jesus Gonzalez Bosquet[c], Richard B. Hayes[c], Nick Orr[c], Kai Yu[c], Amy Hutchinson[b,c], Kevin B. Jacobs[d], Peter Kraft[e], Sholom Wacholder[c], Nilanjan Chatterjee[c], Heather Spencer Feigelson[f], Michael J. Thun[g], W. Ryan Diver[g], Demetrius Albanes[c], Jarmo Virtamo[g], Stephanie Weinstein[c], Jing Ma[b], J. Michael Gaziano[f], Meir Stampfer[b], Fredrick R. Schumacher[a,b], Edward Giovannucci[f], Geraldine Cancel-Tassin[k], Olivier Cussenot[k], Antoine Valeri[k], Gerald L. Andriole[l], E. David Crawford[m], Stephen K. Anderson[n], Margaret Tucker[c], Robert N. Hoover[c], Joseph F. Fraumeni, Jr.[c,2], Gilles Thomas[d], David J. Hunter[a], Michael Dean[a,1], and Stephen J. Chanock[c,1]



LETTER

doi:10.1038/nature10630

A novel recurrent mutation in *MITF* predisposes to familial and sporadic melanoma

Satoru Yokoyama[1*], Susan L. Woods[2*], Glen M. Boyle[2*], Lauren G. Aoude[2*], Stuart MacGregor[2*], Victoria Zismann[3*], Michael Gartside[2], Anne E. Cust[4], Rizwan Haq[5], Mark Harland[6], John C. Taylor[6], David L. Duffy[7], Kelly Holohan[2], Ken Dutton-Regester[2], Jane M. Palmer[2], Vanessa Bonazzi[2], Mitchell S. Stark[2], Judith Symmons[2], Matthew H. Law[2], Christopher Schmidt[4], Cathy Lanagan[4], Linda O'Connor[4], Elizabeth A. Holland[8], Helen Schmid[8], Judith A. Maskiell[8], Jodie Jetann[8], Megan Ferguson[8], Mark A. Jenkins[9], Richard F. Kefford[10], Graham G. Giles[11], Bruce K. Armstrong[12], Joanne F. Aitken[8], John L. Hopper[7], David C. Whiteman[3], Paul D. Pharoah[10], Douglas F. Easton[10], Alison M. Dunning[10], Julia A. Newton-Bishop[5], Grant W. Montgomery[2], Nicholas G. Martin[2], Graham J. Mann[6], D. Timothy Bishop[5], Hensin Tsao[13*], Jeffrey M. Trent[3*], David E. Fisher[1*], Nicholas K. Hayward[2*] & Kevin M. Brown[3,12*]

AJHG

Please cite this article in press as: Colli et al., Altered regulation of DPF3, a member of the SWI/SNF complexes, underlies the 14q24 renal cancer susceptibility locus, The American Journal of Human Genetics (2021), https://doi.org/10.1016/j.ajhg.2021.07.009

ARTICLE

Altered regulation of DPF3, a member of the SWI/SNF complexes, underlies the 14q24 renal cancer susceptibility locus

Leandro M. Colli,[1,2] Lea Jessop,[1] Timothy A. Myers,[1] Sabrina Y. Camp,[1] Mitchell J. Machiela,[1] Jiyeon Choi,[1] Renato Cunha,[2,3] Olusegun Onabajo,[1] Grace C. Mills,[4] Virginia Schmid,[4] Seth A. Brodie,[1] Olivier Delattre,[5] David R. Mole,[4] Mark P. Purdue,[1] Kai Yu,[1] Kevin M. Brown,[1] and Stephen J. Chanock[1,6]

Summary

Our study investigated the underlying mechanism for the 14q24 renal cell carcinoma (RCC) susceptibility risk locus identified by a genome-wide association study (GWAS). The sentinel single-nucleotide polymorphism (SNP), rs4903064, at 14q24 confers an allele-specific effect on expression of the double PHD fingers 3 (*DPF3*) of the BAF SWI/SNF complex as assessed by massively parallel reporter assay, confirmatory luciferase assays, and eQTL analyses. Overexpression of *DPF3* in renal cell lines increases growth rates and alters chromatin accessibility and gene expression, leading to inhibition of apoptosis and activation of oncogenic pathways. siRNA interference of multiple DPF3-deregulated genes reduces growth. Our results indicate that germline variation in *DPF3*, a component of the BAF complex, part of the SWI/SNF complexes, can lead to reduced apoptosis and activation of the STAT3 pathway, both critical in RCC carcinogenesis. In addition, we show that altered *DPF3* expression in the 14q24 RCC locus could influence the effectiveness of immunotherapy treatment for RCC by regulating tumor cytokine secretion and immune cell activation.

Introduction

tibility regions have achieved statistical significance at the genome-wide threshold: 1p32, 2p21, 2q22, 3p22, 3q26,

LETTERS

nature genetics

Genome-wide association study identifies variants in the *ABO* locus associated with susceptibility to pancreatic cancer

Laufey Amundadottir[1,2,55*], Peter Kraft[3,4,55], Rachael Z Stolzenberg-Solomon[2,55], Charles S Fuchs[5,6,55], Gloria M Petersen[7], Alan A Arslan[8–10], H Bas Bueno-de-Mesquita[11], Myron Gross[12], Kathy Helzlsouer[13], Eric J Jacobs[14], Andrea LaCroix[15], Wei Zheng[16], Demetrius Albanes[2], William Bamlet[7], Christine D Berg[17], Franco Berrino[18], Sheila Bingham[19], Julie E Buring[20,21], Paige M Bracci[22], Federico Canzian[23], Françoise Clavel-Chapelon[24], Sandra Clipp[25], Michelle Cotterchio[26], Mariza de Andrade[7], Eric J Duell[27], John W Fox Jr[28], Steven Gallinger[29], J Michael Gaziano[30], Edward L Giovannucci[3,6,31], Michael Goggins[32], Carlos A González[33], Göran Hallmans[34], Susan E Hankinson[3,6], Manal Hassan[35], Elizabeth A Holly[22], David J Hunter[3,6], Amy Hutchinson[2,36], Rebecca Jackson[37], Kevin B Jacobs[2,36,38], Mazda Jenab[27], Rudolf Kaaks[23], Alison P Klein[39,40], Charles Kooperberg[15], Robert C Kurtz[41], Donghui Li[35], Shannon M Lynch[42], Margaret Mandelson[15,43], Robert R McWilliams[44], Julie B Mendelsohn[2], Dominique S Michaud[3,45], Sara H Olson[46], Kim Overvad[47], Alpa V Patel[14], Petra H M Peeters[45,48], Aleksandar Rajkovic[49], Elio Riboli[45], Harvey A Risch[50], Xiao-Ou Shu[16], Gilles Thomas[2], Geoffrey S Tobias[2], Dimitrios Trichopoulos[3,51], Stephen K Van Den Eeden[52], Jarmo Virtamo[53], Jean Wactawski-Wende[54], Brian M Wolpin[5,6], Herbert Yu[50], Kai Yu[2], Anne Zeleniuch-Jacquotte[9,10], Stephen J Chanock[1,2,55], Patricia Hartge[2,55] & Robert N Hoover[2,55]

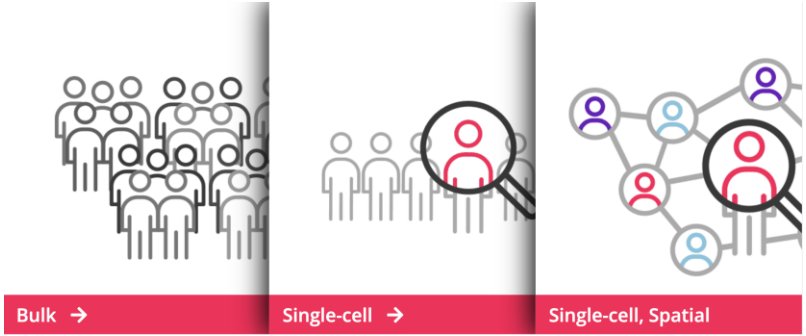
Established 2008

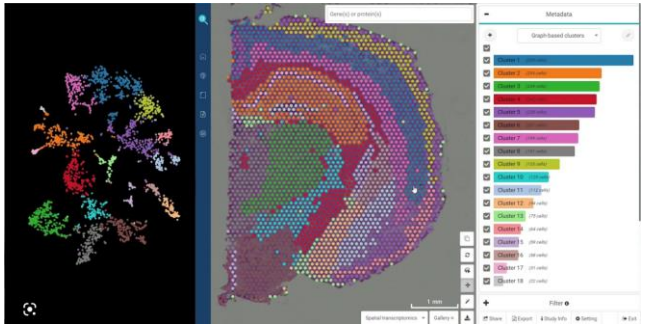
Future Directions

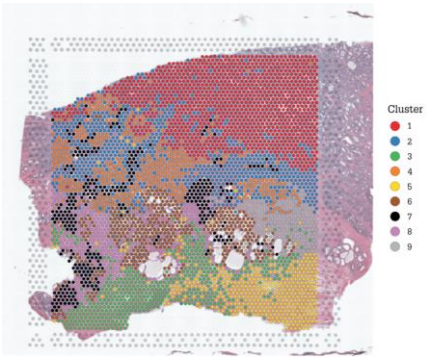
Measured and sustainable growth to support new research areas

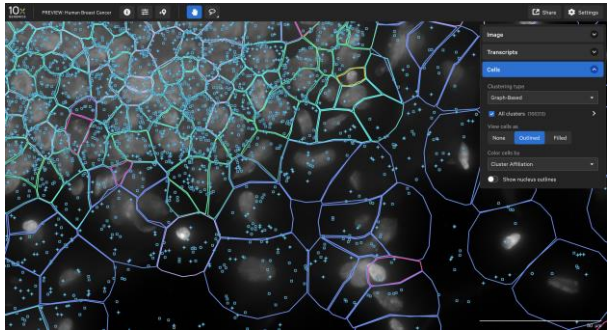
Single Cell and Spatial Biology

- Leveraging established capabilities of CGR laboratory
- Rich DCEG biospecimen resources with key scientific questions









Maintaining currency on sequencing applications

- Enabling cost-effective WGS studies; population scale via short read sequencing, targeted studies for long read
- Proteomics studies via Olink/Illumina
- Liquid biopsy applications requires highly accurate sequencing