

State of the Masonic Cancer Center

April 22, 2020

Douglas Yee, MD

Director, Masonic Cancer Center

Professor of Medicine and Pharmacology

John H. Kersey Chair in Cancer Research



Masonic Cancer Center

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Comprehensive Cancer Center designated by the National Cancer Institute

First (and Only?) Social Distancing Virtual State of the Masonic Cancer Center

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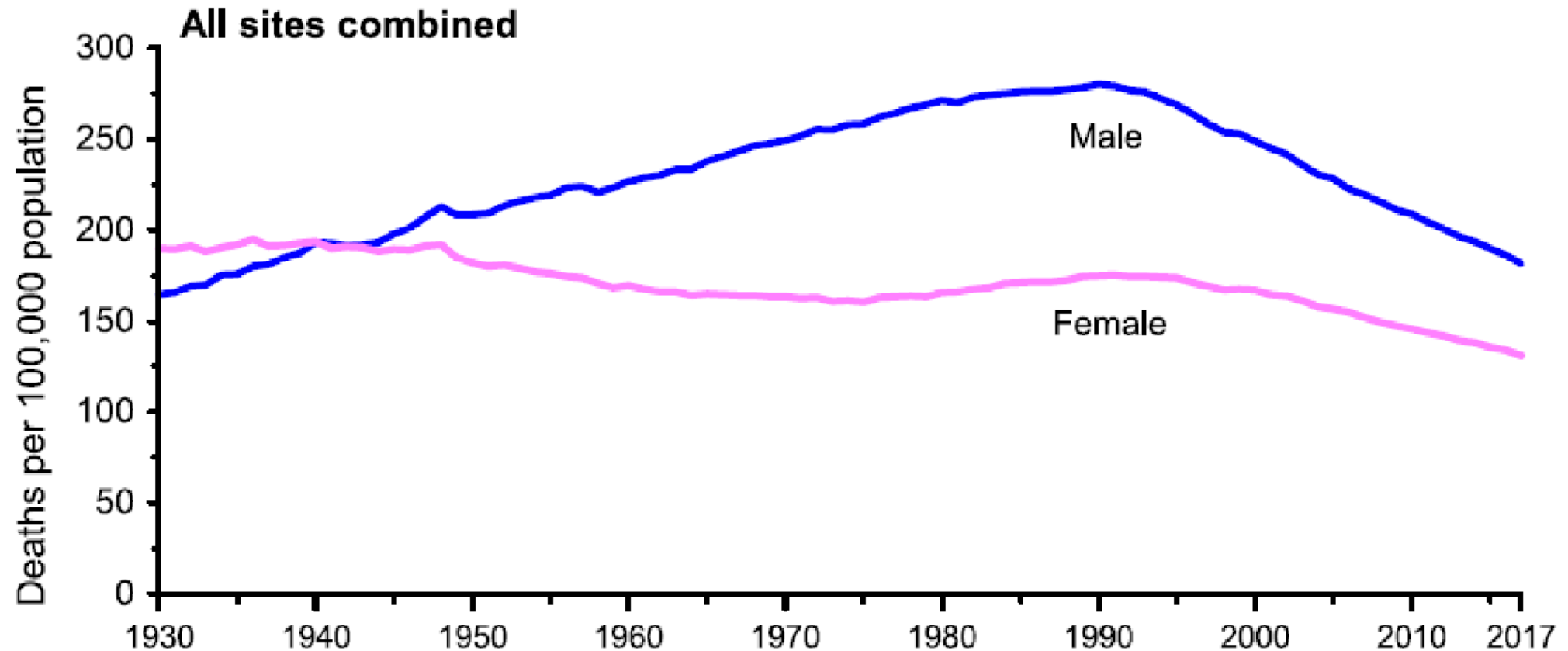


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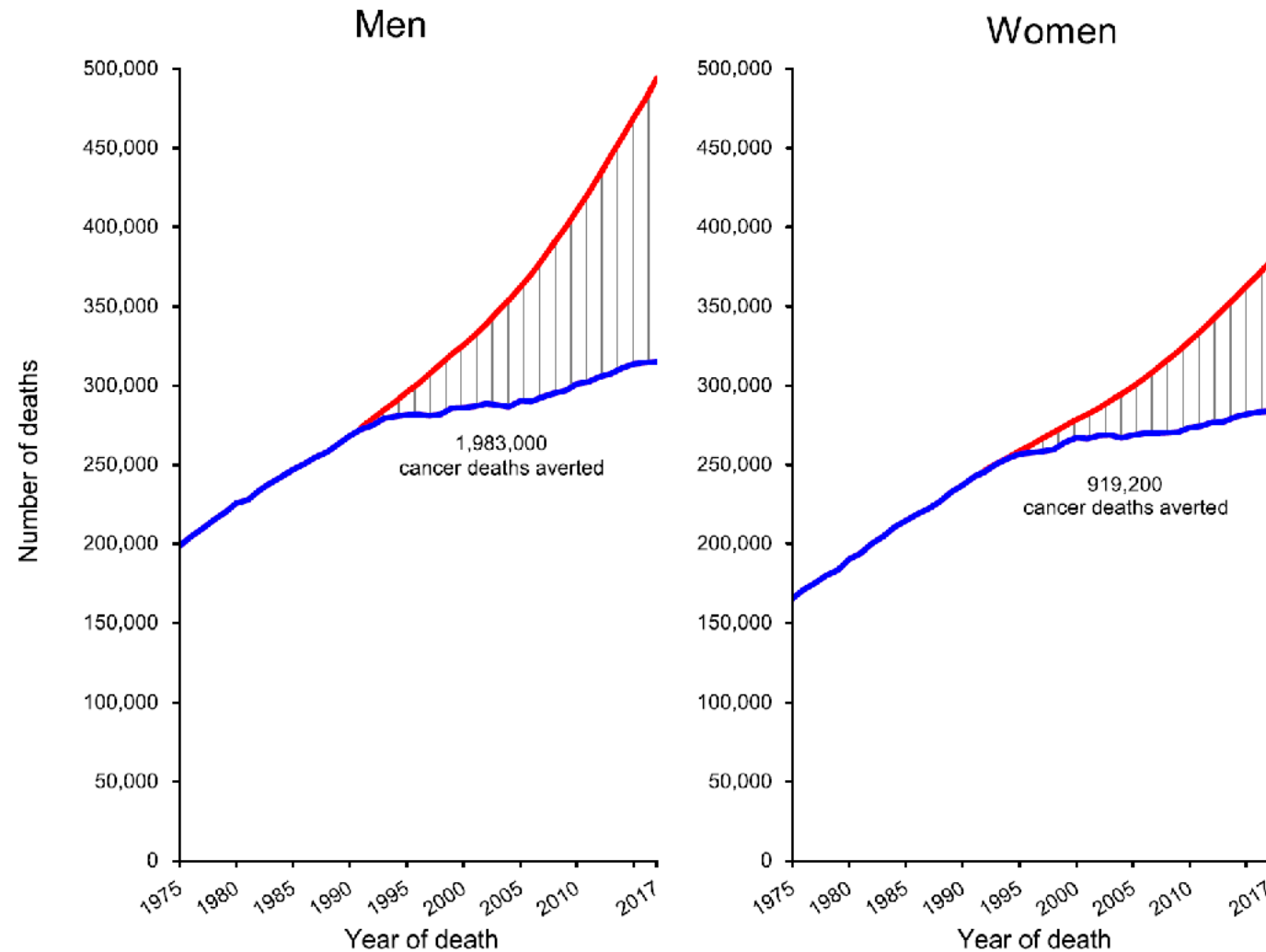
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Cancer Mortality in the US, 1930-2017



Cancer Deaths Reduced - 1975-2017



What Flattened The Curve?

- Population and laboratory science was applied to people
 - Etiology
 - Prevention
 - Screening
 - Therapy
 - Survivorship
- Clinical trials
 - Defined new strategies to prevent and screen cancer
 - Adapted to public health policy
 - Identified new treatment targets
 - New drugs developed
 - Reduced “overtreatment” of some cancers



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Research Funding Highlights

- **\$67M in *NEW* research award funding**

- **Reuben Harris & Douglas Yee**

NCI P01 entitled “APOBEC mutagenesis in breast cancer”

- **Aaron LeBeau**

3 NCI R01s and a DOD grant to develop novel antibody-based molecular imaging agents and targeted therapeutics for metastatic prostate cancer

- **Carol Lange, Julie Ostrander & Kaylee Schwertfeger**

NCI R01 “SRC-3/PELPI complexes drive stem-like phenotypes in luminal breast cancer”

- **Silvia Balbo & Peter Villalta**

NCI R01 “The DNA adductome of lung carcinogenesis”

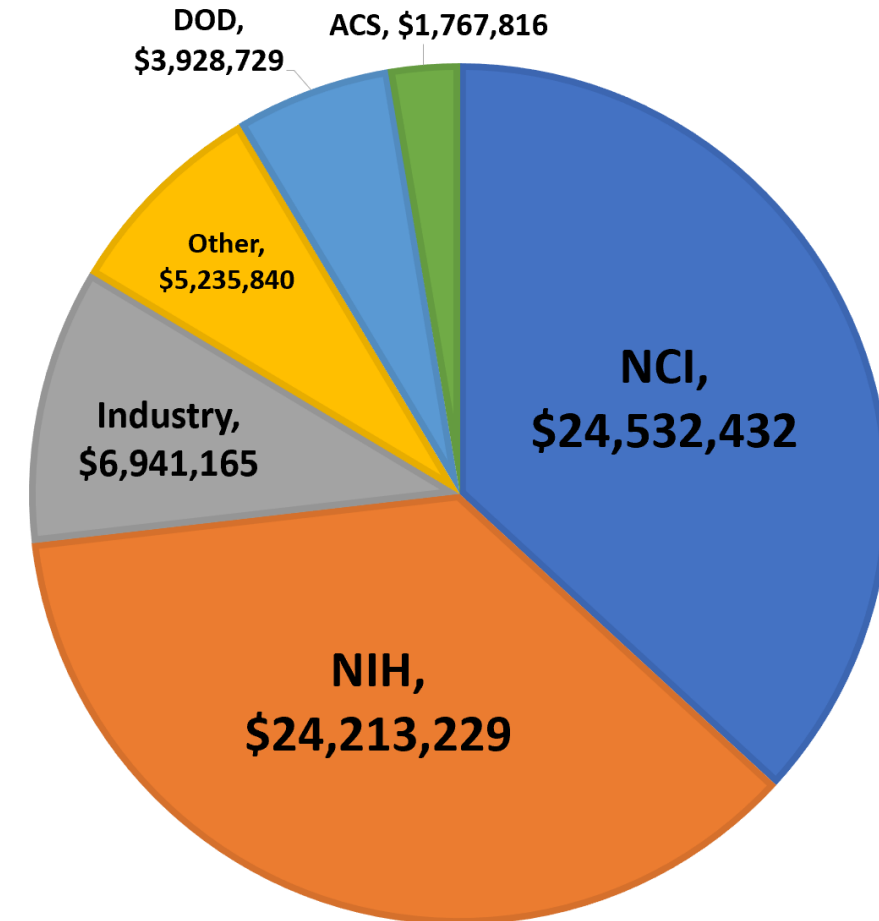
- **Stephen Hecht**

NCI R01 “Clinical Trial of Watercress in Detoxification of Environmental Toxicants and Carcinogens”

- **Peter Gordon**

NCI R37 “Overcoming Leukemia Chemoresistance in the Central Nervous System”

2019 NEW TOTAL AWARD FUNDING - BY SPONSOR



Publication Highlights

- **92 high impact publications across all 6 research programs**

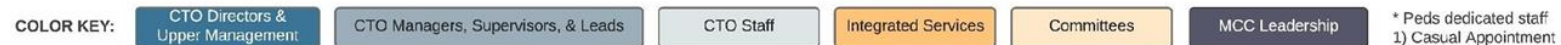
Noteworthy High-Impact Papers in 2019

Investigators	Journal	Title
Veronika Bachanova	NEJM	Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma.
Greg Vercellotti	Nature reviews. Drug discovery	Therapeutic strategies for sickle cell disease: towards a multi-agent approach.
Bruce Blazar	Nature	Absence of NKG2D ligands defines leukaemia stem cells and mediates their immune evasion.
Silvia Balbo Peter Villalta	Science	The human gut bacterial genotoxin colibactin alkylates DNA.
Melissa Geller	The Lancet Oncology	Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): a multicentre, open-label, single-arm, phase 2 trial.
Dorothy Hatsukami	The Lancet Oncology	Smokeless tobacco control in 180 countries across the globe: call to action for full implementation of WHO FCTC measures.
Stephanie Terezakis	The Lancet Oncology	Towards a standard of care in oncology for transgender patients.
Bruce Blazar Tom Griffith	Nature Medicine	Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade.
Clark Chen	Cell	The Extracellular RNA Communication Consortium: Establishing Foundational Knowledge and Technologies for Extracellular RNA Research.

Enhancing Clinical Trial Research

- Created two teams
 - Solid Tumor Unit (STU)
 - Charles Ryan, MD – Co-Associate Director of Clinical Research
 - Emil Lou, MD, PhD – Medical Director
 - Cell, Gene, Immunotherapy (CGI)
 - John Wagner, MD – Co-Associate Director of Clinical Research
 - Shernan Holtan, MD – Medical Director

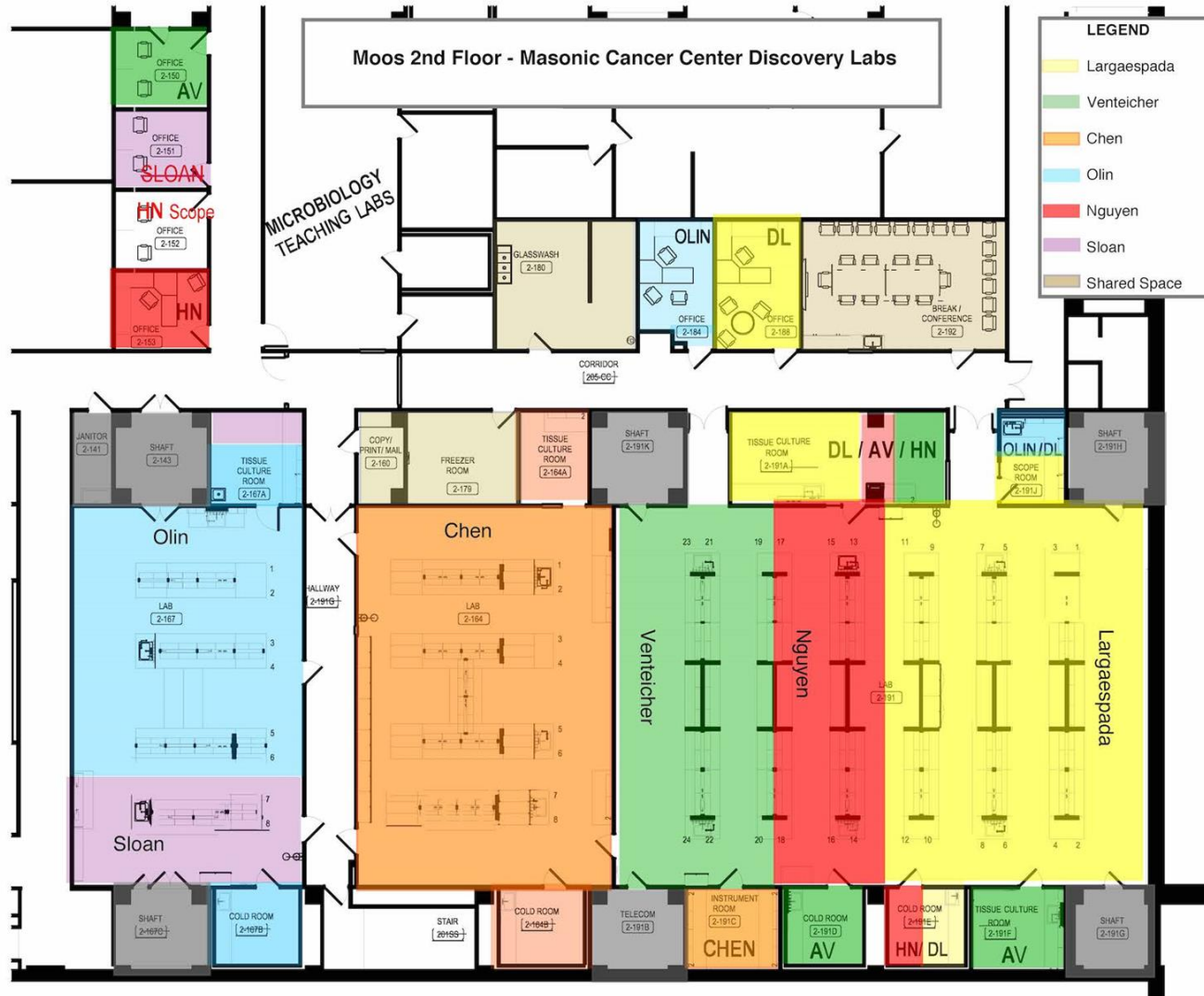




Clinical Trials Milestones: CY 2019

- Accruals
 - 2836 – Total Interventional
 - 364 Interventional Treatment
 - 1706 Health Services Research
 - 69 Ancillary
 - 1376 Observational
- 232 clinical trials studies were open to accrual
 - Solid Tumor Unit = 111
 - Cell, Gene, and Immunotherapy = 121
- 86 new clinical trials were opened during this time
 - Solid Tumor Unit = 46
 - Cell, Gene, and Immunotherapy = 40

Enhancing Laboratory Research Masonic Cancer Center Discovery Labs – Moos Tower 2nd floor



- Andrew Venteicher, MD – Neurosurgeon
- David Largaespada, PhD – Basic research
- Michael Olin, PhD – Basic research
- Lindsey Sloan, MD, PhD – Radiation Oncologist
- Hai Dang Nguyen, PhD – Basic research
- Clark Chen, MD – Neurosurgeon - Chair

Improving Cancer Outcomes

MN Cancer Clinical Trials Network

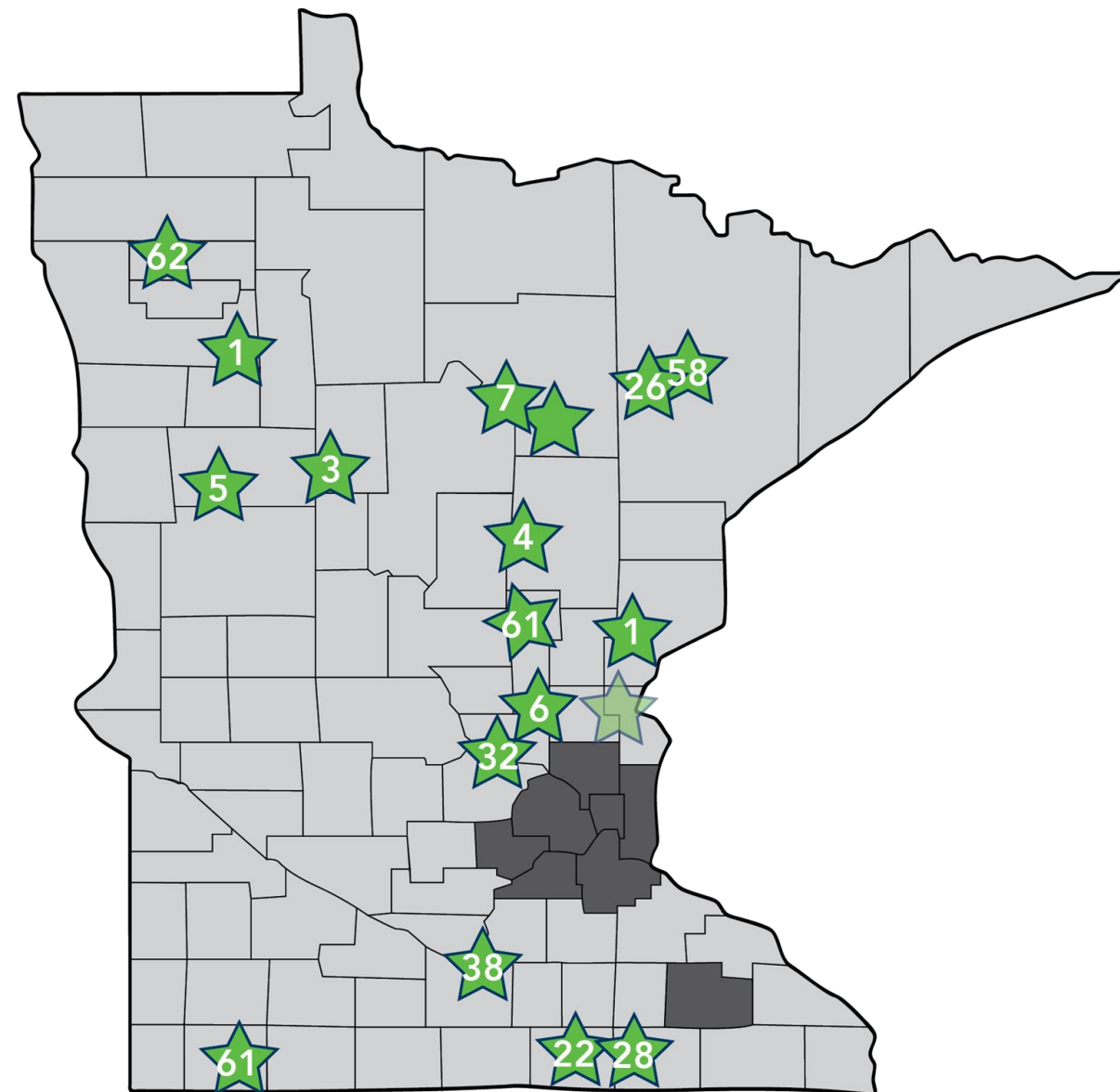
- State-wide initiative to increase participation in interventional clinical cancer research
- Provide infrastructure funding (research staff, equipment, capital upgrades, etc.) at sites state-wide
- Improve access to clinical research by acting as a research coordinating center
 - Identify trials appropriate for network site populations and site skill levels
 - Modifying existing trials or developing trials for MNCCTN
 - Provide project management, regulatory support, budgeting, contracting, etc. for trials going out to sites



MNCCTN

- 415 Minnesotans enrolled in cancer clinical trials
 - 143 enrolled onto MNCCTN-sponsored trials
- 18 sites are enrolling patients
- 46 trials have enrolled participants
- 6 trials in the pipeline

*Data as of January 31, 2020



Enrolling at two locations in Hibbing, MN



Working with MCC Investigators

- MNCCTN team provides project management and regulatory support for therapeutic and non-therapeutic interventional trials
- 18 sites across Greater MN with staff on-site to execute trials
- Currently working on 4 MCC investigator-initiated trials from School of Public Health, Medical School, and College of Pharmacy
- Plan to include under-represented populations in urban centers
- If you are interested in learning more about working with the MNCCTN, reach out to Dr. Yee or Marie Rahne (mrahne@umn.edu)



Enhancing Research Through New Leadership

● Jen Poynter, PhD

- Associate Professor, Division of Epidemiology and Clinical Research, Department of Pediatrics, Medical School
- *New* Associate Director of Community Outreach and Education



● Dan Harki, PhD

- Associate Professor, Department of Medicinal Chemistry, College of Pharmacy
- *New* Co-Leader, Cellular Mechanisms Program



Enhancing Research Through New Leadership

- Anne Blaes, MD

- Associate Professor, Hematology, Oncology, Transplantation, Department of Medicine, Medical School
- *New* Director of Cancer Survivorship Services and Translational Research



- Irina Stepanov, PhD

- Associate Professor, Division of Environmental Health Sciences, School of Public Health
- *New* Director of the Minnesota Institute of Global Prevention



Monday, March 16, 2020:

NCI WebEx COVID-19 with Norman (Ned) Sharpless & Henry Ciolino

● Clinical trials

- Expect decreased accrual
- Do not expect to shut down accrual
- Will not issue mandatory guidelines
 - UMN tiered trials ~ March 18
 - Cancer clinical trials are mostly Tier 2 and required case-by-case approval to enroll

● NCI Funding Questions

- Summer programs – may need to limit, await CDC guidance
 - On campus UMN summer programs are cancelled
- Lab “closure”
 - “Shutting down lab” – means lab to never re-open (retirement, etc). NCI funding would stop
 - “Limited access” – will continue to fund
 - “Repurposed to other duty” – NCI will consider on case-to-case



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NCI Director's Report

Norman E. Sharpless, M.D.

*1st Virtual Joint Meeting of NCI Board of Scientific
Advisors & National Cancer Advisory Board*

April 9, 2020

@NCIDirector
@TheNCI

NCI & COVID-19

- Today's discussion is focused on SARS-CoV-2 and COVID-19
- We will discuss the impact of the pandemic on NCI and the extramural community.
- COVID-19 has affected everything we do at NCI. We've adapted how we do business, and we're embracing opportunities to contribute to COVID research.
- Cancer research and cancer care remain JOB #1 at NCI.
- Even during these difficult times, we are still making progress toward our mission of reducing cancer suffering

UMN/MCC COVID Response & Updates

- COVID clinical trials
 - MCC Leadership in twice weekly “Research Huddles”
 - Losartan (ACE2 inhibitor) approved and enrollment ongoing
 - Remdesivir update: 31 local inpatients enrolled in this study. Completed study 4/19. Awaiting replacement study with JAK inhibitor?
 - NK Cell COVID-19 Trial – Received FDA approval with PI: Dr. Josh Rhein, Jeff Miller is consulting
 - Mesenchymal Stem Cells for severe lung disease – Dr. John Wagner
 - NCI pilot grant application to track COVID infection in bone marrow transplant patients nationally – Dr. Dan Weisdorf, pending
 - NCI Natural History Study of COVID-19 in Cancer - Pending

UMN/MCC COVID Response & Updates

- **Office of Academic and Clinical Affairs Rapid Response Grants**
 - Dr. Amit Kulkarni - Impact of the novel coronavirus COVID-19 on the care and outcomes of patients with cancer: a cohort study
 - Dr. David Odde - Biophysical Modeling of COVID-19 Clinical Trials
 - Dr. Rachel Vogel - Perceptions of COVID-19 and Health
 - Dr. Fang Li - Regulation of the SARS-CoV-2 receptor ACE2 by ADAM17
 - Dr. Mark Osborn - Rapid, Field Deployable COVID-19 Testing
 - Dr. Heather Nelson - Linkage of Cancer Biobanks and Registries to Understand COVID-19 Pathogenesis
 - Dr. Jose Debes - Immune-signature to evaluate COVID-19-related liver injury and outcomes
 - Dr. Louis Mansky - Point of Care Testing of SARS-CoV-2 by Using Smart Phone-Based Fluorescence Imaging
 - Others



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UMN/MCC COVID Response & Updates

- COVID-19 nucleic acid testing – Drs. Andrew Nelson, Sophia Yohe, Kenny Beckman
- COVID-19 antibody testing – Dr. Marc Jenkins
- COVID-19 crystal structure - Drs. Fang Li, Hideki Aihara publish structure of SARS-CoV-2 receptor-binding domain (RBD) in complex with hACE2 - Shang, et al. Nature 2020 PMID: 32225175
- COVID-19 modeling – Drs. Eva Enns, Shalini Kulasingam
- COVID-19 ethics – Drs. Susan Wolf, Debra DeBruin
- NOT-CA-20-042 Notice of Special Interest (NOSI): National Cancer Institute Announcement Regarding Availability of Urgent Competitive Revision and Administrative Supplements on Coronavirus Disease 2019 (COVID-19)
- Others

Clinical Trials Office Activities during COVID-19

1. Developed COVID-19 internal website on the Employee Dashboard for staff to reference with updates, policy changes, and resources
2. Determined technology needs and updated policies to allow all non-essential employees to WFH
3. Surveyed team members for potential risk factors and prioritized their safety by allowing them to work remotely prior to the formal campus-wide reduced operations
4. Created several policies and work instructions to provide guidance to team members during times of "reduced operations"
5. Shared several policies, such as our monitor screening policy, with the research managers across campus and AACI community
6. Developed a staff tracker, updated weekly by our team members, to clearly communicate which members would be in the office for clinical related duties
7. Created a staffing huddle with all of our clinical managers at 8 am every morning to discuss staffing, cross coverage, and shared duties to minimize the number of team members in the office
8. Created a daily managers meeting in the afternoon to discuss updates, check in with management, and provide support
9. Created a daily e-newsletter for the team to keep them informed of the many changes and topics discussed during our managers meetings
10. Partnered with MHealth Fairview and UMP leadership to incorporate research team members in their workflows
11. Submitted a list of 28 volunteers from our office to assist with COVID studies across campus
12. Worked together to rapidly start up and resource COVID-19 cellular therapy trials
13. Provided the team with daily free resources for mental health and wellbeing
14. Donated supplies such as swabs from closed studies that were no longer needed for study purposes
15. Worked with our PIs to create processes to allow for essential research related activities to continue to take place
16. Developed a primary coordinator schedule pre-scrubbing and patient pre-screening policies to ensure patient safety and proactively communicate research needs with our clinical partners
17. Created a photo album to share our experiences during this unusual time

Emerging From COVID-19 – New Faculty

- Melissa Schutten, DVM, PhD
 - DVM/PhD, U Wisconsin
 - Senior Scientist-Pathologist
Genentech
 - Lead Comparative Pathology Shared
Resource



Emerging From COVID-19 – New Faculty

- Lindsey Sloan, MD, PhD
 - MD/PhD, Temple University
 - Radiation Oncology Residency, Johns Hopkins
 - Immune responses post glioblastoma radiation
 - Joining the MCC Discovery Labs



Emerging From COVID-19 – Hormel Institute

- Robert Clarke, PhD, DSc
 - PhD/DSc, Queen's University, Belfast
 - Professor of Oncology, Georgetown University
 - Dean for Research, Georgetown University
 - Co-lead, Breast Cancer Program
 - Offered Executive Director, Hormel Institute



Emerging From COVID-19 – Hormel Institute

- Leena Hilakivi-Clarke, PhD
 - PhD, University of Helsinki, Finland
 - Professor of Oncology, Georgetown University
 - Co-Director, Animal Model Shared Resource, Georgetown University
 - Offered faculty position, Hormel Institute



Chainbreaker Funding

- 2017

- The Role of the Intestinal Microbiota in Cancer Pathogenesis and Clinical Care – PI's: Drs. Alexander Khoruts, Timothy Starr
 - Gut Microbiome Influence On Hematopoietic Cancer And Hematopoietic Cell Transplantation – 4 projects
 - Gut Microbiome Influence On Colon Cancer – 3 projects



Chainbreaker: Gut Microbiome: Co-PI's Alex Khoruts and Tim Starr ***Effects on hematopoietic stem cell transplantation and colon cancer***

- Project 1.** Defining the gut injury/dysbiosis phenotype in high risk allogeneic hematopoietic cell transplantation (HCT) recipients. **Shernan Holtan & Margaret MacMillan**
- Project 2:** The Effect of the Microbiota on Immunosuppressants after HSCT. **Pamela Jacobson**
- Project 3.** Dysbiosis and late effects in long-term survivors of HCT. **Lucie Turcotte**
- Project 4.** Microbiota restoration to strengthen gut integrity and prevent AGVHD, a Phase I clinical trial. **Armin Rashidi & Alex Khoruts**
- Project 5.** Methods for integrating dietary intake, microbial genomics, and polysaccharide degradation with tumor genetics and CRC outcomes. **Dan Knights & Ran Blekhman**
- Project 6.** Interactions between CFTR mutations and the microbiome in CRC. **Alex Khoruts, Patricia Scott & Robert Cormier**
- Project 7.** Functional effects of microbiome on tumor growth, metabolism, immune response and chemotherapy resistance. **Subree Subramanian, Chris Staley & Tim Starr**

Chainbreaker: Gut Microbiome: Co-PI's Alex Khoruts and Tim Starr

Progress

UMN Microbiome Core: Up and running and providing services to UMN community including high-quality characterization of microbiomes and targeted metabolites

Phase I Clinical trial: A Study of FMT in Patients With AML Allo HSCT in Recipients (NCT03678493)

Multiple publications:




Interaction between Host MicroRNAs and the Gut Microbiota in Colorectal Cancer

Ce Yuan,^{a,b} Michael B. Burns,^c Subbaya Subramanian,^{a,b,d} Ran Blekhman^{e,f}



Evaluating the Information Content of Shallow Shotgun Metagenomics

Benjamin Hillmann,^a  Gabriel A. Al-Ghalith,^b Robin R. Shields-Cutler,^c Qiyun Zhu,^d Daryl M. Gohl,^e Kenneth B. Beckman,^e Rob Knight,^{d,f,g} Dan Knights^{a,b,c}



Stress responses, M2 macrophages, and a distinct microbial signature in fatal intestinal acute graft-versus-host disease

Shernan G. Holtan,¹ Ashraf Shabaneh,² Brian C. Betts,¹ Armin Rashidi,¹ Margaret L. MacMillan,³ Celal Ustun,⁴ Khalid Amin,⁵ Byron P. Vaughn,⁶ Justin Howard,⁶ Alexander Khoruts,⁶ Mukta Arora,¹ Todd E. DeFor,⁷ Darrell Johnson,⁸ Bruce R. Blazar,³ Daniel J. Weisdorf,¹ and Jinhua Wang⁹

Cell Host & Microbe

Daily Sampling Reveals Personalized Diet-Microbiome Associations in Humans

Authors

Abigail J. Johnson, Pajau Vangay,
Gabriel A. Al-Ghalith, ..., Ravi Menon,
Katie Koecher, Dan Knights



Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2

Genome Biology

Population dynamics of the human gut microbiome: change is the only constant

Sambhawa Priya and Ran Blekhman^{*}



2021 Ride Event:

- Late summer/early fall
- 1-day: max ride 100 miles
- Family friendly
- New routes
- New donation amounts
- New registration amounts
- University of MN focus

Steering Committee:

- Chair: Chief Creative Officer for Padilla Ad Agency
- UMN Faculty: Largaespada, Jenkins, Madden, Erickson
- Fairview Chief Medical Officer: Mark Welton, MD
- Mortenson, Land O'Lakes, BCBS, Hormel, Sunrise Banks, Mortenson, iHeart Media, MPR, *more*

State of the Masonic Cancer Center

- MCC members are essential to the University's response to COVID-19
- Cancer research remains top priority of MCC
 - Working with University leadership to “re-open” research
- MCC will continue to develop expertise in cancer research
 - Community needs
 - Global cancer prevention
 - Survivorship

Masonic Cancer Center Annual Symposium Abstract Winners



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MCC Symposium Abstract Winners

Andrew Floeder, BS - Graduate Student

Mentor: Silvia Balbo, PhD – “DNA Adductomics of cod exposed to crude oil to identify polycyclic aromatic hydrocarbon biomarkers”



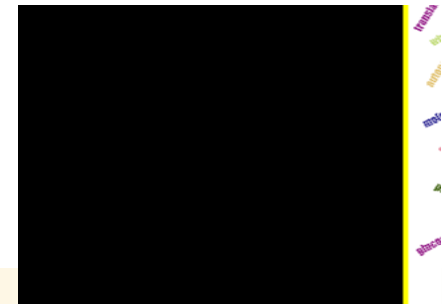
Colleen Longacre, MPH - Graduate Student

Mentor: Beth Virnig, PhD, MPH – “Travel, Treatment Choice, and Survival among Breast Cancer Patients: A Population-Based Analysis”



Carlos Perez Kerkvliet, BS - Graduate Student

Mentor: Carol Lange, PhD – “Glucocorticoid Receptors Enable TGFbeta I Signaling via p38 MAPK in Triple Negative Breast Cancer”



2020 Excellence in Mentoring Award



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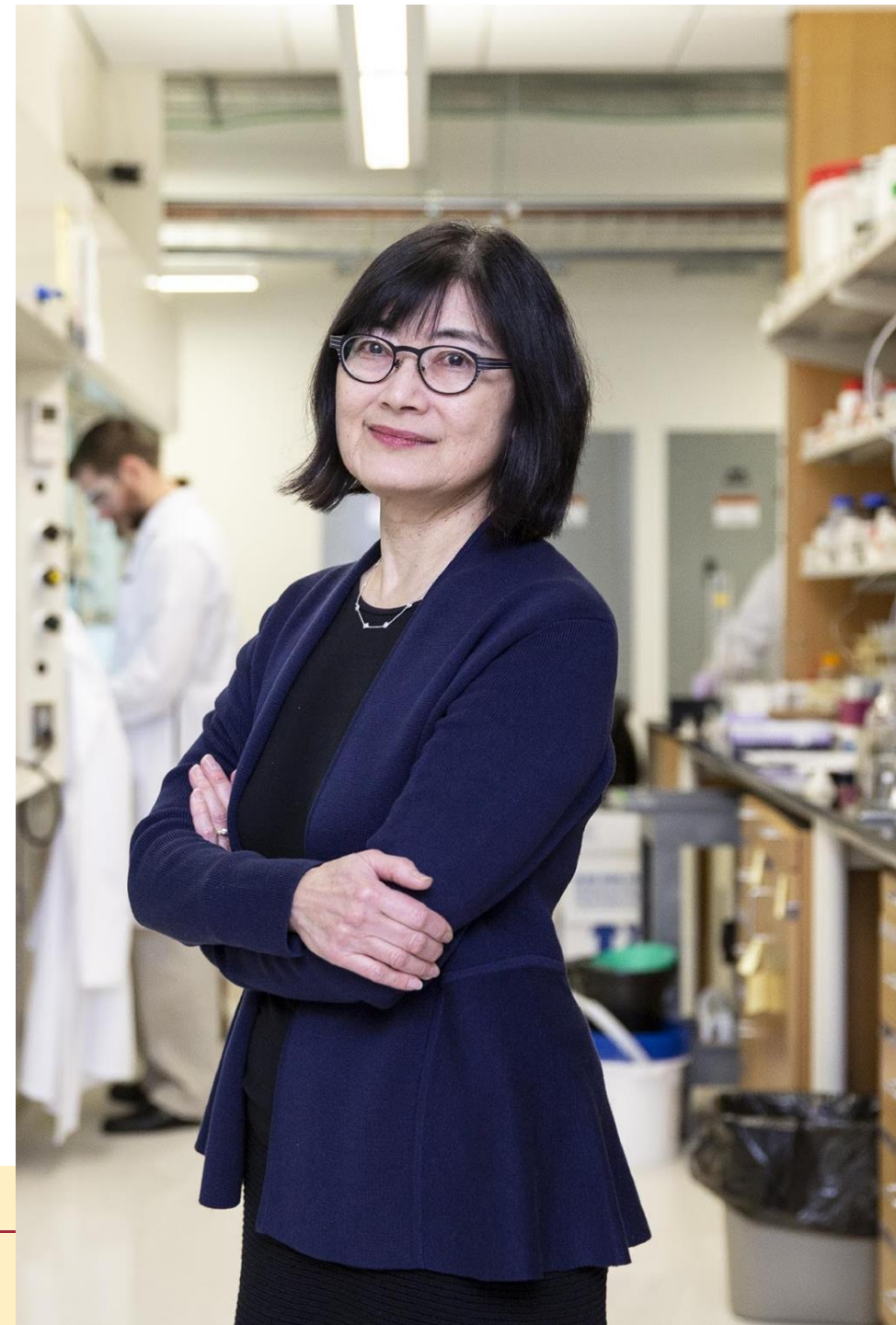
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Excellence in Mentoring Award

Dorothy Hatsukami, PhD

- Professor, Department of Psychiatry
- Associate Director, Cancer Prevention and Control, MCC
- Forester Family Chair in Cancer Prevention
- Nominated by Dana Carroll, PhD, MPH



Planning Committee – Thanks!

- Elizabeth Fedie, Co-Chair (and now Hormel Institute Chief of Staff)
- Aaron Schilz, Co-Chair
- David Largaespada, AD for Basic Science, Science Council
- Jill Siegfried, AD for Translational Research
- Chris Pennell, AD for Education
- Manish Patel, Clinical Research Faculty
- Andrew Nelson, Clinical and Basic Research Faculty
- Deanna Teoh, Clinical Research Faculty
- Ilana Chefetz Menaker, Hormel Institute Faculty
- Marilyn Lingard, MCC Admin
- Lissa Martinez, MCC Events
- Shawn Keenan, UMF





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A large, modern building with a curved glass facade reflecting the sky and surrounding environment. The building is surrounded by a landscaped area with trees and a paved walkway. A person is walking on the path in the foreground.

Advancing Knowledge, Enhancing Care



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