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
First (and Only?) Social Distancing Virtual State of the Masonic Cancer Center
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Cancer Mortality in the US, 1930-2017

All sites combined

Deaths per 100,000 population

Male

Female

Cancer Deaths Reduced - 1975-2017

Siegel, et al. CA Cancer J Clin 70:7 2020 PMID: 31912902
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
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/PELP1 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”
## Publication Highlights

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

### Noteworthy High-Impact Papers in 2019

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Journal</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veronika Bachanova</td>
<td>NEJM</td>
<td>Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma.</td>
</tr>
<tr>
<td>Bruce Blazar</td>
<td>Nature</td>
<td>Absence of NKG2D ligands defines leukaemia stem cells and mediates their immune evasion.</td>
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<tr>
<td>Silvia Balbo</td>
<td>Science</td>
<td>The human gut bacterial genotoxin colibactin alkylates DNA.</td>
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<td>Peter Villalta</td>
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<tr>
<td>Melissa Geller</td>
<td>The Lancet Oncology</td>
<td>Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): a multicentre, open-label, single-arm, phase 2 trial.</td>
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<tr>
<td>Dorothy Hatsukami</td>
<td>The Lancet Oncology</td>
<td>Smokeless tobacco control in 180 countries across the globe: call to action for full implementation of WHO FCTC measures.</td>
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<tr>
<td>Stephanie Terezakis</td>
<td>The Lancet Oncology</td>
<td>Towards a standard of care in oncology for transgender patients.</td>
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<tr>
<td>Bruce Blazar</td>
<td>The Lancet Oncology</td>
<td>Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade.</td>
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<tr>
<td>Tom Griffith</td>
<td>Nature Medicine</td>
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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
  o 2836 – Total Interventional
    o 364 Interventional Treatment
    o 1706 Health Services Research
  o 69 Ancillary
  o 1376 Observational

• 232 clinical trials studies were open to accrual
  o Solid Tumor Unit = 111
  o Cell, Gene, and Immunotherapy = 121

• 86 new clinical trials were opened during this time
  o Solid Tumor Unit = 46
  o 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
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
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

https://nci.rev.vbrick.com/#/videos/6fa7bd32-ff67-4c05-a674-a8372209998f
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
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
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
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 Blekhmane,f

Evaluating the Information Content of Shallow Shotgun Metagenomics
Benjamin Hillmann,a Gabriel A. Al-Ghalith,h Robin R. Shields-Cutler,c Qiyun Zhu,b Daryl M. Gohl,e Kenneth B. Beckman,e Rob Knight,b,c Dan Knightsa,b,c

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

Genome Biology
Population dynamics of the human gut microbiome: change is the only constant
Sambhava Priya and Ran Blekhman

Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2
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
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 TGFbeta1 Signaling via p38 MAPK in Triple Negative Breast Cancer”
2020 Excellence in Mentoring Award
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