NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis

Office of Cancer Complementary and Alternative Medicine

Strategic Workshop on Rigor and Reproducibility: Precision Fecal Microbiota Transplant and Microbiome Cancer Therapeutics

September 5th, 2019
(7:30am-4:00pm)

NCI-Shady Grove Campus
Room: Seminar 408/410
9609 Medical Center Dr.
Rockville, MD 20850

Agenda

Goals:

•Assess the current states of FMT, pre/probiotics and microbiome-based cancer therapeutic research
•Discuss the knowledge gaps, challenges, needs and future opportunities to enhance the safety, rigor and reproducibility of clinical research
•Provide feedback to NCI & NIH regarding future priority areas in enhancing precision mechanism-based rigor and reproducibility of FMT and defined microbiome based therapeutic translational and clinical research for cancer and other diseases.

Workshop Outcome:

White Paper will assist grant applicants and researchers in enhancing rigor and reproducibility of translational and clinical research and fostering data sharing and collaborations.

Session Format:

There will be a 15 min scientific presentation for each speaker, followed by a about 30 min discussion in each session.

7:30 am **Registration**

8:00 am **Welcome**
Jeffrey White, M.D. Director of Office of Cancer Complementary and Alternative Medicine, DCTD

Meeting Introduction and Objectives
Dan Xi, Ph.D. *Meeting Chair*, Program Director, Office of Cancer Complementary and Alternative Medicine, DCTD, NCI.

8:10-8:50 am **Overview (Moderator: Dan Xi, Ph.D. NCI)**

- **Microbiome and Cancer Preclinical Study Overview**
  Giorgio Trinchieri, M.D. (National Cancer Institute) (15 min)

- **FMT and Microbiome Clinical Trial Overview (15 min)**
  Jennifer Wargo, M.D. (MD Anderson Cancer Center) (15 min)

10 min Panel Discussion

Session 1: Mechanism, Clinical Efficacy and Safety

8:50-10:30 am **(1) FMT and Microbial Consortia Cancer Immunotherapy Clinical Trials**
(Moderator: Jennifer Wargo, M.D. MD Anderson Cancer Center)

Goals: discuss variables and confounding variables (e.g. diet, antibiotics, lifestyle, environmental factors, host and diseases), mechanism and rationale of clinical trial design, efficacy, safety, PK/PD of FMT and microbial-based therapy, FMT and live biological product manufacture, FMT donor selection, and biomarkers/omics.

- **FMT and Cancer Immunotherapy Melanoma Trial**
  Hassane Zarour, M.D. (University of Pittsburgh) (15 min)
- **FMT and Re-induction Immunotherapy in Refractory Metastatic Melanoma Patients**
  Gal Markel, M.D., Ph.D. and Ben Boursi, M.D. (Tel Aviv University, Israel) (15 min)
- **Microbial Consortia as Therapeutic Co-interventions in Cancer Immunotherapy. MET-4-IO and ROMA-IO**
  Bryan Coburn, M.D., Ph.D., FRCPC. (University Health Network, Canada) (15 min)-***(Remote-WebEx)***
- **Fecal Microbiota Transplantation for Cancer Immunotherapy Induced Colitis**
  Yinghong Wang, M.D., Ph.D. (MD Anderson Cancer Center) (15 min)

10 min Break

40 min Panel Discussion

10:40-12:20pm **(2) FMT and Microbiota Therapeutic Preclinical Model and Human Study**
(Moderator: Dan Xi, Ph.D. and Nina Lukinova, Ph.D. NCI)

Goals: discuss variables (e.g. diet, environmental factors, antibiotics, age, circadian clock), bioinformatic tools, genetic engineering, clinically relevant models and preclinical research approaches to enhance rigor and reproducibility and inform clinical trial design.

- **Role of Gut Microbiota in Modulating Immune Checkpoint Inhibitory Therapy for Cancer**
  Andrew Koh, M.D. (U T Southwestern Medical Center) (15 min)
- **Nutrition, Microbiome, and Mucus Axis in Febrile Neutropenia**
  Robert Jenq, M.D. (MD Anderson Cancer Center) (15 min)
- **Intermittent Fasting-induced Gut Microbiome Modulation of CNS Autoimmunity.**
  Yanjiao Zhou, M.D., Ph.D. (U Conn Health Connecticut) (15 min) ***(Remote-WebEx)***
- **Engineering Probiotic Cancer Therapeutics Using Synthetic Biology**
  Tal Danino, Ph.D. (Columbia University) (15 min)-(***Remote-WebEx)***

40 min Panel Discussion

12:20-1:05 pm **45 min Lunch on Your Own (Cafeteria)**

1:05 -2:10 pm **Session 2. Microbiome Measurements and Biomarkers**
(Moderator: Gabriela Riscuta, M.D, NCI, PPWG)

Goals: discuss variables (e.g. diet, lifestyle, environmental factors, host and diseases), measurement SOP, assays and microbiome reference.

- **Standards for Microbiome Measurements: Ongoing Efforts at NIST**
  Scott Jackson, Ph.D. (The National Institute of Standards and Technology) (15 min)
- **Correlative Studies in Large Human Population: Microbial Factors for Cancer Development & Progression**
  Ahn Jiyoung, Ph.D. (New York University) (15 min***)-(Remote-WebEx)***
- **Diet, the Human Microbiome, and its Metabolome: Rigor and Reproducibility**
  Gary Wu, M.D. (University of Pennsylvania) (15 min)

20 min Panel Discussion

2:10-2:15pm **5 min Break**

2:15 pm-3:20pm **Session 3: Clinical Trial Design, Intervention Standardization and FDA Regulatory Issue**
(Moderator: Ryan Ranallo, Ph.D. NIAID)

Goals: discuss clinical variables (e.g. donor screen, patient selection and stratify, age, sex and health disparity), FMT safety, product manufacture and quality control, clinical research design, PK/PD, and IND.

- **Assessment of Safety, Potency, and Mechanism of FMT Using a Mouse Model of Clostridium Difficile Infection**
  Paul Carlson, Ph.D. (The Food and Drug Administration) (15 min)
- **The AGA National FMT Registry**
  Gary Wu, M.D. (University of Pennsylvania) (15 min)
- **Regulatory Considerations for Gut Microbiota-based Cancer Therapy**
  Ke Liu, M.D., Ph.D. (The Food and Drug Administration) (15min)

20 min Panel Discussion

5 min Break

3:25-4:00 pm ***No WebEx Session***
Session 4: Data Sharing, Collaboration and Summary
(Moderator: Dan Xi, Ph.D. NCI and Jennifer Wargo, M.D. MD Anderson Cancer Center)

Goals: outline summary- the variables and confounding variables, the challenge, gap, opportunity and recommendation. Discuss the next steps and infrastructure needs toward data sharing and collaboration/consortium to enhance rigor and reproducibility in clinical trial research.

- **All Speakers and Panelists**

4:00 pm Meeting Adjourn

Panelists-Remote WebEx
Ami Bhatt, M.D. (Stanford University)
Arthur Frankel, M.D.
Florencia McAllister, M.D. (MD Anderson Cancer Center)

FMT and Microbiome Cancer Therapeutic, Rigor and Reproducibility Strategic Workshop Planning Working Group:
NCI:
Dan Xi, Ph.D., OCCAM/DCTD (Chair), Nina Lukinova, Ph.D. CDP/DCTD; Gabriela Riscuta, M.D., PPWG
NIAID: Ryan Ranallo, Ph.D.
FDA: Ke Liu, M.D., Ph.D.
Academic: Jennifer Wargo, M.D., MD Anderson Cancer Center