BIOGRAPHICAL SKETCH

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NAME: Daniel N. Frank

eRA COMMONS USER NAME (credential, e.g., agency login): DANIELFRANK

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Illinois, Urbana, IL	B.S.	08/1982	05/1986	Honors Biology
University of Illinois, Urbana, IL	B.S.	08/1982	05/1986	Biochemistry
University of California, San Francisco, CA	Ph.D.	09/1986	07/1993	Biochemistry/ Biophysics
Indiana University, Bloomington, IN	Post-doc	07/1993	05/1996	Microbial Ecology
University of California, Berkeley, CA	Post-doc	06/1996	06/1999	Microbial Ecology

A. Personal Statement

I currently am an Associate Professor at the University of Colorado School of Medicine, Division of Infectious Diseases. My research program explores the mechanisms by which myriad human-associated microorganisms impact our health and wellbeing. This work entails culture-independent characterization of complex microbial communities through high-throughput sequencing and analysis of 16S rRNA gene and metagenomic sequences. We have conducted several large, multi-centered, international studies in both infants and adults that have achieved a significantly deeper understanding of human microbiology in health and disease, including obesity and metabolic disease. As PI or co-Investigator on several NIH and foundation-funded grants, I have developed a research group consisting of both bench scientists and bioinformaticians who collectively have the requisite skills to complete the proposed research project. Ongoing projects and publications that I would like to highlight include (project personnel highlighted in bold):

Current Funding:

R01DK126710 **(PI:** Tang) 02/01/2021 – 01/31/2026
NIH/NIDDK
Dietary influence on infant growth and the gut microbiota.
Role: co-investigator

R21DE033826 **(MPI: Frank** & Lu**)** 9/01/2024 - 8/31/2026
NIH/NIDCR
Functional roles of the human microbiome and metabolome in oral cancer

R01AI175239 **(MPI:** Ramakrishnan & **Frank)** 9/01/2023 - 08/30/2028
NIH/NIAID
CRS Microbiome: Multi-omic Integrative Longitudinal Experimental (CRS-MILE) Study

Past Funding:

R01DK113957 (MPI: Krebs and **Reisdorph**), 07/01/2018 – 06/30/2023
NIH/NIDDK

Predicting health outcomes of Mediterranean diet via metabolomics of food and biospecimens.
Role: Co-Investigator

Citations:

1. Reisdorph NA, Hendricks AE, Tang M, Doenges KA, Reisdorph RM, Tooker BC, Quinn K, Borengasser SJ, Nkrumah-Elie Y, **Frank DN**, Campbell WW, Krebs NF. Nutrimetabolomics reveals food-specific compounds in urine of adults consuming a DASH-style diet. *Scientific reports.* 2020;10(1):1157. PMCID: PMC6981146.
2. Tang M, Matz KL, Berman LM, Davis KN, Melanson EL, **Frank DN**, Hendricks AE, Krebs NF. Effects of Complementary Feeding With Different Protein-Rich Foods on Infant Growth and Gut Health: Study Protocol. *Frontiers in pediatrics.* 2021;9:793215. PMCID: PMC8793676.
3. Hill EB, Konigsberg IR, Ir D, **Frank DN**, Jambal P, Litkowski EM, Lange EM, Lange LA, Ostendorf DM, Scorsone JJ, Wayland L, Bing K, MacLean PS, Melanson EL, Bessesen DH, Catenacci VA, Stanislawski MA, Borengasser SJ. 2023. The Microbiome, Epigenome, and Diet in Adults with Obesity during Behavioral Weight Loss. *Nutrients* 15
4. Hill EB, Reisdorph RM, Rasolofomanana-Rajery S, Michel C, Khajeh-Sharafabadi M, Doenges KA, Weaver N, Quinn K, Sutliff AK, Tang M, Borengasser SJ, **Frank DN**, O'Connor LE, Campbell WW, Krebs NF, Hendricks AE, Reisdorph NA. 2024. Salmon Food-Specific Compounds and Their Metabolites Increase in Human Plasma and Are Associated with Cardiometabolic Health Indicators Following a Mediterranean-Style Diet Intervention. *J Nutr* 154: 26-40

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2017-	Associate Professor, University of Colorado, Denver, CO
2016	Co-Director, Microbiome Core, GI and Liver Innate Immunity Program University of Colorado, Denver, CO.
2014-	Faculty, Graduate Program in Microbiology, University of Colorado, Denver, CO
2013-	Affiliate, University of Colorado Center for Global Health, Denver, CO
2010-2017	Assistant Professor, University of Colorado, Denver, CO
1999-2010	Research Associate, University of Colorado, Boulder, CO

Other Experience and Professional Memberships

Member, American Society for Microbiology
Member, Society for Mucosal Immunology
Member, AAAS
Member, Mucosal and Vaccine Research Program Colorado

2019	*Ad hoc* NIH Study Section Member: Integrative Nutrition and Metabolic Processes
2019	*Ad hoc* NIH Study Section Member: ZRG1 PSE-H(70)
2021	*Ad hoc* NIH Study Section Member: ZRG1_BDCN-Q

Honors

1982-84	James Scholar, University of Illinois
1986	Phi Beta Kappa, University of Illinois
1986	Bronze Tablet, University of Illinois
1986	Summa Cum Laude, University of Illinois
1986-89	National Science Foundation Predoctoral Fellow, National Science Foundation
1993-96	American Cancer Society Postdoctoral Fellow, American Cancer Society
2013	ASPIRE Investigator Award in Adult Vaccines Research
2024	CU Anschutz Campus Research Award: Research Faculty Collaborator Award

C. Contributions to Science

1. Early Studies of the Human Microbiome. My studies of the human microbiome began in 1999 while a Research Associate in the lab of Prof. Norman R. Pace (University of Colorado, Boulder), who pioneered the application of culture-independent, DNA sequence-based approaches to studying microbial communities. During this time, I worked primarily on an NIH-funded study of Crohn's disease, which was one of the first very large-scale surveys (>150 subjects) of the human microbiome. The resulting paper (reference d), which

demonstrated the loss of commensal *Clostridia spp.* and *Bacteroides spp.* in a subset of IBD patients, has been extensively cited. Other of my papers during this time helped to establish the basic techniques and analytic approaches that have become standards for analysis of the human microbiome.

a. **Frank DN**, Spiegelman GB, Davis W, Wagner E, Lyons E, et al. Culture-independent molecular analysis of microbial constituents of the healthy human outer ear. J Clin Microbiol. 2003 Jan;41(1):295-303. PubMed PMID: 12517864; PubMed Central PMCID: PMC149572.

b. St Amand AL, **Frank DN**, De Groote MA, Pace NR. Use of specific rRNA oligonucleotide probes for microscopic detection of *Mycobacterium avium* complex organisms in tissue. J Clin Microbiol. 2005 Apr;43(4):1505-14. PubMed PMID: 15814959; PubMed Central PMCID: PMC1081365.

c. Dalby AB, **Frank DN**, St Amand AL, Bendele AM, Pace NR. Culture-independent analysis of indomethacin-induced alterations in the rat gastrointestinal microbiota. Appl Environ Microbiol. 2006 Oct;72(10):6707-15. PubMed PMID: 17021222; PubMed Central PMCID: PMC1610281.

d. **Frank DN**, St Amand AL, Feldman RA, Boedeker EC, Harpaz N, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A. 2007 Aug 21;104(34):13780-5. PubMed PMID: 17699621; PubMed Central PMCID: PMC1959459.

2. The Gut Microbiome in Cancer and other Chronic Diseases. Although disrupted gut microbiota have been demonstrated in multiple diseases, the causes and consequences of dysbiosis are only now being elucidated. The work of my group has demonstrated several mechanisms by which dysbiosis may arise and mediate disease risk in a variety of anatomical sites, disease states, and hosts (human, mouse, rat, macaque), including host genetics. Furthermore, we are actively pursuing novel means of remediating dysbiosis through microbiome transplants, nutritional interventions, probiotics, and other products.

a. **Frank DN, Robertson CE**, Hamm CM, Kpadeh Z, Zhang T, Chen H, Zhu W, Sartor RB, Boedeker EC, Harpaz N, Pace NR, Li E. Disease phenotype and genotype are associated with shifts in intestinal-associated microbiota in inflammatory bowel diseases. *Inflamm Bowel Dis.* 2011;17(1):179-184. .

b. Markle JG, **Frank DN**, Mortin-Toth S, **Robertson CE**, Feazel LM, Rolle-Kampczyk U, von Bergen M, McCoy KD, Macpherson AJ, Danska JS. Sex Differences in the Gut Microbiome Drive Hormone-Dependent Regulation of Autoimmunity. *Science.* 2013;339(6132):1084-1088.

c. Son JS, Khair S, Pettet DW, 3rd, Ouyang N, Tian X, Zhang Y, Zhu W, Mackenzie GG, **Robertson CE**, Ir D, **Frank DN**, Rigas B, Li E. Altered interactions between the gut microbiome and colonic mucosa precede polyposis in APCMin/+ mice. *PLoS One.* 2015;10(6):e0127985.

d. Nycz BT, Dominguez SR, Friedman D, Hilden JM, Ir D, **Robertson CE, Frank DN**. Evaluation of bloodstream infections, *Clostridium difficile* infections, and gut microbiota in pediatric oncology patients. *PLoS One.* 2018;13(1):e0191232.

3. Airway and Head & Neck Microbiota. I have extensive experience in applying culture-independent and culture-based microbiological methodologies to analyses of the human upper airways, oral cavity, and ear canals. These studies have focused on the environmental (e.g., bioaerosol and cigarette smoke exposures) and host immunological and genetic factors shaping the commensal microbiome in health and disease (e.g., chronic rhinosinusitis, otitis media). Of particular interest has been understanding the factors underlying upper airway colonization by the opportunistic pathogen *Staphylococcus aureus*.

a. Feazel LM, Baumgartner LK, Peterson KL, **Frank DN,** Harris JK, Pace NR. Opportunistic pathogens enriched in showerhead biofilms. *Proc Natl Acad Sci U S A.* 2009;106(38):16393-16399.

b. Bessesen MT, Kotter CV, Wagner BD, Adams JC, Kingery S, Benoit JB, Robertson CE, Janoff EN, **Frank DN**. MRSA colonization and the nasal microbiome in adults at high risk of colonization and infection. *J Infect.* 2015;71(6):649-657.

c. Ramakrishnan VR**, Frank DN**. Impact of cigarette smoking on the middle meatus microbiome in health and chronic rhinosinusitis. *Int Forum Allergy Rhinol.* 2015;5(11):981-989.

d. **Frank DN**, Giese APJ, Hafren L, … **Robertson CE** … and Santos-Cortez RLP. Otitis media susceptibility and shifts in the head and neck microbiome due to SPINK5 variants. *J Med Genet.* 2020;10.1136/jmedgenet-2020-106844.

4. Microbiome Analysis Tools. In conducting studies of the human microbiome, my group has contributed to the development of analysis software for both 16S rRNA and meta-transcriptomic sequencing. This work has

been funded through grants from the NIH Human Microbiome Project (UH2 and R21) as well as the Canadian Institutes of Health Research.

a. **Frank DN**. XplorSeq: a software environment for integrated management and phylogenetic analysis of metagenomic sequence data. BMC Bioinformatics. 2008 Oct 7;9:420. PubMed PMID: 18840282; PubMed Central PMCID: PMC2577119.

b. **Frank DN**. BARCRAWL and BARTAB: software tools for the design and implementation of barcoded primers for highly multiplexed DNA sequencing. BMC Bioinformatics. 2009 Oct 29;10:362. PubMed PMID: 19874596; PubMed Central PMCID: PMC2777893

c. **Robertson CE**, Harris JK, Wagner BD, Granger D, Browne K, Tatem B, Feazel LM, Park K, Pace NR, and **Frank DN**. Explicet: graphical user interface software for metadata-driven management, analysis and visualization of microbiome data. Bioinformatics. 2013 Dec 1;29(23):3100-1. PubMed PMID: 24021386; PubMed Central PMCID: PMC3834795.

d. Carpenter CM, **Frank DN**, Williamson K, Arbet J, Wagner BD, Kechris K, Kroehl ME. tidyMicro: A pipeline for microbiome data analysis and visualization using the tidyverse in R. *BMC bioinformatics.* 2021;22(41).

5. Phylogeny and Structure of Functional RNAs. My first exposure to the use of RNA sequences as markers of microbial ecology and cellular evolution came as an undergraduate in the laboratory of Prof. Carl Woese (Univ. of Illinois), where I isolated and sequenced several archaeal small structural RNA genes. My graduate thesis research with Prof. Christine Guthrie (University of California, San Francisco), supported by a National Science Foundation predoctoral award, used the model eukaryote *Saccharomyces cerevisiae* to probe structure/function relationships in a small nuclear RNA required for pre-mRNA processing. Following graduate school, I was awarded an American Cancer Society fellowship to pursue postdoctoral research in the laboratory of Prof. Norman Pace (University of Colorado, Boulder). There I investigated the structure and catalytic activity of the RNA subunit of ribonuclease P (RNase P), the ubiquitous and essential component of pre-tRNA processing machinery in all cellular life.

a. **Frank D**, Guthrie C. An essential splicing factor, SLU7, mediates 3' splice site choice in yeast. *Genes Dev.* 1992 Nov;6(11):2112-24. PubMed PMID: 1427075.

b. **Frank DN**, Harris ME, Pace NR. Rational design of self-cleaving pre-tRNA-ribonuclease P RNA conjugates. *Biochemistry*. 1994 Sep 6;33(35):10800-8. PubMed PMID: 8075082.

c. **Frank DN**, Ellington AE, Pace NR. In vitro selection of RNase P RNA reveals optimized catalytic activity in a highly conserved structural domain. *RNA*. 1996 Dec;2(12):1179-88. PubMed PMID: 8972768; PubMed Central PMCID: PMC1369446.

d. **Frank DN**, Pace NR. *In vitro* selection for altered divalent metal specificity in the RNase P RNA. *Proc Natl Acad Sci U S A*. 1997 Dec 23;94(26):14355-60. PubMed PMID: 9405616; PubMed Central PMCID: PMC24975.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1nwB2V5UvVnQJ/bibliography/43235528/public/?sort=date&direction=descending