

My Academic Journey

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Expertise.

- 1) Protein evolution. I use and develop tools to examine how protein structure and function is maintained in response to sequence changes. I have a special interest in identifying the role that variable positions play in protein evolution. I have long taught an undergraduate course protein sequence annotation.
- 2) Composition and function of the human and other microbiomes. I use and develop tools to examine 16S rRNA gene composition, gene content and expression of mixed population samples (meta-genomes and meta-transcriptomes), and metabolomic analysis of clinical samples. I have experience in metagenomic binning and annotation.
- 3) Computational biology and the application of techniques for compositional data analysis to the above problems. My primary contribution is ALDEx2 tool in Bioconductor for the analysis of high throughput experiments that generate counts per sequence tag: 16S rRNA gene sequencing, transcriptomics and selex-type experiments. I teach a graduate course, and have delivered many workshops, on the use of compositional data analysis techniques to examine transcriptomes, microbiomes and other types of complex data sets derived from high throughput sequencing.

Historical and Current Projects

- Bacteriophage Mu molecular biology (PhD)
 - a lot of sequencing and time spent in cold-rooms
- Gene targeting and DNA double-strand break repair (PDF - 2008)
 - first demonstration of gene targeting in a live metazoan (*Drosophila*)
 - the ‘synthesis dependent strand annealing’ model of DSB repair
- Protein coevolution (2005 - present)
 - my first foray into computational biology
 - worked out methods to remove the largest source of bias in covariation analysis.
- 16S rRNA gene based microbiome profiling by Illumina sequencing (2010 - present)
 - developed dual-index barcode system for Illumina sequencing (before Illumina did!)
- Compositional Data Analysis (2013 - present)
 - recognized that high throughput sequencing data are non-linear and compositional and adapted methods for compositional data analysis to the microbiome and transcriptome fields
 - maintainer of the ALDEx2 R package on Bioconductor (top 15%)
 - developer of and advocate for effect-size plots in place of volcano and MA plots
- Meta-transcriptomics and meta-genomics (2013 - present)
 - current focus is on functionalizing microbiomes using meta-genomic and meta-transcriptomic approaches.
 - working with environmental and human samples
 - identifying non-chromosomal elements
 - hold provisional patent on specific modulation of microbiome composition using conjugative plasmids to deliver site-specific nucleases

Speaking and Workshops (past 5 years)

- nine visiting academic lectures
- sixteen invited conference presentations
- seven workshops organized and presented

Methods

- Anova-like differential expression (ALDEx) analysis for mixed population rna-seq. PLoS One, 8(7):e67019, 2013.
- Unifying the analysis of high-throughput sequencing datasets: characterizing RNA-seq, 16S rRNA gene sequencing and selective growth experiments by compositional data analysis. Microbiome, 2:15.1–15.13, 2014.
- Expanding the UniFrac toolbox. PLoS One, 11(9):e0161196, 2016.
- Displaying variation in large datasets: Plotting a visual summary of effect sizes. Journal of Computational and Graphical Statistics, 25(3C):971–979, 2016.
- It’s all relative: analyzing microbiome data as compositions. Ann Epidemiol, 26(5):322–9, May 2016.
- Assessment of variation in microbial community amplicon sequencing by the microbiome quality control (mbqc) project consortium. Nat Biotechnol, 35(11):1077–1086, Nov 2017. (Consortium member)
- Microbiome datasets are compositional: And this is not optional. Front Microbiol, 8:2224, 2017.
- From RNA-seq to biological inference: Using compositional data analysis in meta-transcriptomics. Methods Mol Biol, 1849:193–213, 2018.

Vaginal microbiome

- Microbiome profiling by Illumina sequencing of combinatorial sequence-tagged PCR products. PLoS One, 5(10):e15406, 2010.
- Changes in vaginal microbiota following antimicrobial and probiotic therapy. Microb Ecol Health Dis, 26:27799, 2015.
- A multi-platform metabolomics approach identifies highly specific biomarkers of bacterial diversity in the vagina of pregnant and non-pregnant women. Sci Rep, 5:14174, 2015.

Gut microbiome

- The gut microbiota of healthy aged chinese is similar to that of the healthy young. mSphere, 2(5):e00327–17, 2017.
- Stool substitute transplant therapy for the eradication of *Clostridium difficile* infection: ‘repopulating’ the gut. Microbiome, 1(1):3, Jan 2013.

- Administration of defined microbiota is protective in a murine *Salmonella* infection model. Sci Rep, 5:16094, 2015.
- Probiotic administration attenuates myocardial hypertrophy and heart failure after myocardial infarction in the rat. Circ Heart Fail, 7(3):491–9, May 2014.
- Evidence for greater production of colonic short-chain fatty acids in overweight than lean humans. Int J Obes (Lond), 38(12):1525–31, Dec 2014.
- Metabolic products of the intestinal microbiome and extremes of atherosclerosis. Atherosclerosis, 273:91–97, Jun 2018.
- Associations with metabolic products of the intestinal microbiome, carotid plaque burden, and renal function. Nutrients, 10(6), Jun 2018.

Genomes, shotgun meta-genomics and meta-transcriptomics

- A new genomic blueprint of the human gut microbiota. Nature, Feb 2019.
- At the crossroads of vaginal health and disease, the genome sequence of *Lactobacillus iners* AB-1. Proc Natl Acad Sci U S A, 108 Suppl 1:4688–95, Mar 2011.
- Genome sequence of *Lactobacillus pentosus* KCA1: Vaginal isolate from a healthy premenopausal woman. PLoS One, 8(3):e59239, 2013.
- Comparative meta-RNA-seq of the vaginal microbiota and differential expression by *Lactobacillus iners* in health and dysbiosis. Microbiome, 1(1):12, Apr 2013.

Fungal Typing

- New primers for discovering fungal diversity using nuclear large ribosomal DNA. PLoS One, 11(7):e0159043, 2016.

Microbiome Modulation

- Efficient inter-species conjugative transfer of a 1 CRISPR nuclease for targeted bacterial biofilm modulation. Nature Comm: under revision