Using Omics in Research: Insights from the P30 Center on Symptoms and Metabolomics

EMORY | NELL HODGSON WOODRUFF SCHOOL OF NURSING

Brittany Butts, Nicholas Giordano, Laura Kimble, Laren Narapareddy, Irene Yang, and Sandra B Dunbar

SNRS Pre-Conference Workshop

March 1, 2023

Disclosures

- This study was funding by the National Institutes of Health, NINR [P30 NR018090].
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- Effort for NG is supported by NIDA [K23DA057415].

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Workshop Introduction

- P30 Center for the Study of Symptom Science, Metabolomics, & Multiple Chronic Conditions overview
- Omics overview
- Applications of omics in nursing research
- How to do omics research without a basic science background
- Sample collection in omics research
- Analyzing and presenting data in omics and research
- Social determinants of health
- My first omics research: lessons learned

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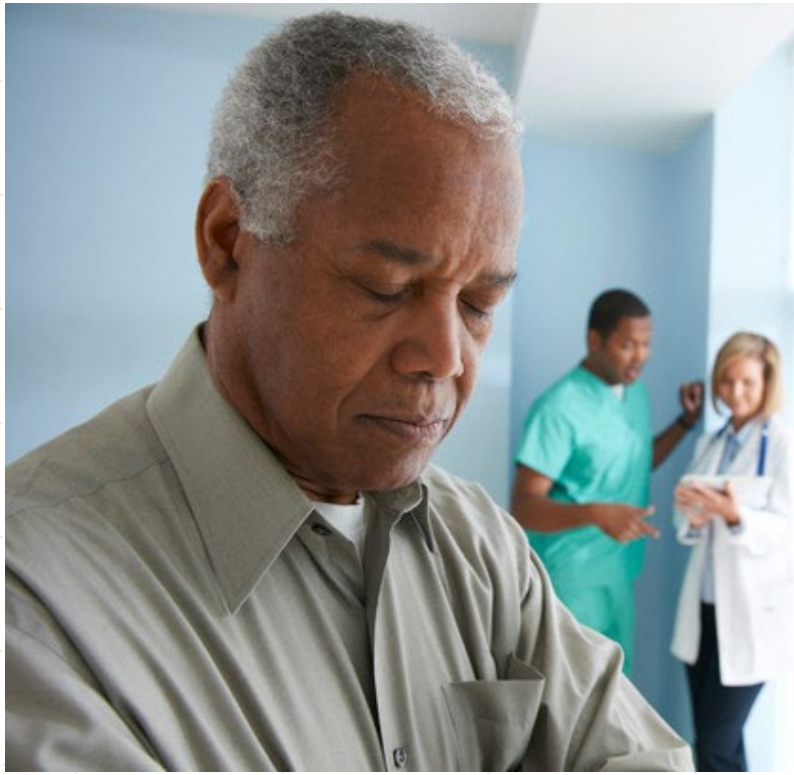
P30 Center Overview



Nell Hodgson Woodruff
School of Nursing

Emory University Atlanta, GA

Funding NINR P30 NR018090

Core Directors & Pilot PIs

- Linda McCauley, Center Director
- Kate Yeager, Associate Center Director
- Sandra Dunbar, Pilot Core Director
- Irene Yang, Enrichment Core Director
- Vicki Hertzberg, Data Science Core Director
- Drenna Waldrop-Valverde, Center Evaluator
- Pilot PIs: Glenna Brewster & Jessica Wells, Brittany Butts, Laren Narapareddy, Nick Giordano
- Supplement Pilot PIs: Irene Yang, Laura Kimble

Overall Center Objectives

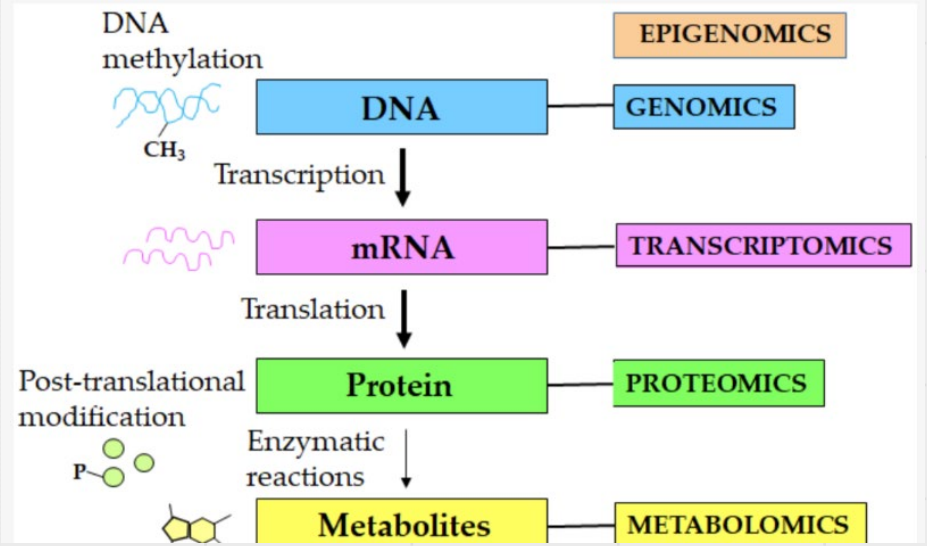
Create and manage a Center that provides **resources and infrastructure** to support **cutting-edge research** using **metabolomics and microbiomic technologies** and **data analytic strategies** to **reduce symptoms** (fatigue, depression and anxiety) in adult **African Americans** with **multiple chronic conditions** (MCC).

Promote the **success of junior faculty**.

Disseminate Center discoveries through publications, summer institutes and conferences.

Research Aim

- Apply next-generation **metabolomics** technology and sophisticated **data analytic** strategies to stimulate discovery of the **metabolites and metabolic pathways** present in **African Americans** with **multiple chronic conditions**, focusing on metabolites and pathways that **synergize** across health conditions and associate with severe **fatigue, depression or anxiety or** underly their **clustering**.



Toward Precision nursing: uncovering who experiences what and why others do not?

WHY AFRICAN AMERICANS AND WHY THESE AIMS?

African Americans disproportionately suffer MCC

The symptoms of fatigue and depression and anxiety often cluster and carry negative consequences for health and well-being

Symptom severity in those with even the same MCC varies, suggesting that the mechanisms driving symptoms in MCC are not fixed but vary in ways that may make them amenable to targeted intervention

POTENTIAL METABOLITES & METABOLIC PATHWAYS CONTRIBUTING TO FATIGUE, ANXIETY, &/or DEPRESSSION

FATIGUE	Inflammation (cytokines); Energy (Krebs Cycle)
DEPRESSION	Inflammation (cytokines); Energy (Krebs Cycle); tryptophan, serotonin
ANXIETY	Catecholamines, HPA axis

P30 Pilots and PIs: Metabolomic pathways to fatigue, depression, or anxiety in Black adults:

- **Who are Family Caregivers with Obesity and HTN – Dr. Glenna Brewster Glasgow**

- **With HIV and HTN – Dr. Jessica Wells**

- **With Heart Failure (HFrEF) and HTN – Dr. Brittany Butts**

P30 Pilots and PIs

Metabolomic pathways to fatigue, depression, or anxiety in Black adults:

- 

  With Polycystic Ovarian Syndrome (PCOS) and HTN
  Dr. Laren Narapareddy

With Sleep Apnea, Diabetes, and HTN – Dr. Nick Giordano

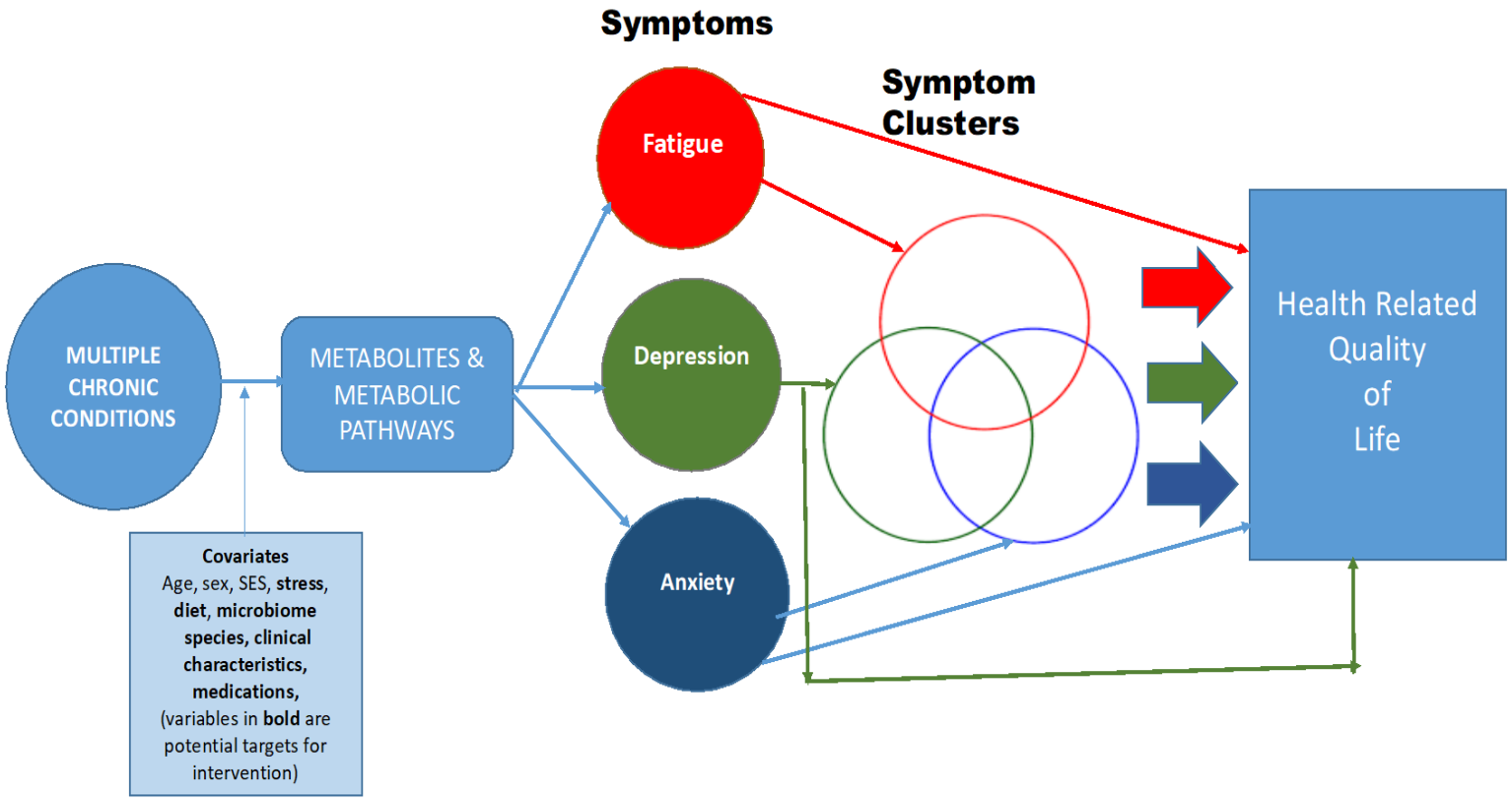
P30 Pilots and PIs Supplements

Metabolomic pathways to fatigue, depression, or anxiety in Black adults:

Who are family caregivers of persons with CA and HTN – Dr. Irene Yang

With Lupus and HTN – Dr Laura Kimble

A NEW MODEL FOR SYMPTOM SCIENCE



The Theoretical Framework

- Individuals with multiple chronic conditions and a ***unique mixture of covariates*** produce an ***equally unique phenotype of metabolites and metabolic pathways*** that associated with the symptoms of fatigue, depression, and/or anxiety.
- ***The metabolites and metabolic pathways*** produced in those with MCC, ***may synergize positively or negatively*** with each other ***and/or may contribute to a cluster*** of symptoms.
- Depending on severity and synergy, these complex pathways may impact an individual's health and quality of life.

P30 Center: Opportunities for the School and its Faculty, Fellows, and Students

Infrastructure: Data Science Center

Enrichment: Conferences and Workshops

Supplemental funding

New grant proposals

Dissemination of New Science: publications, presentations, and webinars

Team Science

Infrastructure for Student Trainees

THE P30

Center for the Study of Symptom Science, Metabolomics and Multiple Chronic Conditions

THANK YOU for YOUR INTEREST!!

Omics – A Brief Overview

Brittany Butts

Omics – A Brief Overview

- What is omics?

“omics”

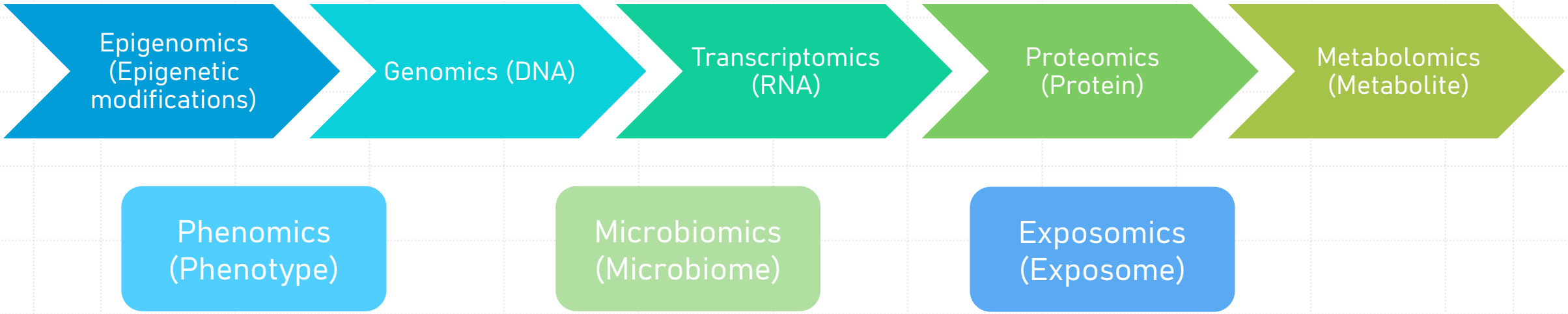
The word you've entered isn't in the dictionary. Click on a spelling suggestion below or try again using the search bar above.

Omics – A Brief Overview

- What is omics?
- Probing and analyzing large amounts of data representing the structure and function of an entire makeup of a given biological system at a particular level

Omics – A Brief Overview

- What is omics?
- Probing and analyzing large amounts of data representing the structure and function of an entire makeup of a given biological system at a particular level
- A group of words that end in omics



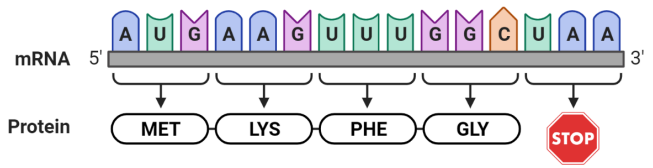
Central Dogma of Molecular Biology

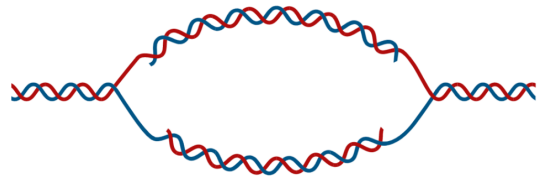
DNA - encodes our genes

Transcription

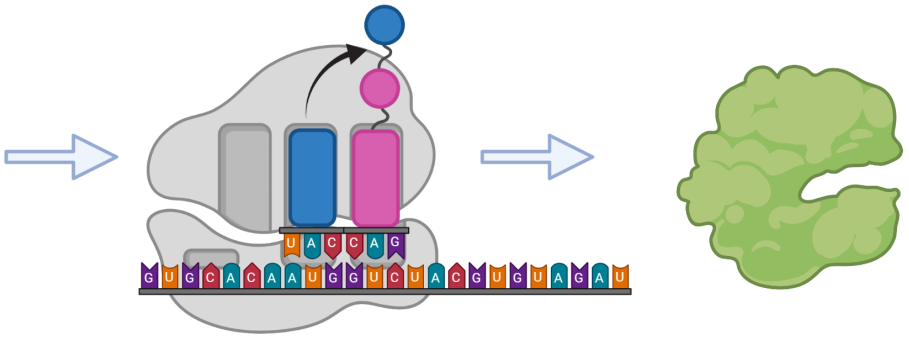
mRNA contains the codes for new proteins

Translation





DNA replication occurs during cell division.



Genomics

- Study of the structure, function, evolution, and mapping of genomes

Basic Genomics

- Genes (exons) comprise about 2% of the human genome
- The remainder 98% consists of noncoding regions (introns), whose functions may include providing chromosomal structural integrity and regulating where, when, and in what quantity proteins are made.
- The human genome sequence is almost (99.9%) exactly the same in all people.

Source: Genome Management Information System, Oak Ridge National Laboratory

Genomic Medicine Goal: DNA to treatments

The ultimate goal of genomic medicine is personalized health care that integrates one's

- genotype (the genetic constitution of an individual)
- phenotype (the biochemical, physiological and morphological characteristics of an individual)
- and environmental factors

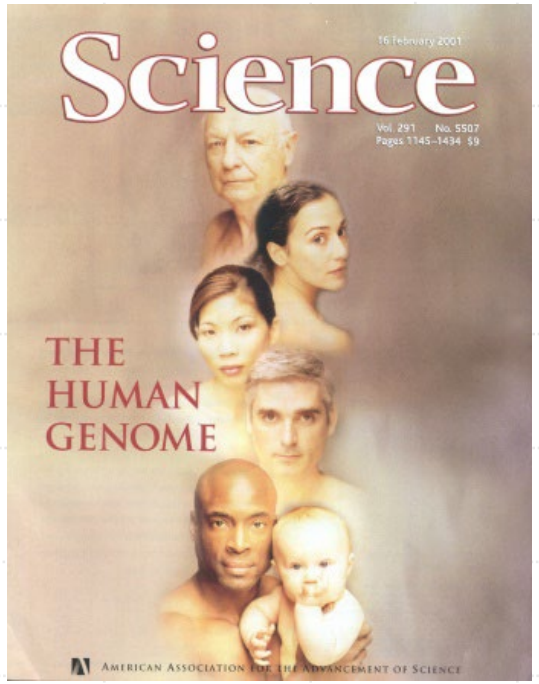
in order to formulate prevention and treatment options for complex disorders.

Genomics

- Study of the structure, function, evolution, and mapping of genomes

Genetic Mapping: Human Genome Project

- The Human Genome Project began in 1990
- 2001 Rough Draft then in 2003 Completed sequence
- It took 13 years and 3 billion dollars



Human Genome Project

- The project goals were to:
- *identify* all the approximately 20,000–25,000 genes in human DNA,
- *determine* the sequences of the 3 billion chemical base pairs that make up human DNA,
- *store* this information in databases,
- *improve* tools for data analysis,
- *transfer* related technologies to the private sector
- *address* the ethical, legal, and social issues (ELSI) that may arise from the project.

2003 National Human Genome Research Institute (NHGRI) launched a public research consortium named ENCODE, the **Enc**yclopedia **O**f **D**NA **E**lements

Genomics

Science Times

TUESDAY, SEPTEMBER 4, 2007

The New York Times

DECODING HIMSELF A team led by J. Craig Venter, above, has finished the first mapping of a full, or diploid, genome, made up of DNA inherited from both parents. The genome is Dr. Venter's own.

Genes highlighted above are linked to specific traits but do not mean the conditions are inevitable.

In the Genome Race, the Sequel Is Personal

By NICHOLAS WADE

The race to decode the human genome may not be entirely over: the loser has come up with a new approach that may let him prevail in the end.

In 2003, a government-financed consortium of academic centers announced it had completed the human genome, fending off a determined challenge from the biologist J. Craig Venter. The consortium's genome comprised just half the DNA contained in a normal cell, and the DNA used in the project came from a group of people from different racial and ethnic backgrounds.

But the loser in the race, Dr. Venter, could still have the last word. In a paper published today, his research team is announcing that it has decoded a new version of the human genome that some experts believe may be better than the

Using his own DNA, a pioneering biologist and his team have decoded a new version of the human genome.

consortium's.

Called a full or5 diploid genome, it consists of the DNA in both sets of chromosomes, one from each parent, and it is the normal genome possessed by almost all the body's cells. And the genome the team has decoded belongs to just one person: Dr. Venter.

The new genome, Dr. Venter's team reports, makes clear that the variation in the genetic programming carried by an individual is much greater than expected. In at least 44 percent of Dr. Venter's genes, the copies inherited from his mother differ from those inherited from his father, according to the analysis published in today's issue of PLoS Biology.

Huntington F. Willard, a geneticist at Duke University who has had early ac-

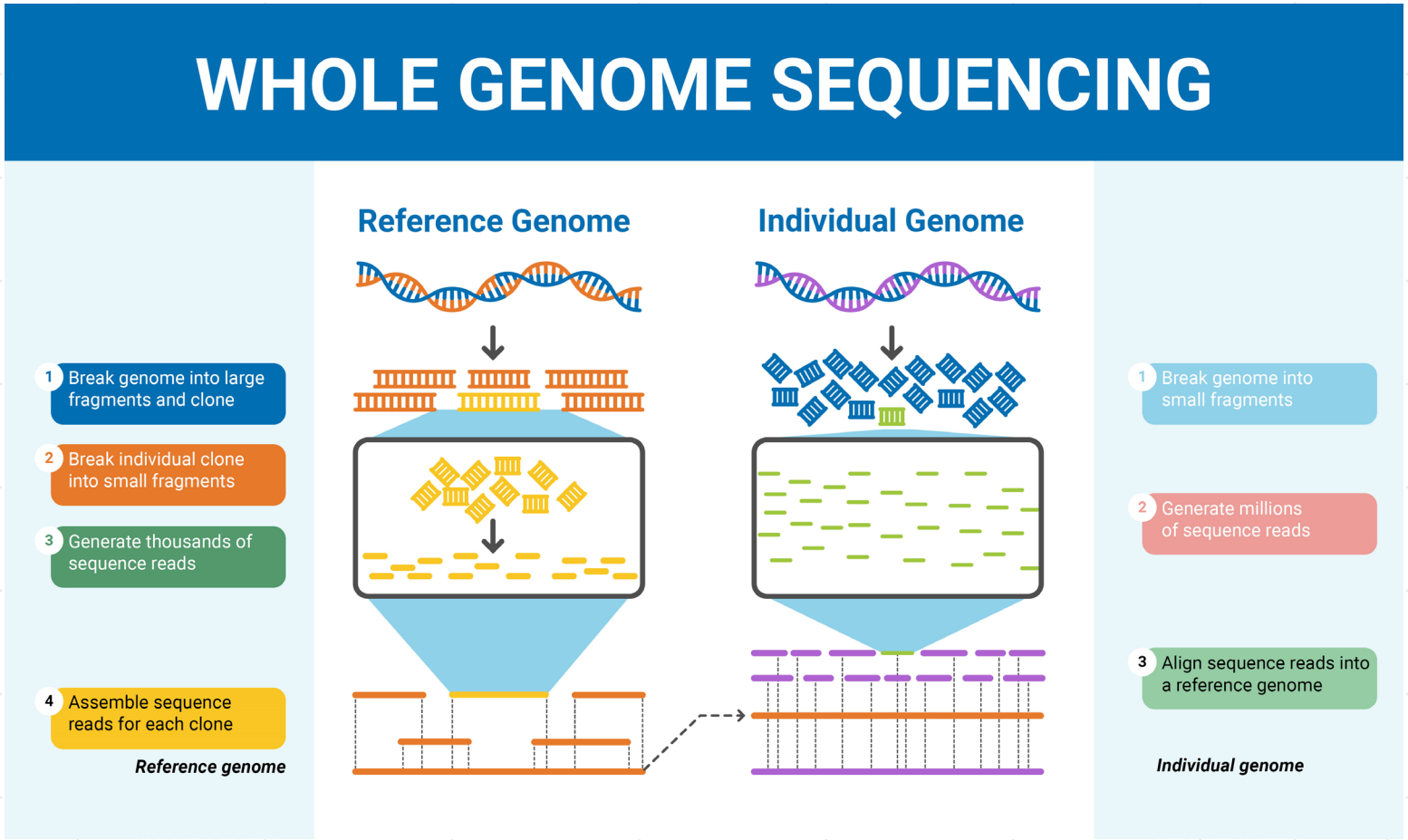
Continued on Page 4

Advancements in Genome Sequencing

- 2007 – J. Craig Venter decoded a full diploid genome – his and James Watson's
- Took 3 months and $300,000 each
- Currently it takes around 30 minutes and $600

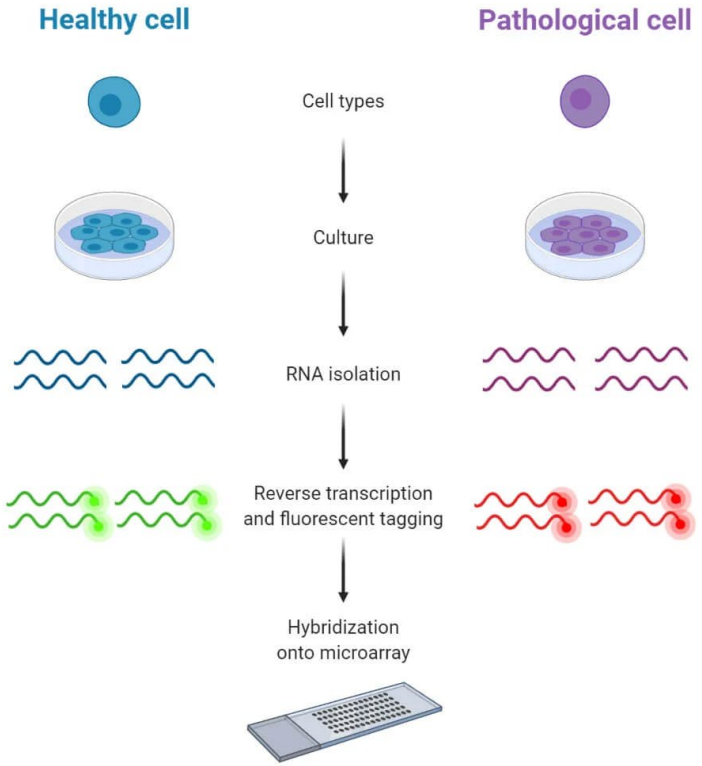
Genomics

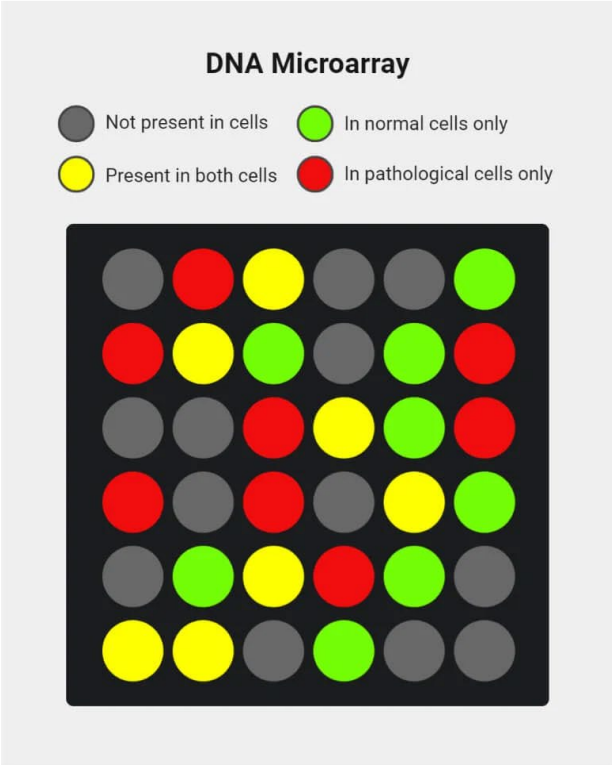
- Study of the structure, function, evolution, and mapping of genomes
- May use DNA sequencing



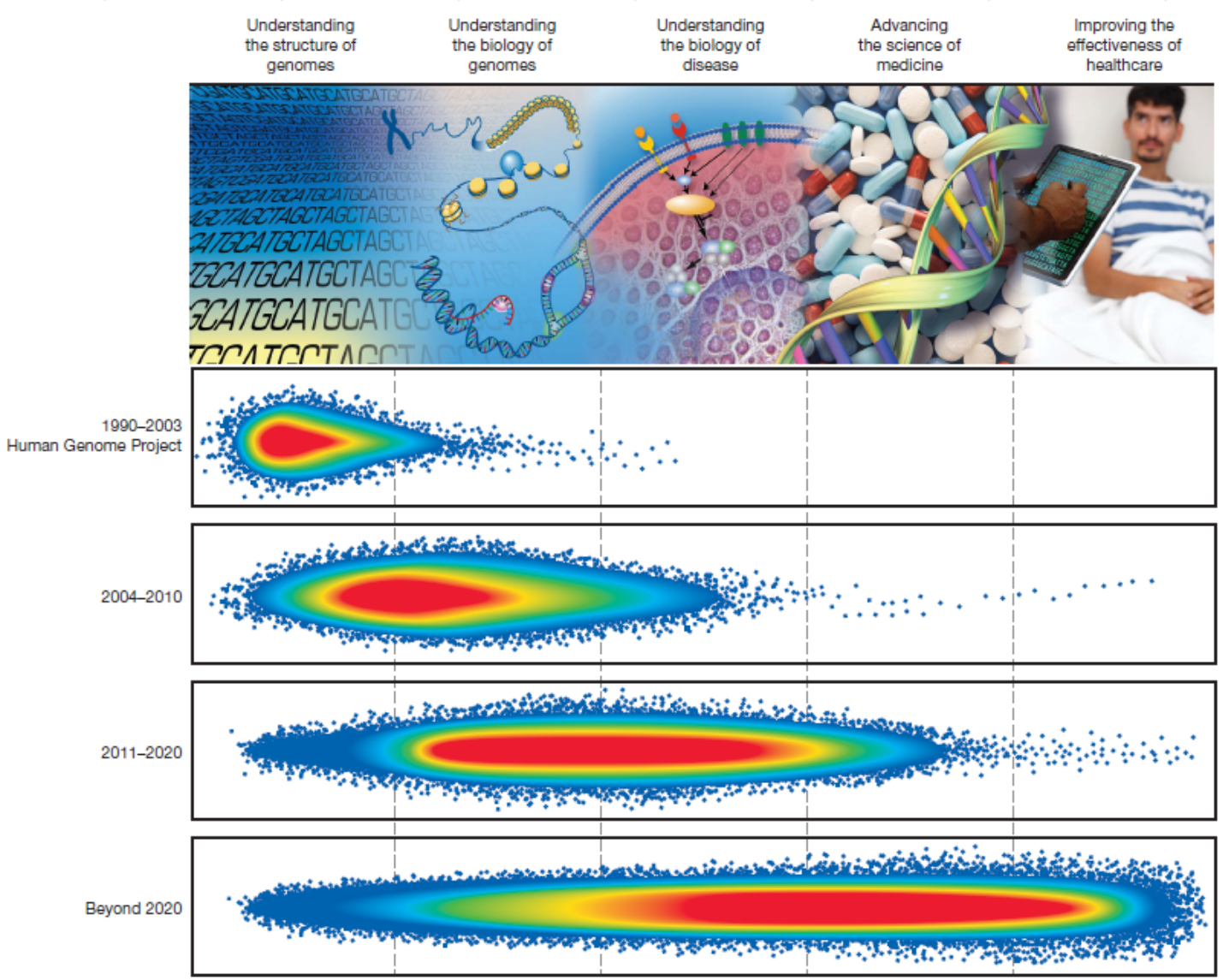
Genomics

- Study of the structure, function, evolution, and mapping of genomes
- Often use microarray technology





From base pairs to bedside



Eric Green, Mark Guyer & National Human Genome Research Institute (NHGRI)

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Genomics

What are some applications for genomics in research and healthcare?

- Gene discovery and diagnosis of rare genetic disorders
- Identification of genetic factors that contribute to chronic disease
- Pharmacogenetics and targeted therapy
- Prenatal testing
- Infectious disease and vaccine development
- Personalized medicine
- Gene therapy
- Genomic editing?

Epigenomics

- The study of the complete set of epigenetic modifications on the genetic material of a cell (epigenome)

What is Epigenetics?

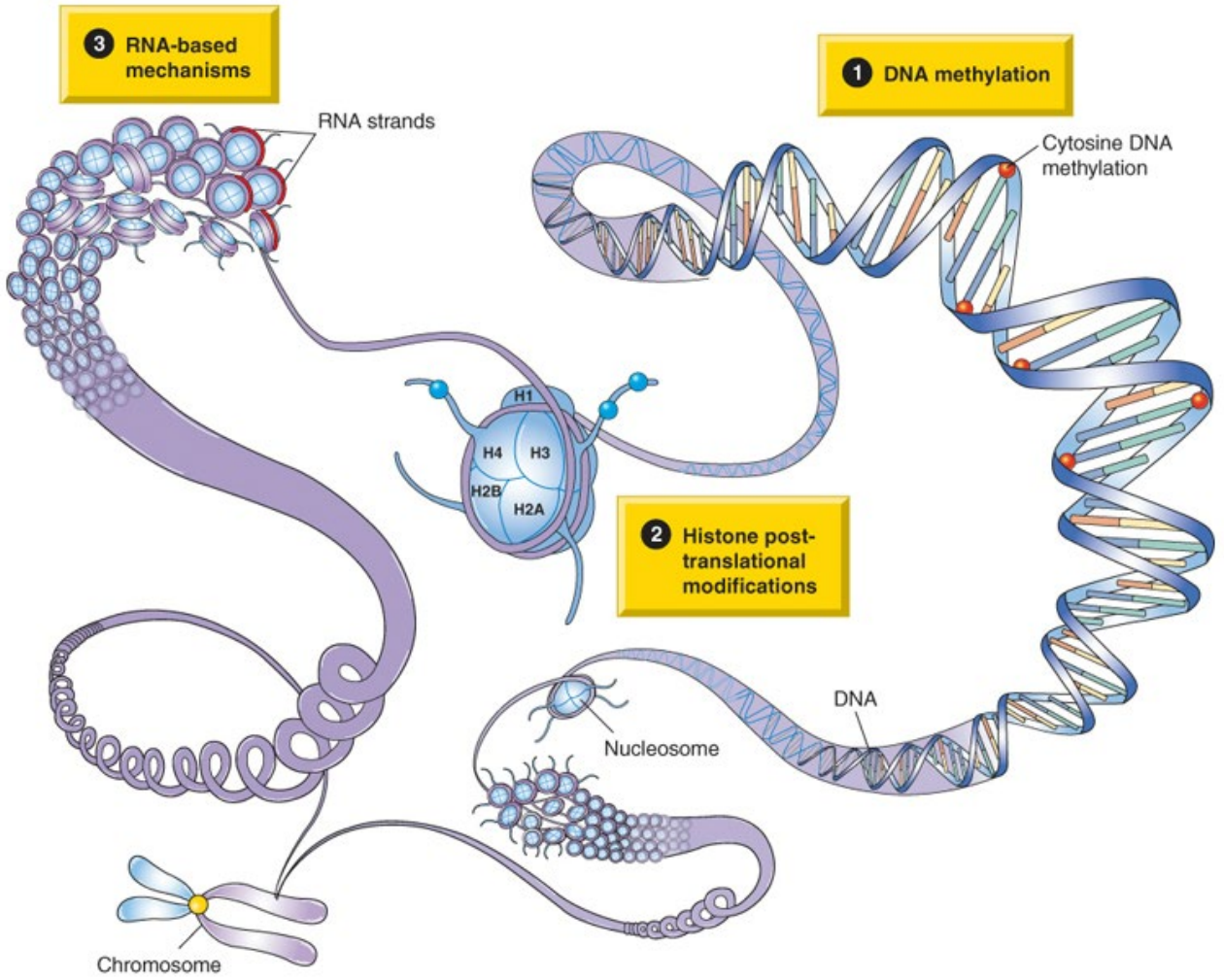
Changes in **gene expression** caused by mechanisms OTHER THAN changes in DNA sequence

Maintained in successive mitotic cell divisions

Environmental factors (diet, chemical exposure) can → epigenetic modifications

Types of epigenetic changes

- DNA Methylation
- Histone modification
- RNA-based mechanisms



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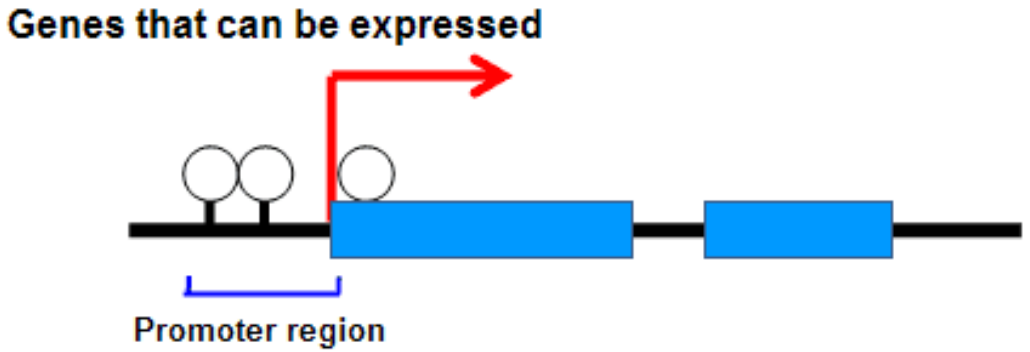
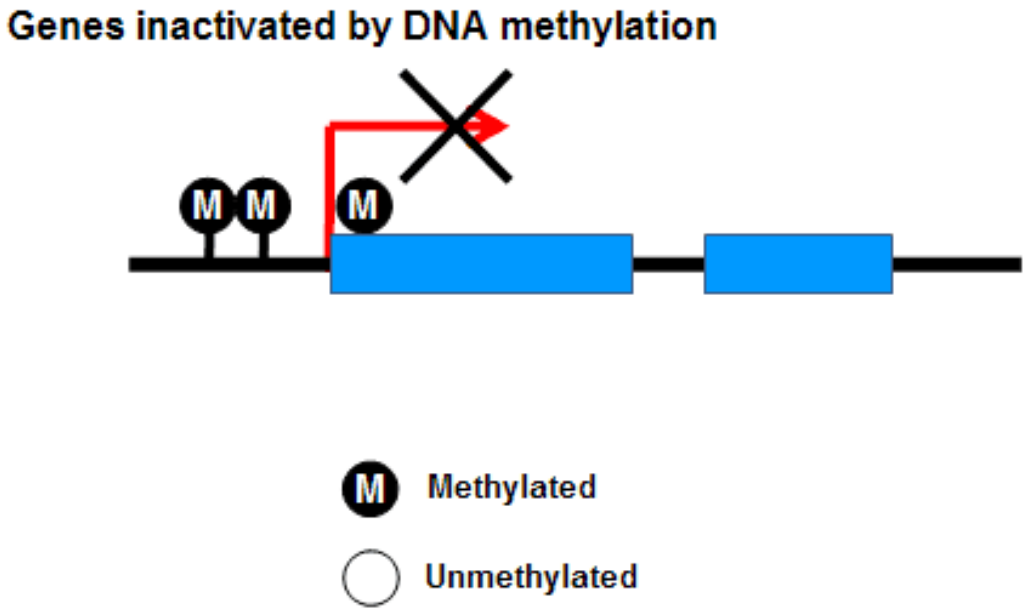
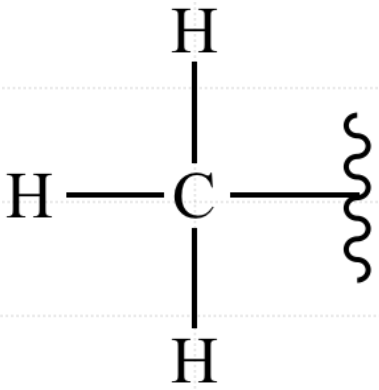


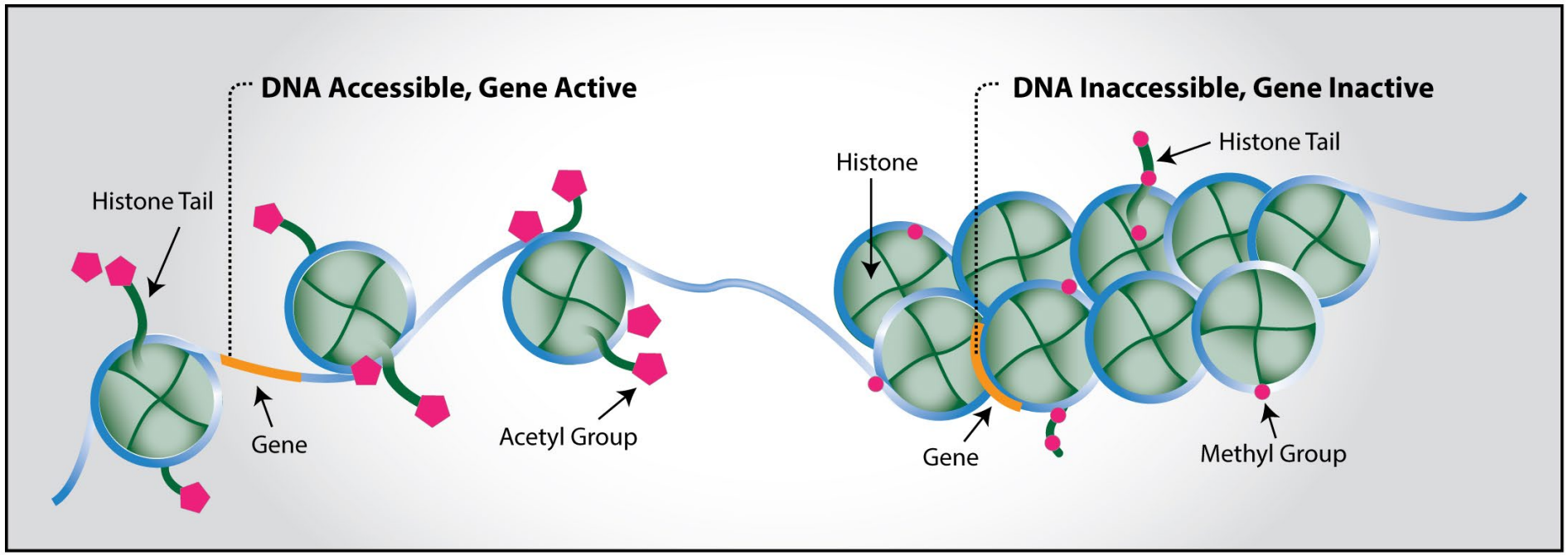




Methyl group

Types of epigenetic changes

- DNA Methylation
- **Histone modification**
- RNA-based mechanisms



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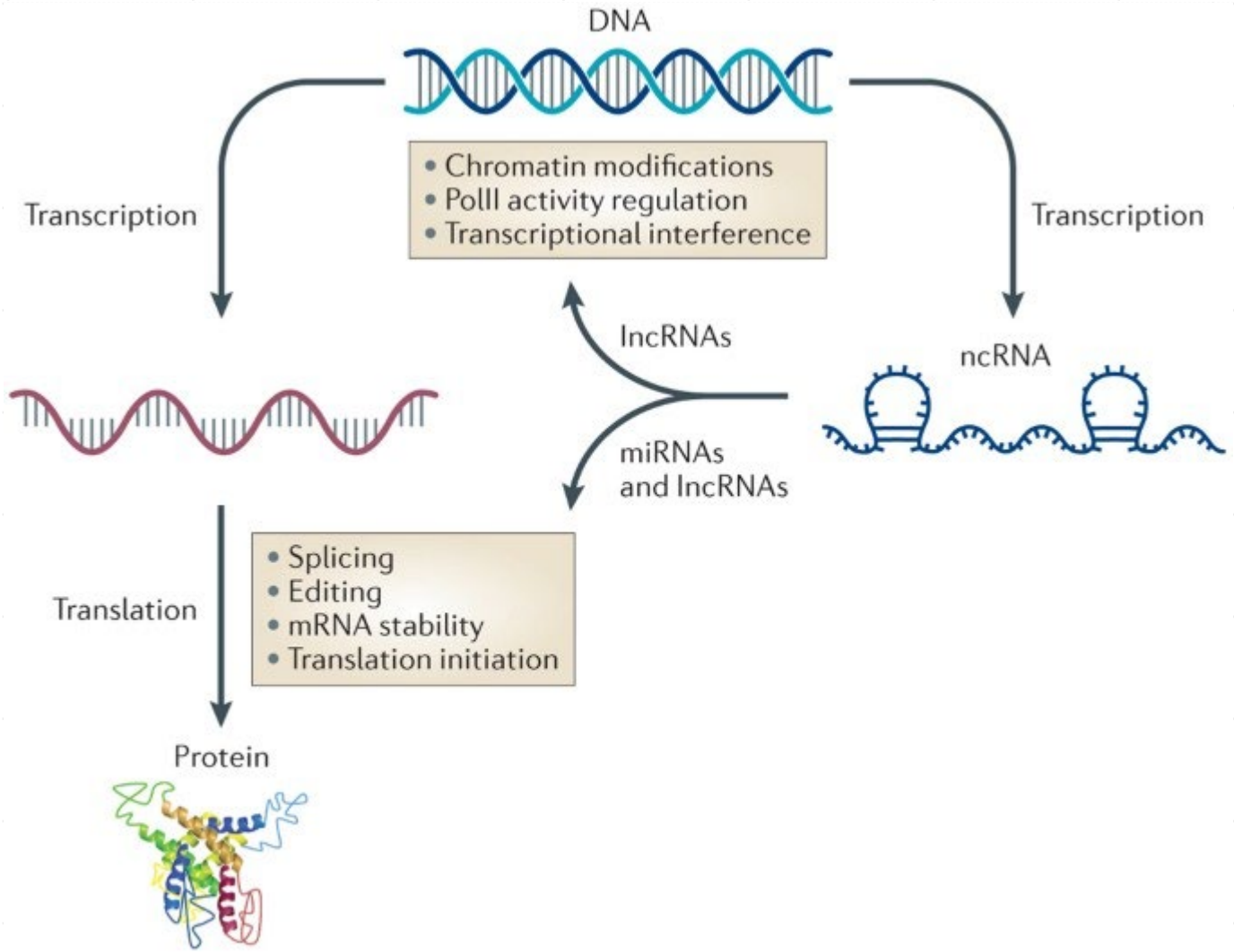


Wahlestedt C. Targeting long non-coding RNA to therapeutically upregulate gene expression 2014 Jan;13(1):79]. *Nat Rev Drug Discov*. 2013;12(6):433-446. doi:10.1038/nrd4018

Physiologic Role of Epigenetic Modifications

- Important in embryogenesis to turn genes on/off → cell differentiation

- Remember: ALL cells have ALL genes, BUT only certain genes are turned on → specific cell morphology and function

Do you want more or less in epigenetics?

- It depends on where the DNA methylation occurs along the DNA, what gene is involved
- Examples:
  - BRCA1 hypermethylation → breast cancer
  - Peptidyl arginine deiminase 2 (PADI2) hypomethylation → multiple sclerosis
  - Inappropriate histone modifications
    - IFNγ aberrant acetylation → SLE
    - IL-6 aberrant methylation → type I diabetes

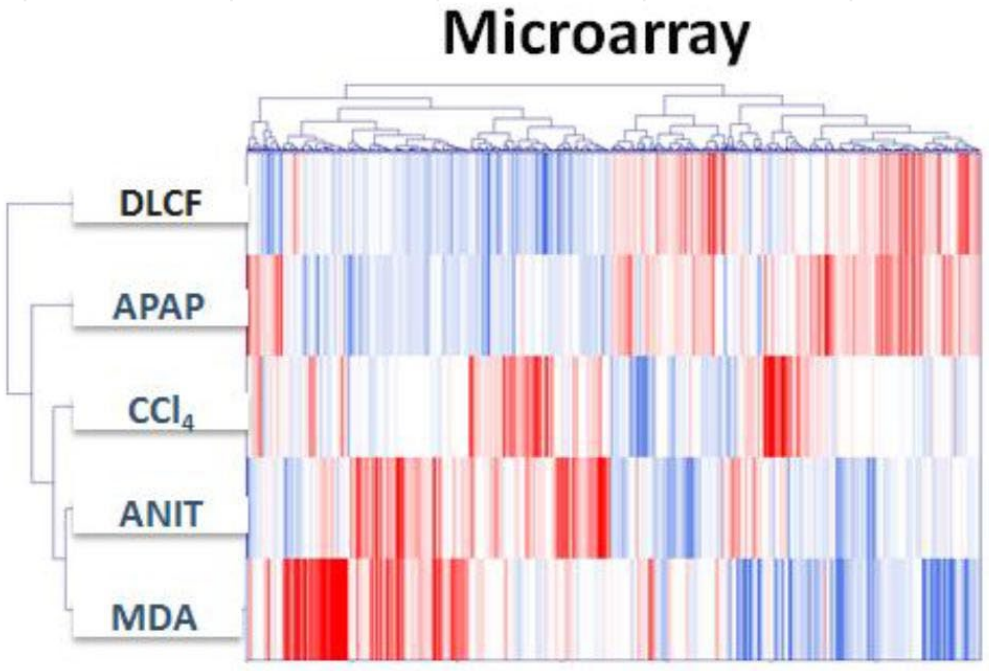
Epigenomics

- What are some applications for epigenomics in research and healthcare?
- Drugs that target the epigenome
  - Can target writers (add), readers (interpretation), or erasers (remove)
  - DNA methyltransferase (DNMT) inhibitors
  - Histone deacetylase (HDAC) inhibitors
- Lifestyle interventions

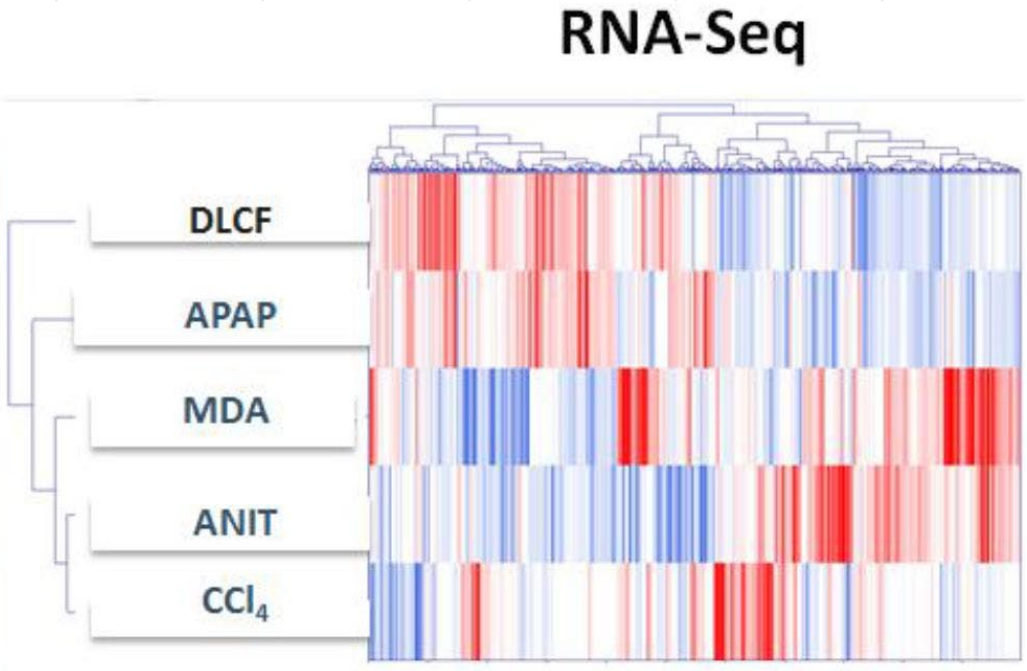
Transcriptomics and Proteomics

- Transcriptomics – large-scale study of mRNA transcripts
- Proteomics – large-scale study of proteins
- **Transcriptomics provides a useful overview of global gene expression**
- **Proteomics is often used as a complementary technique that provides a comprehensive insight into the protein profile of an organism**

Transcriptomics Methods

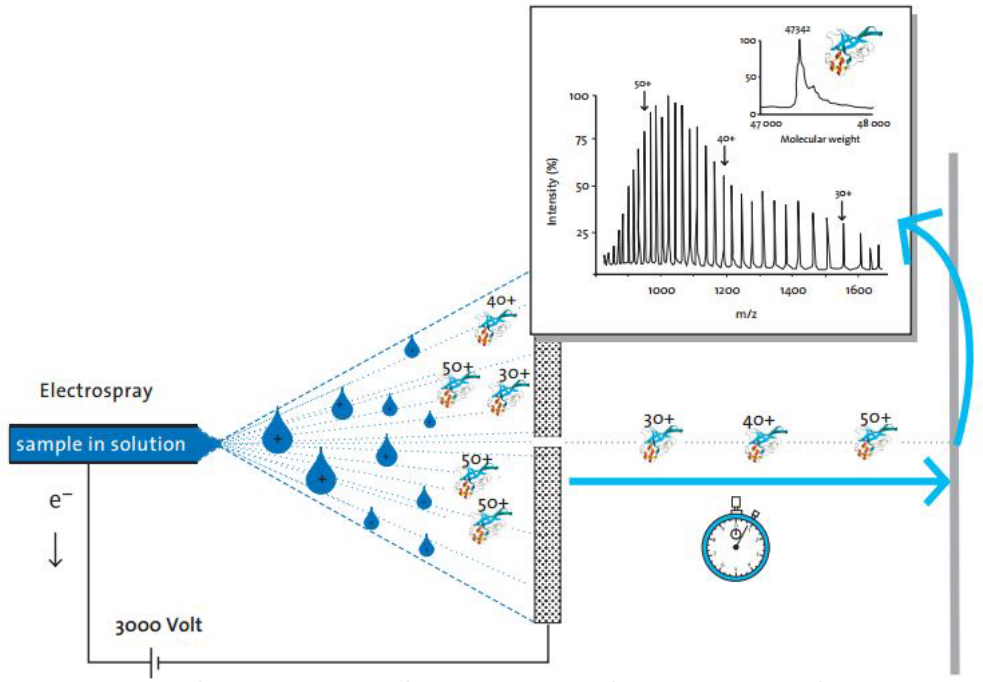


Hybridization assay



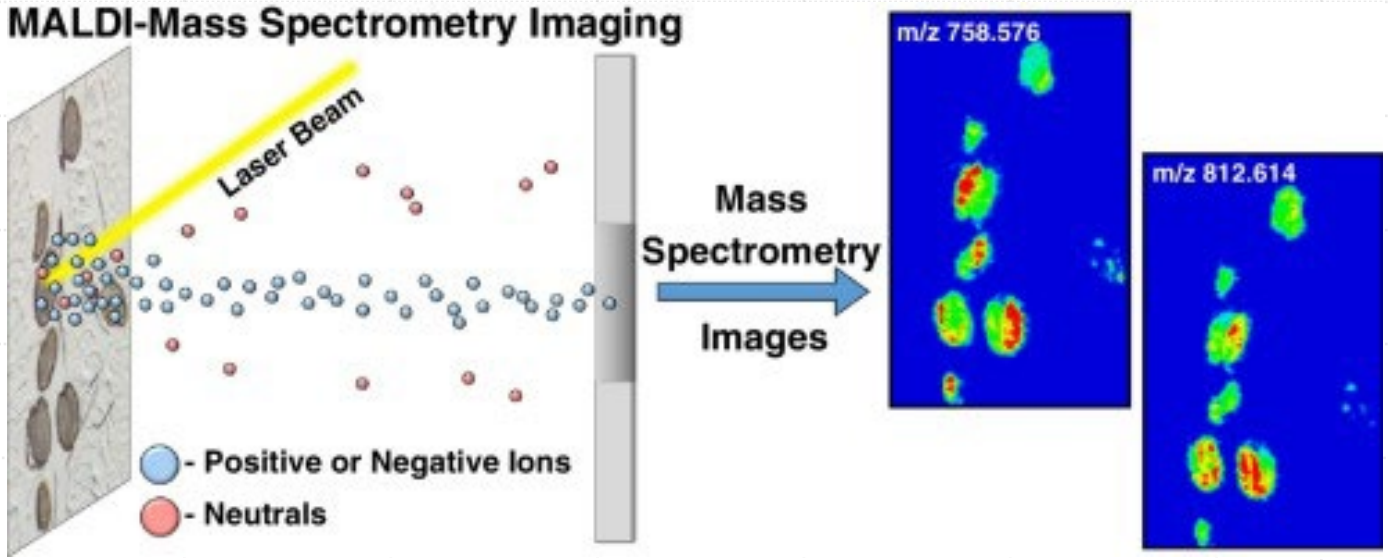
Quantitative RNA sequencing

Mass spectrometry – measures mass-to-charge ratio of ions.
Sample is ionized and hit with a beam of electrons.
Molecules break into charged fragments separated according to mass-to-charge ratio.
Molecules identified based on known mass.



Mass spectrometry

Proteomics Methods



Transcriptomics and Proteomics

- What are some potential research and clinical applications?

- Most chronic diseases have complex genetic contributions. Looking at gene expression can be more informative in looking at what genes contribute to multifactorial diseases

Metabolomics

- Large-scale study of small molecules – metabolites – within cells, biofluids, tissues or organisms

Metabolomics

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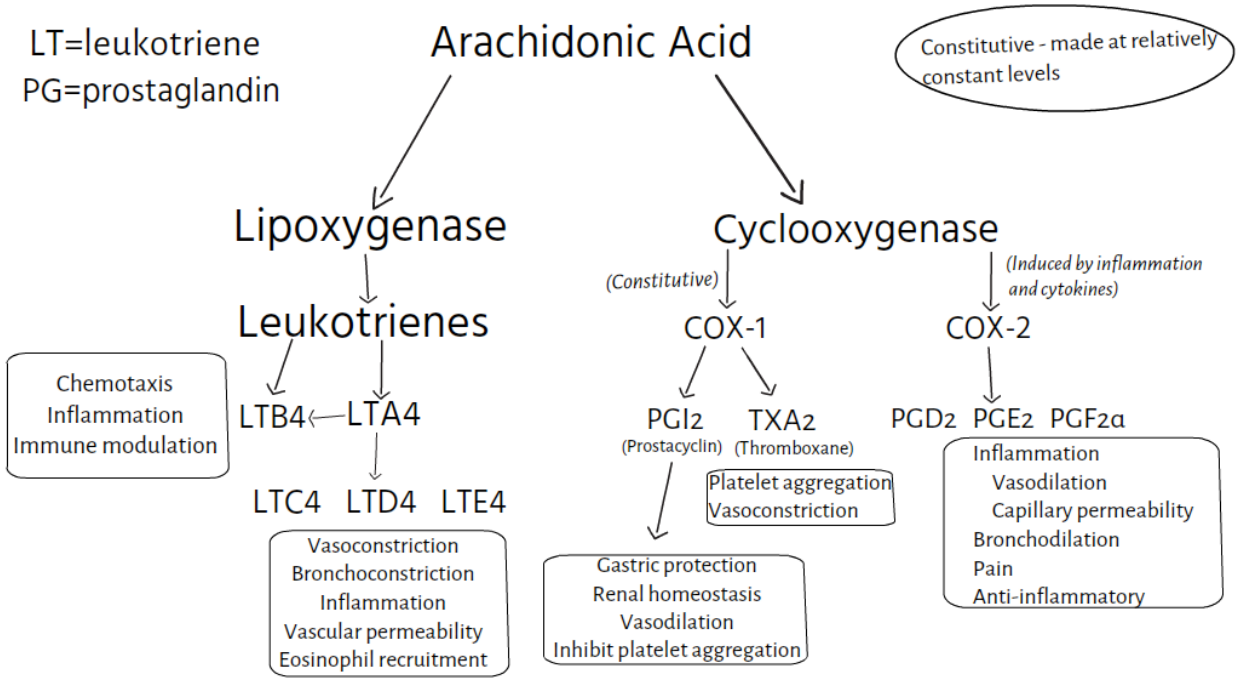
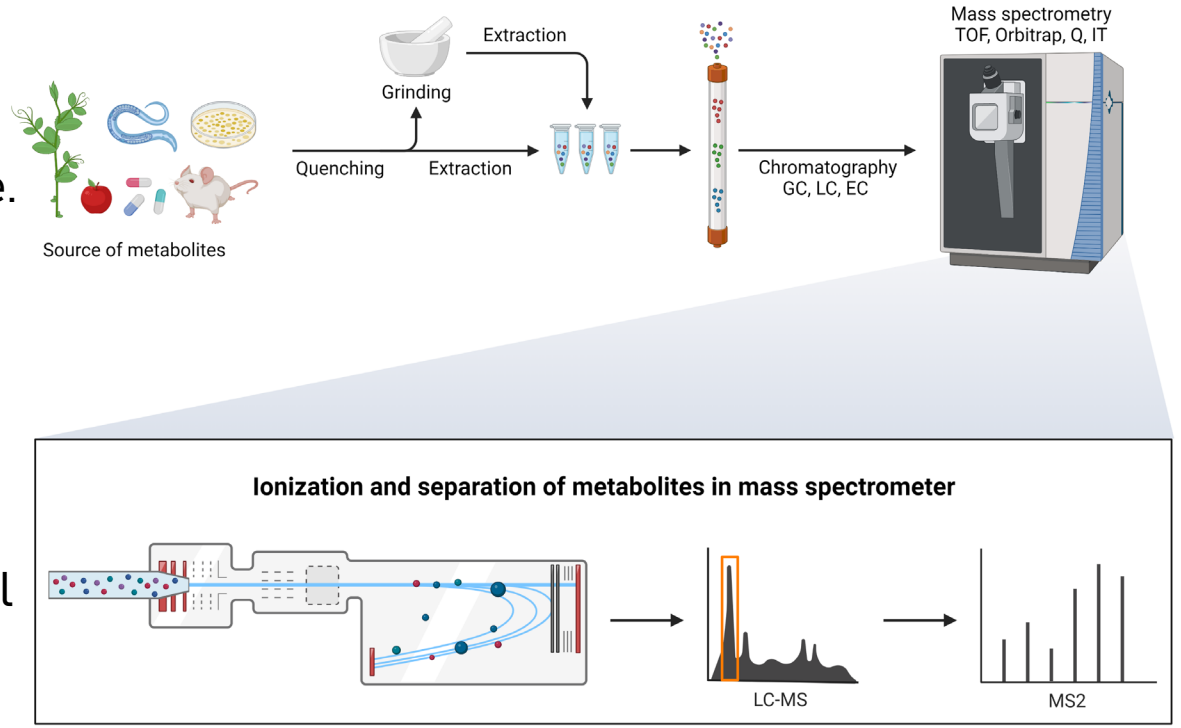


Learn more about arachidonic acid metabolism:
https://www.youtube.com/watch?v=CN85DkGCYkk&t=297s

Metabolomics Overview

Chromatography – separates components of a mixture.

- Mixture is dissolved in a substance (mobile phase), which carries it through a second substance (stationary phase).
- The different components of the mixture travel through the stationary phase at different speeds, causing them to separate from one another.
- Substances are separated based on speeds of travel through the stationary phase.



Examples:
Gas chromatography – mixture vaporized and run through metal/glass with inert gas (He, N)
Liquid chromatography – mixture dissolved in liquid, run through silica

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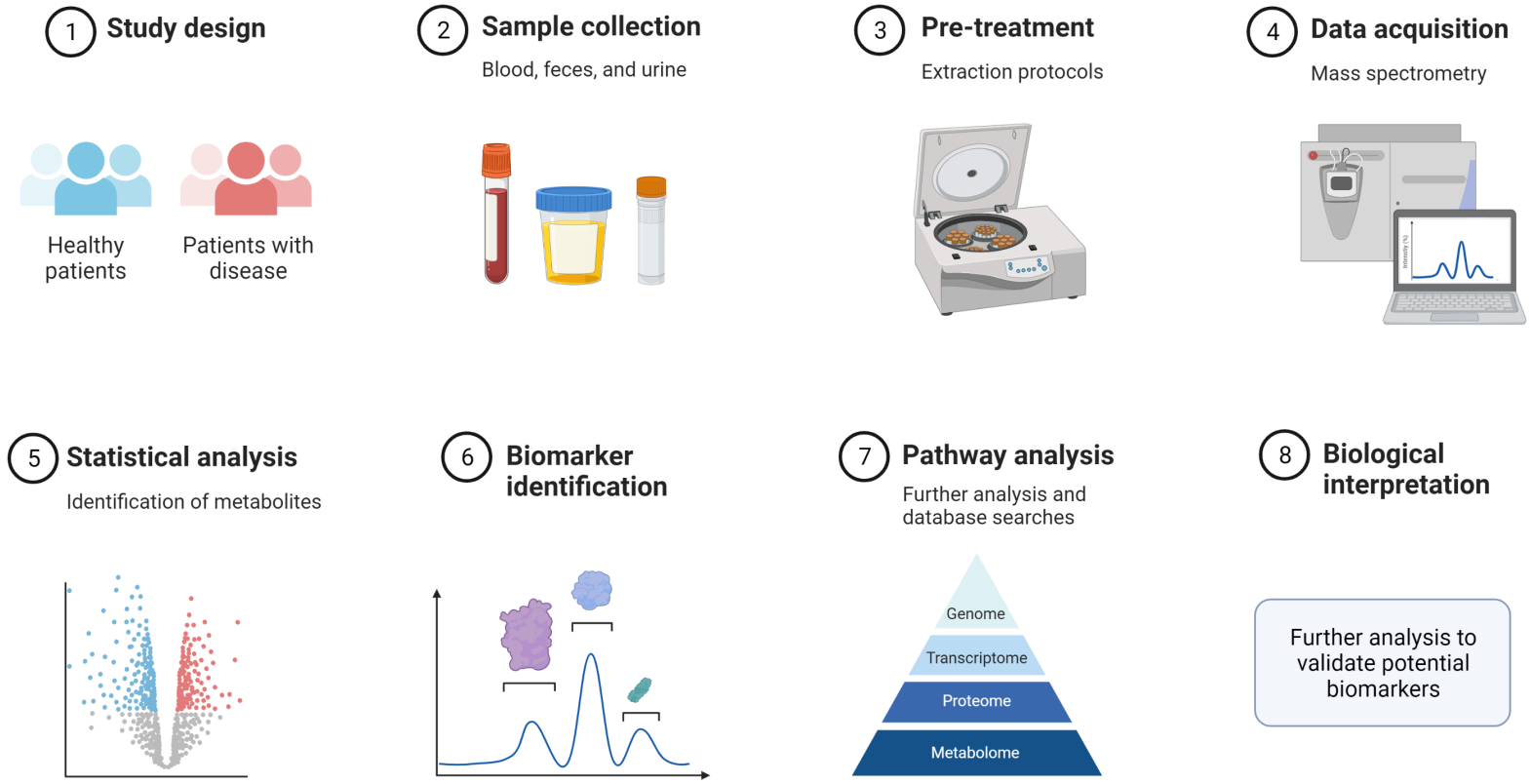
Untargeted Metabolomics for Discovery of Disease Biomarkers

- Analyzes all metabolites present in an organism.
- Usually compare groups
  - Healthy vs disease state
  - With or without a comorbidity
  - Treatment



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Metabolomics

- How could we use metabolomics in research and healthcare?

- Metabolomics allows us to better understand pathways related to disease, sequelae, and patient outcomes
- Investigation of pathways that differ between 2 groups of people

Microbiomics

- The study of all microorganisms in a given community.

Microbiome

- The collection of all microbes, such as bacteria, fungi, viruses, and their genes, that naturally live on our bodies and inside us

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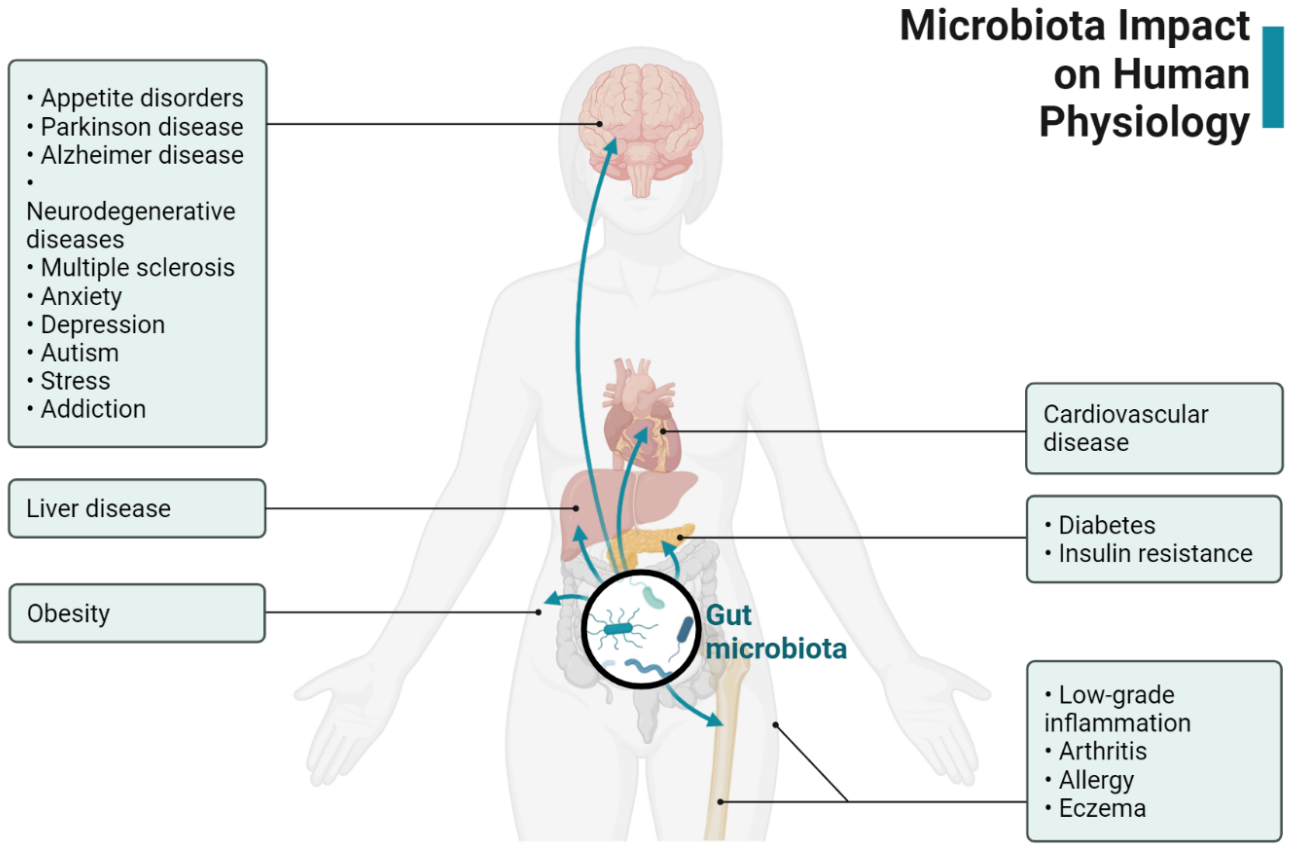

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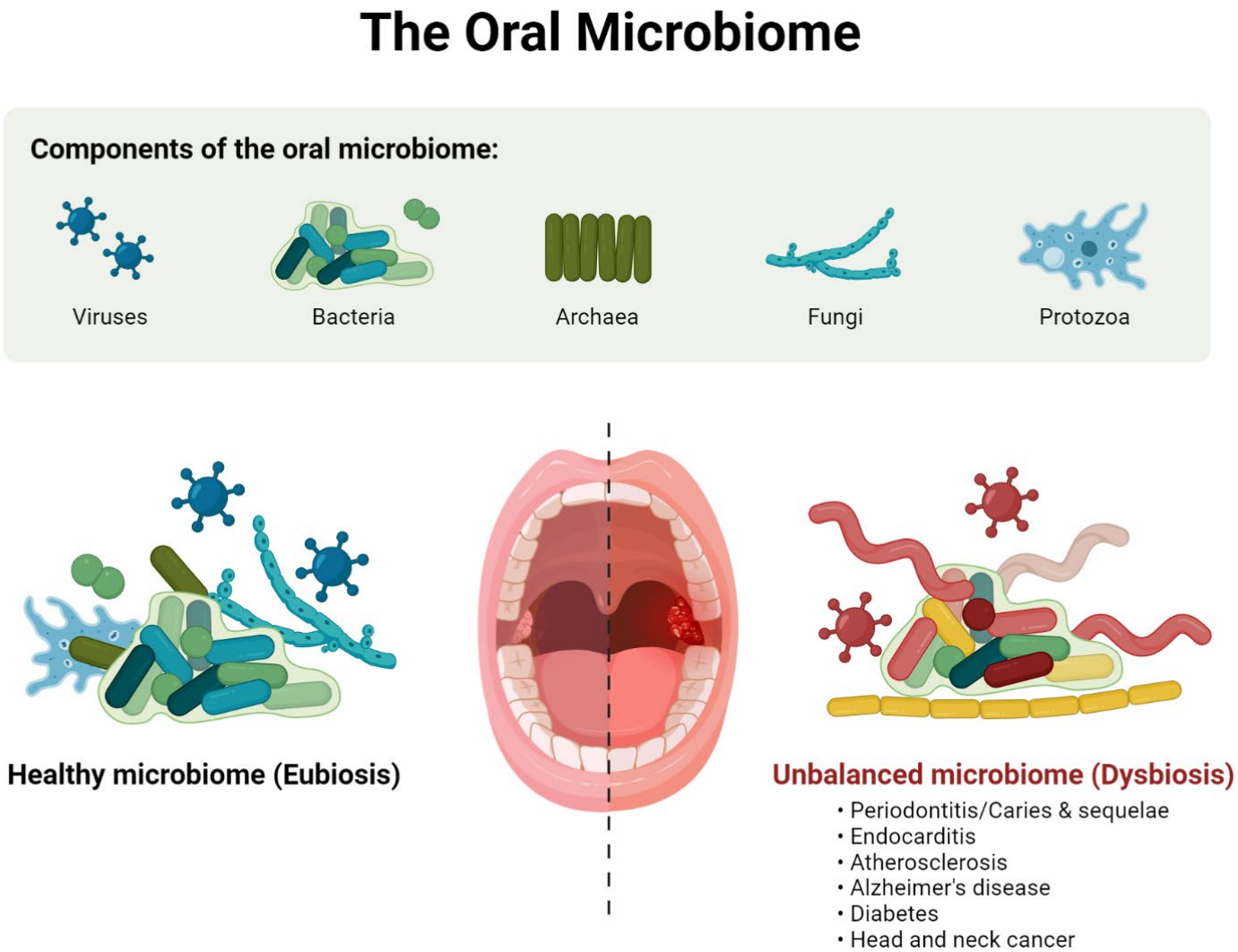
Microbiome


The Oral Microbiome
Components of the oral microbiome:
Viruses
Bacteria
Archaea
Fungi
Protozoa
Healthy microbiome (Eubiosis)
Unbalanced microbiome (Dysbiosis)
• Periodontitis/Caries & sequelae
• Endocarditis
• Atherosclerosis
• Alzheimer's disease
• Diabetes
• Head and neck cancer
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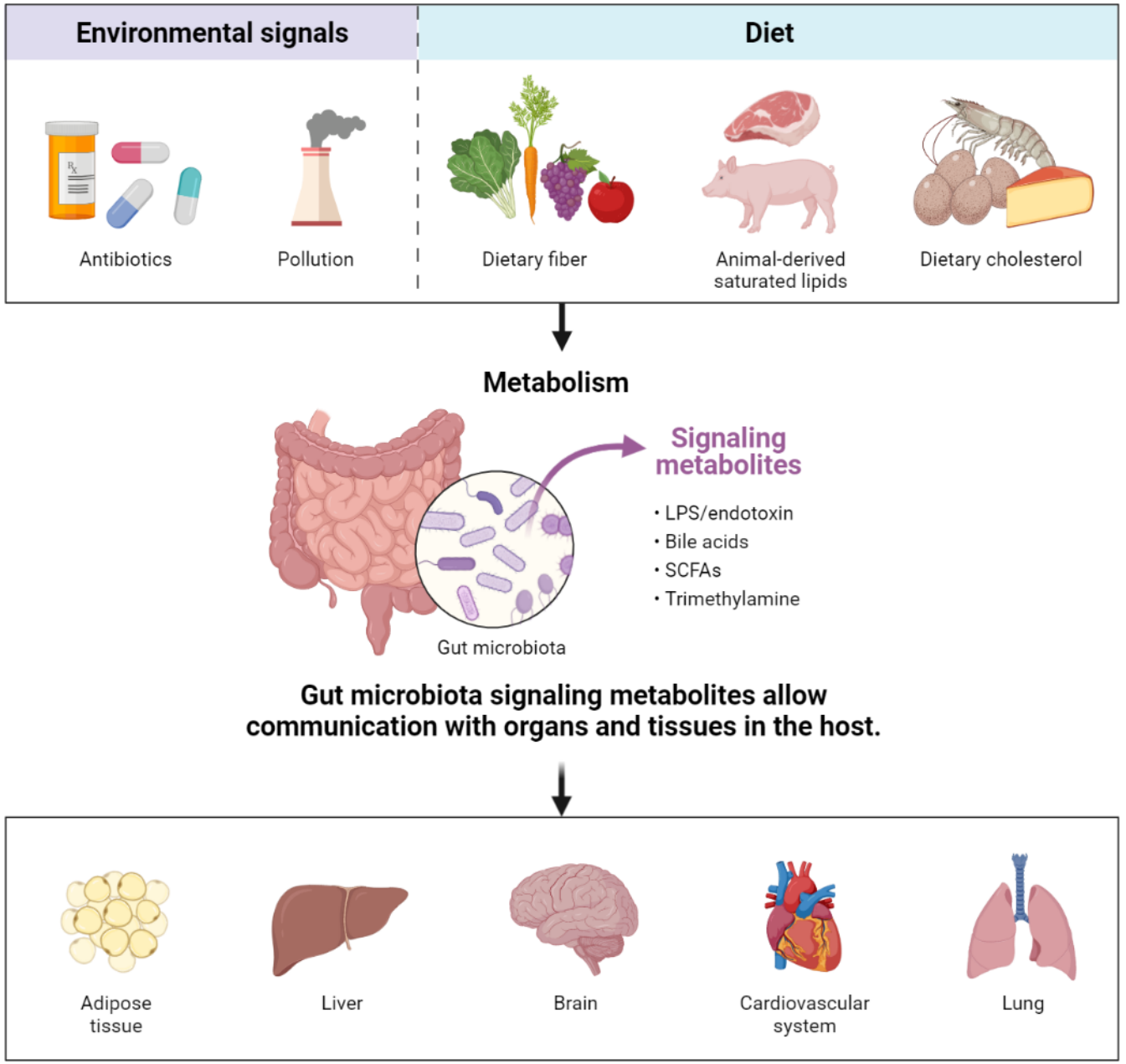
Microbiome



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Microbiomics

- How could we use microbiomics in research and healthcare?

- Different types of bacteria may influence health and disease states
- Some bacteria are involved in metabolism of substances in our body. Having the wrong type of bacteria may lead to harmful metabolites.

Applications of Omics in Nursing Research

How are omics used in Nursing Research?

Omics in Research

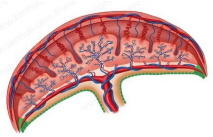
Published in final edited form as:
Nurs Res. 2022 ; 71(2): 128–137. doi:10.1097/NNR.0000000000000574.

Adaptation of Metabolomics and Microbiomic Research Protocols During the COVID-19 Pandemic

Brittany Butts, PhD, RN [Assistant Professor], Taqiyya Alford, MPH, CRC [Clinical Research Coordinator], Glenna Brewster, PhD, RN, FNP-BC [Assistant Professor], Nicole Carlson, PhD, CNM [Assistant Professor], Ebony Coleman, CRC [Clinical Research Coordinator], Erica Davis, BSN, RN [PhD Candidate], Erin Ferranti, PhD, MPH, RN, FAHA [Assistant Professor], Laura P. Kimble, PhD, RN, FAAN [Professor], Laren Narapareddy, PhD, RN [Assistant Professor], Jessica Wells, PhD, RN, WHNP-BC [Assistant Professor], Irene Yang, PhD, RN [Assistant Professor]
Emory University Nell Hodgson Woodruff School of Nursing, Atlanta, GA

DOI: 10.1002/ajp.23101

RESEARCH ARTICLE



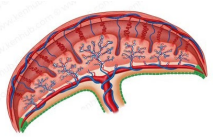
AMERICAN JOURNAL OF PRIMATOLOGY WILEY

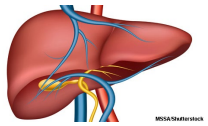
Maternal weight affects placental DNA methylation of genes involved in metabolic pathways in the common marmoset monkey (*Callithrix jacchus*)

Laren Narapareddy[1] | Derek E. Wildman[2] | Don L. Armstrong[3] | Amy Weckle[4] | Aleeca F. Bell[5] | Crystal L. Patil[5] | Suzette D. Tardif[6] | Corinna N. Ross[7] | Julienne N. Rutherford[5]

DOI: 10.1096/fj.202002744R

RESEARCH ARTICLE





THE FASEB JOURNAL

Sex-specific effects of in vitro fertilization on adult metabolic outcomes and hepatic transcriptome and proteome in mouse

Laren Narapareddy[1,2] | Eric A. Rhon-Calderon[2] | Lisa A. Vrooman[2] | Josue Baeza[3] | Duy K. Nguyen[2] | Clementina Mesaros[4] | Yemin Lan[2] | Benjamin A. Garcia[3] | Richard M. Schultz[5] | Marisa S. Bartolomei[2,4]

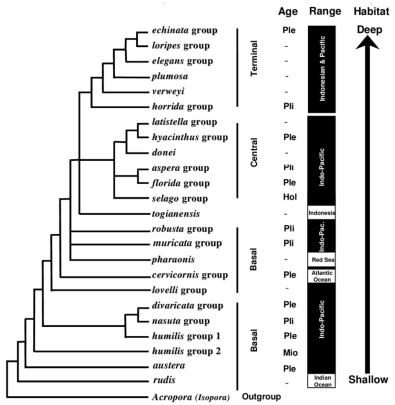
Characterizing the ORAL MICROBIOME as an entry point to understanding the Oral-Systemic connection

- Populations:
  - Pregnant persons
  - Vapers
  - Individuals with cognitive impairment
  - Caregivers
- Specimen matrices
  - Subgingival plaque
  - Soft tissue swabs
  - Saliva
- Additional markers to elucidate the oral microbiome-systemic relationship
  - Salivary metabolomics
  - Immune system mediators (salivary, systemic, CSF)

Animal omics: from coral to humans

Undergraduate

Evolutionary biology of Acropora coral species



Marshall, B and Romano, S. (November 2004) Molecules and morphology may support different hypotheses about the evolutionary history of species of the common reef-building coral, *Acropora*. Poster presentation, Annual Biomedical Research Conference for Minority Students, Dallas, TX.

Marshall, B and Romano S. (February 2004) Are morphological species of *Acropora* coral supported by genetic differences? Oral presentation, NSF HBCU-UP National Conference at North Carolina Agriculture and Technology University in Greensboro, NC.

Graduate

Effects of exercise on epigenetic control of an inflammatory pathway in persons with heart failure

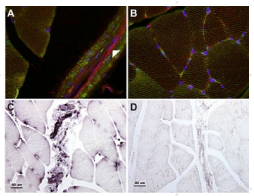
BASIC SCIENCES

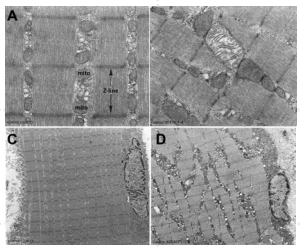
Effects of Exercise on *ASC* Methylation and IL-1 Cytokines in Heart Failure

BRITTANY BUTTS[1], JAVED BUTLER[2], SANDRA B. DUNBAR[3], ELIZABETH CORWIN[3], and REBECCA A. GARY[3]

[1]*Division of Cardiovascular Disease, University of Alabama at Birmingham School of Medicine, Birmingham, AL;* [2]*Division of Cardiology, Stony Brook University, Stony Brook, NY; and* [3]*Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA*

(No omics research in postdoc)
I did do cool work with tissues, pericardial fluid, and other fun stuff.





Faculty

Metabolomic Pathways to Fatigue, Depression, Anxiety, and Dyspnea in Black Adults with Heart Failure and Hypertension

Specific Aim 1: Using high resolution metabolomics **a)** examine the associations among the circulating metabolites and metabolic profiles with the severity of each of the symptoms of fatigue, depression, or anxiety, and **b)** compare the circulating metabolites and metabolic pathways that associate with symptom severity in participants with **HF** versus participants with that **HF *plus* HTN**

Specific Aim 2: Identify the relationships among demographic, clinical, psychosocial and behavioral covariates (e.g., sex as a biological variable, body mass index, stress, SES, diet, smoking, medications, comorbidities, disease severity), metabolites and metabolic pathways, severity levels of symptoms of fatigue, depression, or anxiety, symptom synergy and heath related quality of life

Exploratory Aim: Explore the contribution of the gut microbiome (dominant species, ratios of species) and microbiome-associated metabolites and metabolic pathways as potential covariates associated with self-report of severity of symptoms of fatigue, depression, and anxiety

Microbiome in nursing science

Precision Health

- How does the gut microbiome change in disease states such as colorectal cancer, Alzheimer's disease, frailty and aging etc.?
- What is the relationship between human microbiome and cancer risk?
- What is the relationship between gut microbiome and metabolic diseases?

Mechanism(s) of Symptoms

- What is the relationship between changes in the gut microbiome and depression in the elderly?
- What is the role of the gut-brain axis in psychoneurological symptoms in children with chemotherapy?
- What is the relationship between gut microbiome and maternal stress in pregnancy?

Microbiome in nursing science

Nursing-based Practice/Interventions

- How does oral care impact the oral microbiome in patients who are intubated over time and its impact on lung diseases?
- How does therapeutic dogs influence children's skin microbiome?
- Does administration of pre-/probiotics alleviate psychological conditions (e.g., depression and anxiety) in certain populations?
- How does the microbiome change in neonates and young children? How do microbiome changes affect disease in this population?

Big Data

- Develop methods and tools to mine microbiome data?
- Integrate microbiome data to understand mechanism(s) of symptoms, patient outcomes et al?

Microbiome in nursing science

Biomarker Discovery

- Are there microbial biomarkers that can be sampled from the oral microbiome that predict disease? (e.g., inflammatory bowel disease)?
- Are specific microbial strains as biomarkers of cognitive impairments in dementia?

Health Disparities

- What are the differences in vaginal microbiome and symptoms in African American women with gynecologic cancers vs healthy controls?
- What are the impacts of maternal stress on the gut-brain axis in African American infants?
- What are the relationships between microbiome, environment and neurodevelopmental delay in African Americans infants?

How to Do Omics Without a Basic Science Background

Laura P. Kimble, PhD, RN, FNP-C, FAHA, FAAN

Clinical Professor and Associate Dean for Academic Operations

School of Nursing Emory University

How Did I End Up Doing Omics Research?

- Supplement to the P30 Center Funded to Engage in Research Training
- “Metabolites and metabolic pathways associated with symptoms among African Americans with systemic lupus erythematosus and hypertension”
- Implications:
  - Systems Biology/Biochemistry
  - Metabolomics (Theory & Methods)
  - Rheumatology (Systemic Lupus Erythematosus)
  - Immunology (Autoimmunity)

Research Supplements to Promote Re-entry and Re-integration into Health-Related Research Careers

The notice of special interest (NOSI) titled *Research Supplements to Promote Re-Entry and Re-integration into Health-Related Research Careers (NOT-OD-21-134)* announced administrative supplements to be given to existing NIH research grants to support full- or part-time research by women or men returning to the scientific workforce. The supplements are designed to bring scientists' existing research skills and knowledge up to date so that by the end of the supplement period, they will be prepared to apply for a fellowship (F), a career development (K) award, a research grant (R), or another type of independent research support.

The **Re-entry Supplements Program** provides mentored research training opportunities for a minimum of 1 year to scientists who have had at least 6 months of interruption in their careers for family responsibilities or other qualifying circumstances so they can re-enter active research careers. Most candidates for the re-entry supplements will have a doctoral degree or an equivalent degree; however, some awarding NIH Institutes, Centers, and Offices (ICOs) may allow predoctoral students, including those enrolled in dual-degree programs, to apply.

The **Re-integration Program** addresses the critical need of scientists who have been adversely affected by unsafe or discriminatory environments resulting from unlawful harassment to rapidly transition into new research environments that are safe and supportive. Predoctoral and postdoctoral students are eligible to apply for re-integration supplements to allow them to transition to safe, supportive research environments and complete their graduate degrees.

HOW TO APPLY

Systemic Lupus Erythematosus

- Systemic lupus erythematosus (SLE) chronic, life-threatening, autoimmune disease with no known cure-affects 300,000 in US (Agarwal et al. , 2016)
- SLE more prevalent in minority women of childbearing age (15 to 44 years) (Williams et al., 2016);
  - 90% SLE patients are women, highest prevalence among Black women 1:537
- Individuals with SLE lose 13 billion annually because of decreased work productivity- inability to work full-time or unable to work at all (Gordon et al, 2013)

SYSTEMIC LUPUS ERYTHEMATOSUS

LOSS OF TOLERANCE OF SELF

PREDISPOSING FACTORS

GENES

High Hazard Ratios (≥6);

Deficiencies of C1q,C2,C4 (rare)
TREX1 mutations affecting DNA degradation (rare)

Affecting Ag presentation or persistence, e.g., phagocytosis of immune complexes

HLA-DRB1 (*1501,*0301), DR3, DQA2
CR2, FCGR2A/B

Enhance Innate Immunity, including production of IFNs

TNFAIP3, IRF5/TNPO3, IRF7/PHRF1, ITGAM, ICAMs

Alter Adaptive Immunity B and/or T Cell Signaling

BANK1, STAT4, MSHS, IZKF3, TCF7

GENES FOR LUPUS NEPHRITIS

HLA-DR3, STAT4, APOL1 (African Americans), FCGR3A, ITGAM, IRF5, IRF7, TNFSF4 (Ox40L), DNAse1

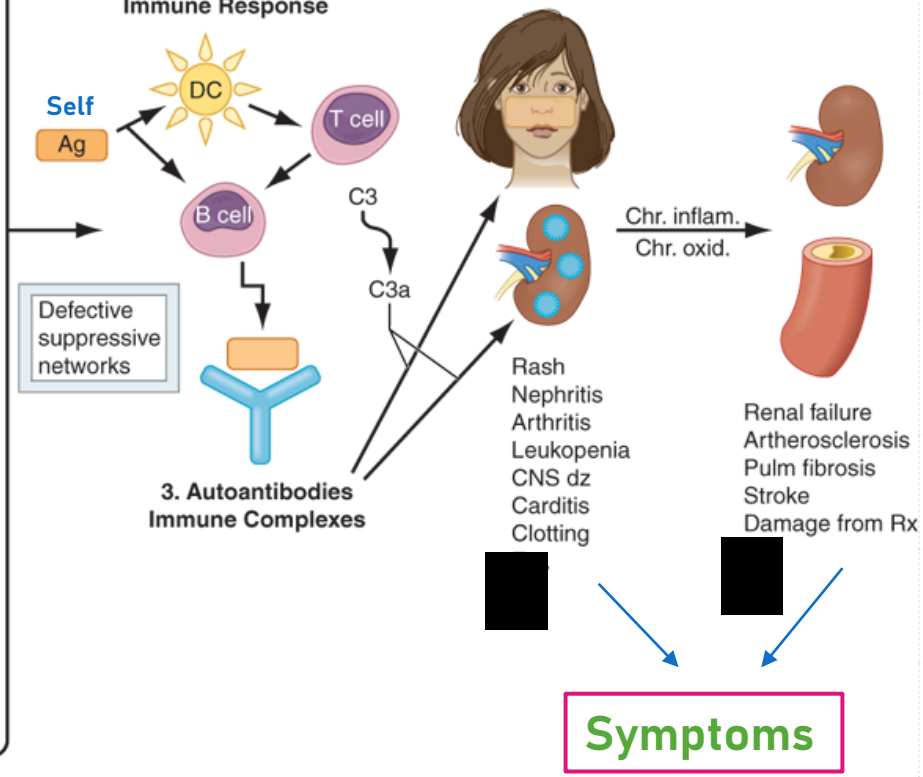
ENVIRONMENT/MICROENVIRONMENT

Ultraviolet Light, Smoking, Crystalline Silica, ?EBV infection
Femaleness

EPIGENETICS

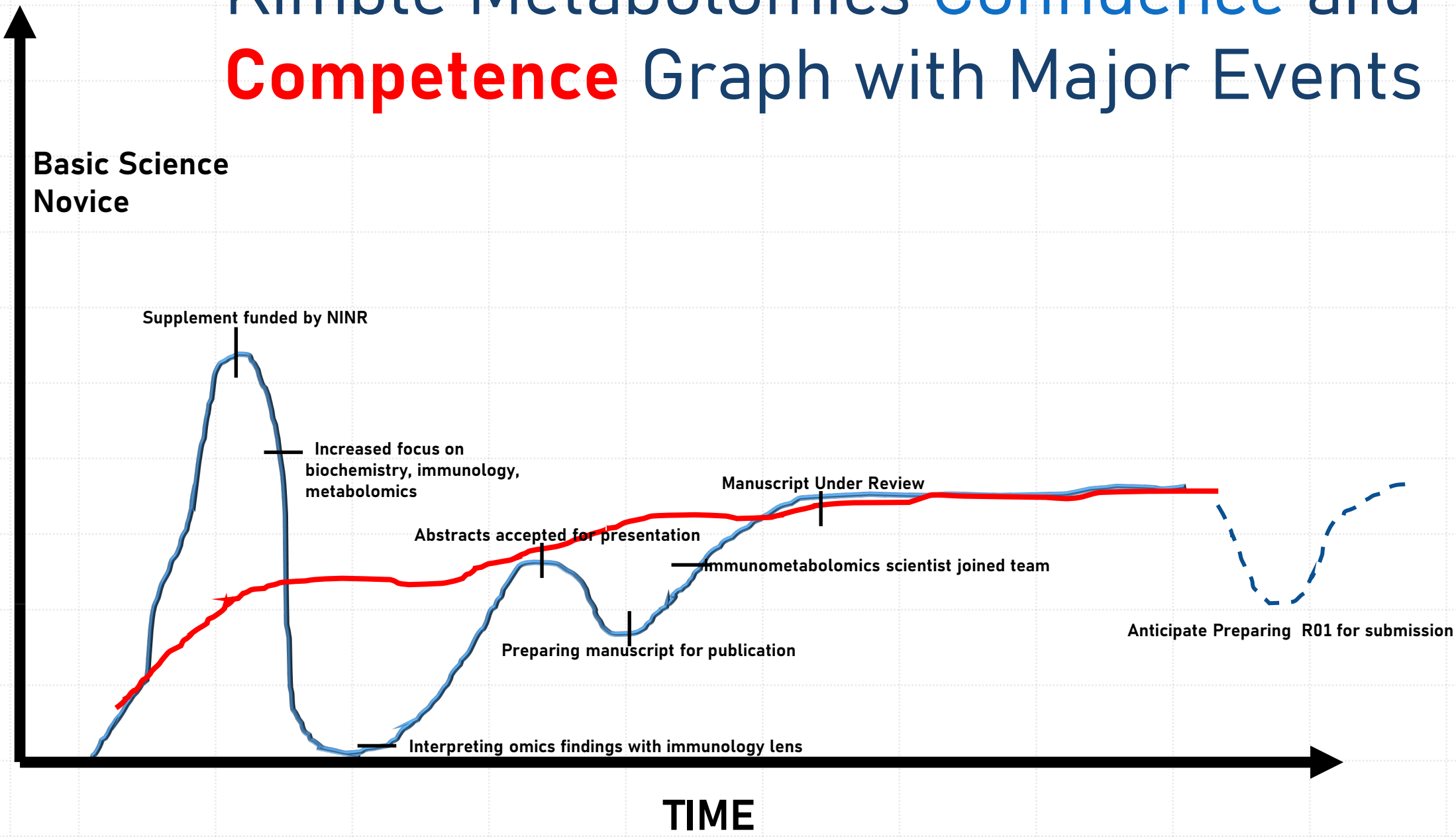
Hypomethylation of DNA: In CD4+T, B and monocytes
Some affect IFN production
Histone modifications: Some increase expression of predisposing genes and/or IFN production
MicroRNA affecting gene expression

Mir-21, -146A, -155, -569, -30A, Let-7a



Hahn, 2018

Kimble Metabolomics Confidence and **Competence** Graph with Major Events



Key Points:

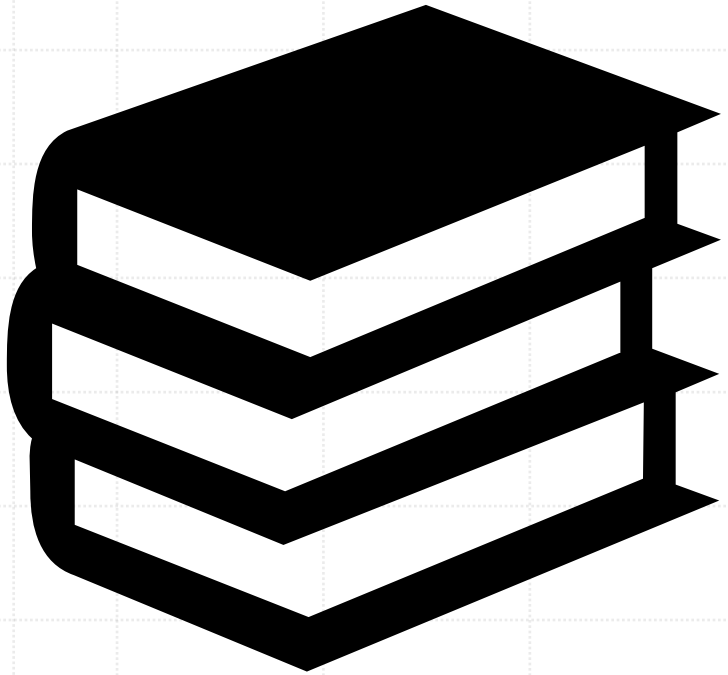
Leverage your existing knowledge and strengths

Participate in high quality/high impact learning as feasible

Integrate scholarship into omics learning activities

Disseminate omics work strategically

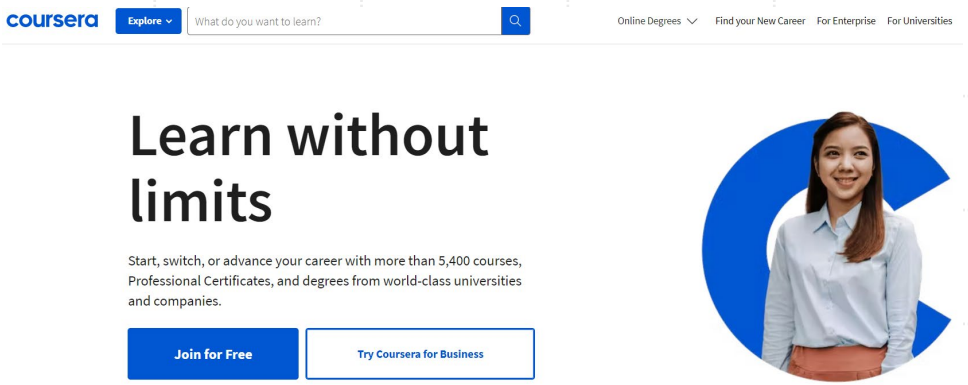
Build a strong team

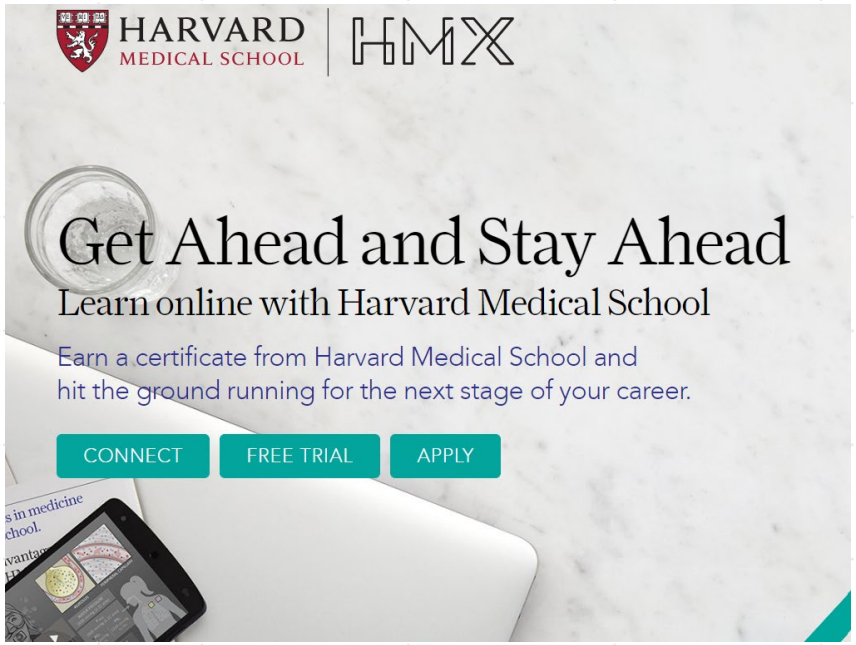


Leverage Your Existing Knowledge and Strengths:

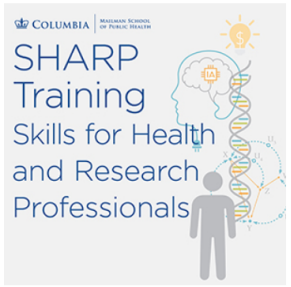
- PhD from University of Rochester with cognate area in social psychology
- Very strong training and experience in biostatistics, research design, and statistical analysis (SPSS)
- Track record with extramural grant funding from NIH/NINR and American Heart Association
- Track record as symptom scientist in cardiovascular disease
- Highly motivated for pilot and training to succeed

Participate in High Quality/High Impact Structured Learning:





SHARP Training: Skills for Health And Research Professionals



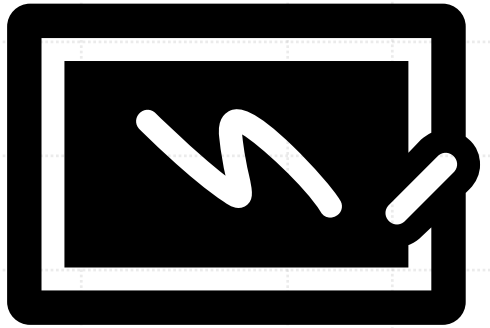
Registration is open for summer trainings! Check out this year's topics below.

Our SHARP Program consists of short, intensive boot camps led by field experts to teach in-demand research skills and methods to investigators at all career levels and from any organization. Check out the official flyer with all 2023 topics to share with your colleagues.

SUBSCRIBE FOR UPDATES

Join the Columbia SHARP email list to hear about program updates! For specific training updates, visit that training page below.

Do you have recommendations for future trainings? Share your suggestions.



Participate in High Quality/High Impact Structured Learning:

HMX Fundamentals

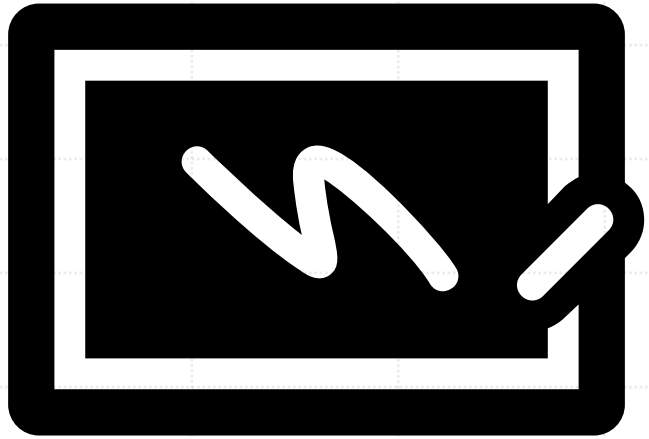
Immunology

Get an in-depth look at how the body fights disease – and how new therapies can help.

Microbial life forms are an ever-present, extremely dangerous threat to our survival, against which the immune system must constantly defend.

In HMX Fundamentals Immunology, you'll learn about the processes that enable our immune systems to respond to evolving threats, and learn about new, immunology-based disease treatments.

APPLY NOW FREE TRIAL



HMX Fundamentals

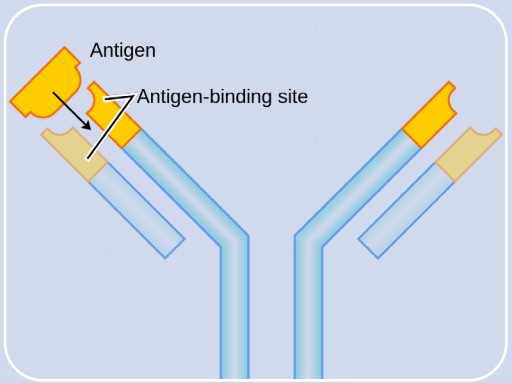
Biochemistry

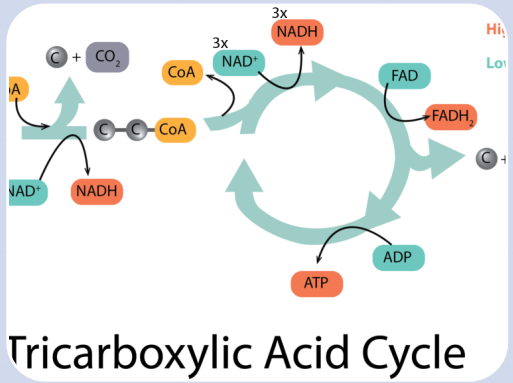
Learn why human health is dependent on chemistry, and what that means for clinical care.

Understanding biochemistry is an excellent foundation for learning all of biology, but it can be difficult to make sense of the complexity of biochemical systems.

In HMX Fundamentals Biochemistry, you'll learn about the principles governing the interactions of individual molecules, and how those same principles apply at the scale of cells and organisms. Along the way, you'll see how biochemistry intersects with human disease and clinical care.

APPLY NOW FREE TRIAL





Tricarboxylic Acid Cycle


Exposome Boot Camp: Measuri
osures on an Omic Scale

Registration is Open! Join us for t
next Exposome Boot Camp on Ju
21, 2023.

The Exposome Boot Camp is a two-day intensiv
camp of seminars and hands-on analytical sessic
provide an overview of concepts, techniques, ar
analysis methods used in studies of the exposor
Register here.

HMX Immunology

10 weeks online

$500

HMX Biochemistry

10 weeks online

$500

Columbia SHARP

Exposome Bootcamp

2 day intensive

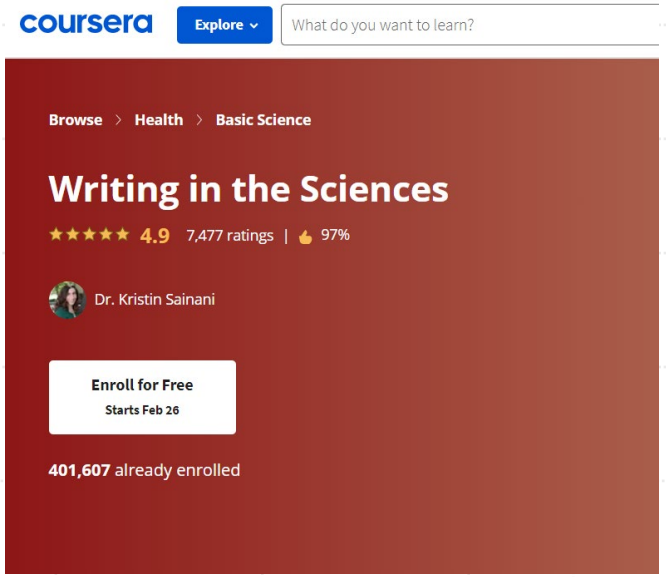
$1,375

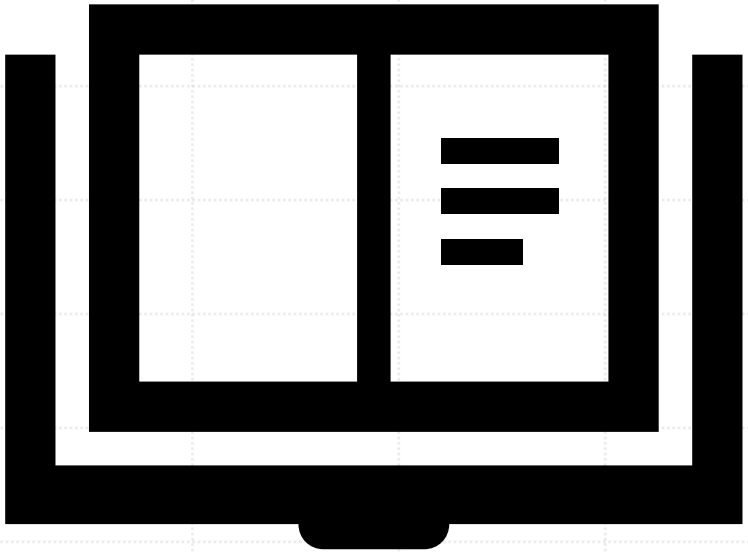
Websites:

https://onlinelearning.hms.harvard.edu/hmx/

https://www.publichealth.columbia.edu/research/precision-prevention/sharp-training-skills-health-and-research-professionals

https://www.coursera.o





Integrate Scholarship into Omics Learning Activities:

- Needed rapid understanding of metabolomics studies/methods
- Understanding state of the science of omics in nursing important
- Leveraged expertise in the School for a mutually beneficial scholarship effort
- Involved mentees in learning activities

Biological Research For Nursing
Volume 22, Issue 4, October 2020, Pages 436-448

https://doi-org.proxy.library.emory.edu/10.1177/1099800420940041

Special Section Article

Metabolomics Research Conducted by Nurse Scientists: A Systematic Scoping Review

Laura P. Kimble, PhD, RN, FNP-C, FAHA, FAAN [1], **Sharon Leslie, MSLS, AHIP** [2], **and Nicole Carlson, CNM, PhD, RN, FACNM** [1]

Abstract

Metabolomics, one of the newest omics, allows for investigation of holistic responses of living systems to myriad biological, behavioral, and environmental factors. Researcher use metabolomics to examine the underlying mechanisms of clinically observed phenotypes. However, these methods are complex, potentially impeding their uptake by scientists. In this scoping review, we summarize literature illustrating nurse scientists' use of metabolomics. Using electronic search methods, we identified metabolomics investigations conducted by nurse scientists and published in English-language journals between 1990 and November 2019. Of the studies included in the review ($N = 30$), 9 (30%) listed first and/or senior authors that were nurses. Studies were conducted predominantly in the United States and focused on a wide array of clinical conditions across the life span. The upward trend we note in the use

Body Image, Depression Symptoms, and Health-Related Quality of Life in Black Women With Systemic Lupus Erythematosus

Madeline M. Jones & Laura P. Kimble

ABSTRACT

Objective: To examine relationships among body image, depression symptoms, and quality of life in Black women with systemic lupus erythematosus (SLE).

Design: Descriptive, correlational design.

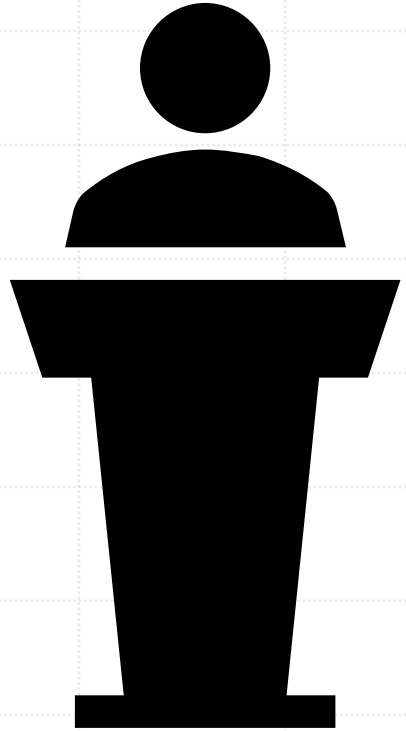
Setting/Sample: Using social media advertising, we recruited Black women with self-reported SLE to complete a web-based survey.

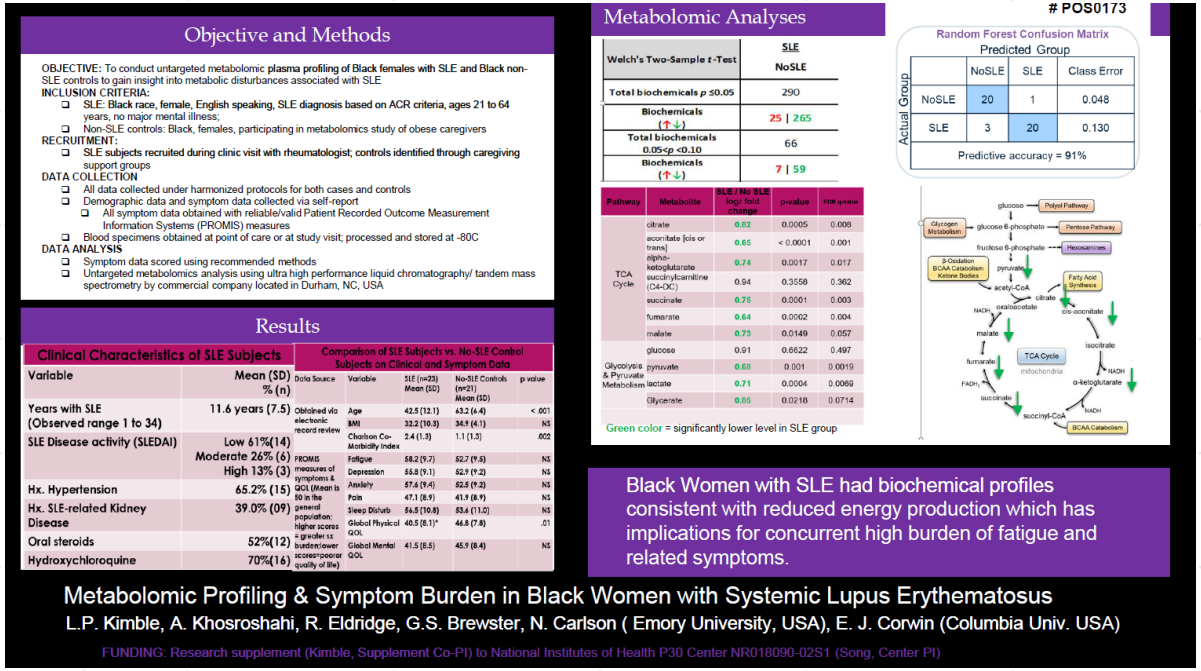
greater depression symptoms than reported by the general population. Greater body image disturbance was significantly associated with greater depression symptoms and poorer quality of life in the area of role disruption.

Conclusion: Depression and body image disturbance among Black women with SLE should be routinely assessed and

Disseminate Omics Findings Strategically:

- Consider when submitting whether presenting to basic scientists vs. clinical scientists
- Submit to clinical/translational science venues when possible





POS0173

- Submitted in basic and translational research category
- Challenges in discussing work, but received great recommendation for expert to join team

Home › Annual Meeting › Abstracts › Submission

Registration
Program
Abstracts
Submission
Presentation
Embargo Policies
Permissions and Reprints

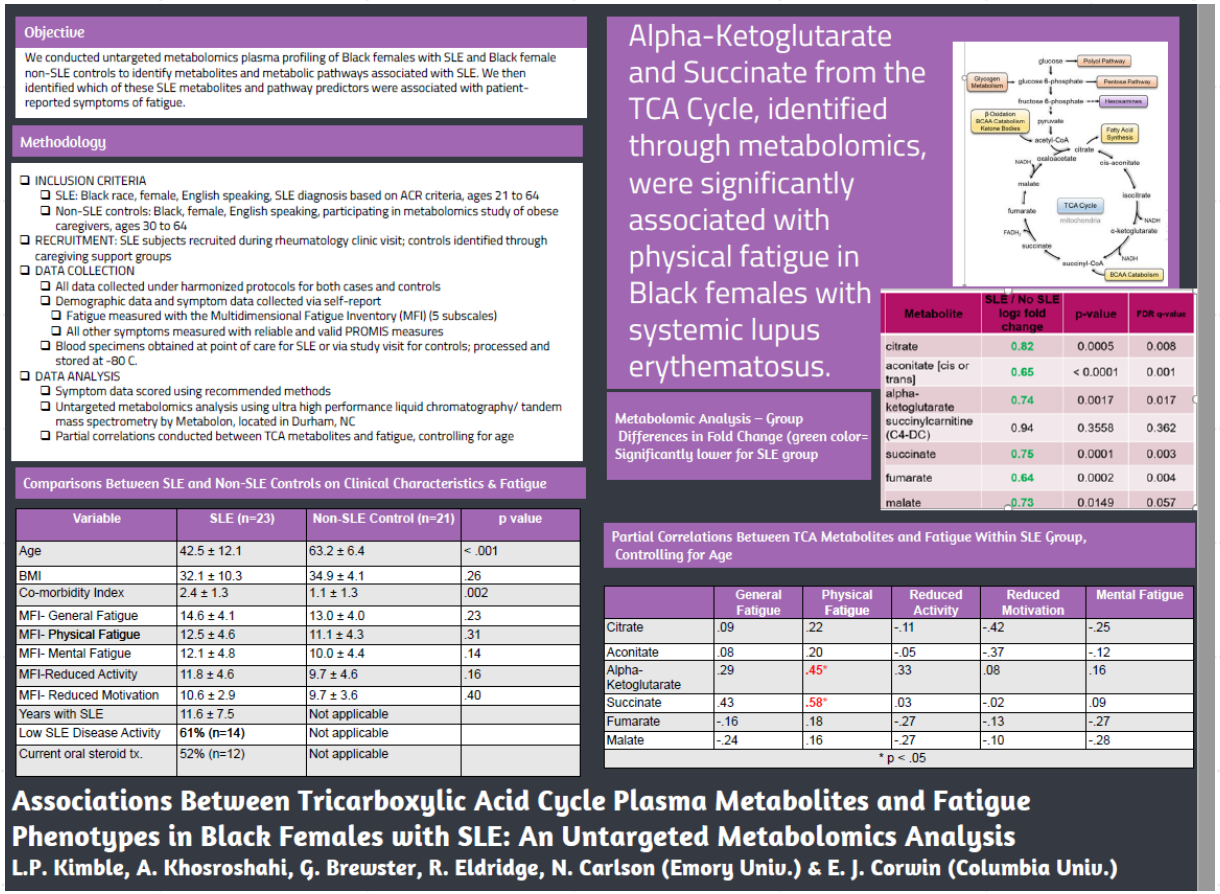
Abstract Submission

The American College of Rheumatology and Association of Rheumatology Professionals invite you to submit an abstract to ACR Convergence and take advantage of the opportunity to have your work peer reviewed by experts in the field.

Abstracts News

Abstracts Available

- Submitted to clinical research category
- Less interest in abstract (few individuals attended presentation), but potentially easier to explain findings
- More appropriate venue for level of omics knowledge



Objective

We conducted untargeted metabolomics plasma profiling of Black females with SLE and Black female non-SLE controls to identify metabolites and metabolic pathways associated with SLE. We then identified which of these SLE metabolites and pathway predictors were associated with patient-reported symptoms of fatigue.

Methodology

- INCLUSION CRITERIA
  - SLE: Black race, female, English speaking, SLE diagnosis based on ACR criteria, ages 21 to 64
  - Non-SLE controls: Black, female, English speaking, participating in metabolomics study of obese caregivers, ages 30 to 64
- RECRUITMENT: SLE subjects recruited during rheumatology clinic visit; controls identified through caregiving support groups
- DATA COLLECTION
  - All data collected under harmonized protocols for both cases and controls
  - Demographic data and symptom data collected via self-report
    - Fatigue measured with the Multidimensional Fatigue Inventory (MFI) (5 subscales)
    - All other symptoms measured with reliable and valid PROMIS measures
  - Blood specimens obtained at point of care for SLE or via study visit for controls; processed and stored at -80 C.
- DATA ANALYSIS
  - Symptom data scored using recommended methods
  - Untargeted metabolomics analysis using ultra high performance liquid chromatography/ tandem mass spectrometry by Metabolon, located in Durham, NC
  - Partial correlations conducted between TCA metabolites and fatigue, controlling for age

Comparisons Between SLE and Non-SLE Controls on Clinical Characteristics & Fatigue

Variable	SLE (n=23)	Non-SLE Control (n=21)	p value
Age	42.5 ± 12.1	63.2 ± 6.4	< .001
BMI	32.1 ± 10.3	34.9 ± 4.1	.26
Co-morbidity Index	2.4 ± 1.3	1.1 ± 1.3	.002
MFI- General Fatigue	14.6 ± 4.1	13.0 ± 4.0	.23
MFI- Physical Fatigue	12.5 ± 4.6	11.1 ± 4.3	.31
MFI- Mental Fatigue	12.1 ± 4.8	10.0 ± 4.4	.14
MFI-Reduced Activity	11.8 ± 4.6	9.7 ± 4.6	.16
MFI- Reduced Motivation	10.6 ± 2.9	9.7 ± 3.6	.40
Years with SLE	11.6 ± 7.5	Not applicable	
Low SLE Disease Activity	**61% (n=14)**	Not applicable	
Current oral steroid tx.	52% (n=12)	Not applicable	

Alpha-Ketoglutarate and Succinate from the TCA Cycle, identified through metabolomics, were significantly associated with physical fatigue in Black females with systemic lupus erythematosus.

Metabolomic Analysis – Group Differences in Fold Change (green color= Significantly lower for SLE group

Metabolite	SLE / No SLE log2 fold change	p-value	FDR q-value
citrate	0.82	0.0005	0.008
aconitate [cis or trans]	0.65	< 0.0001	0.001
alpha-ketoglutarate	0.74	0.0017	0.017
succinylcarnitine (C4-DC)	0.94	0.3558	0.362
succinate	0.75	0.0001	0.003
fumarate	0.64	0.0002	0.004
malate	0.73	0.0149	0.057

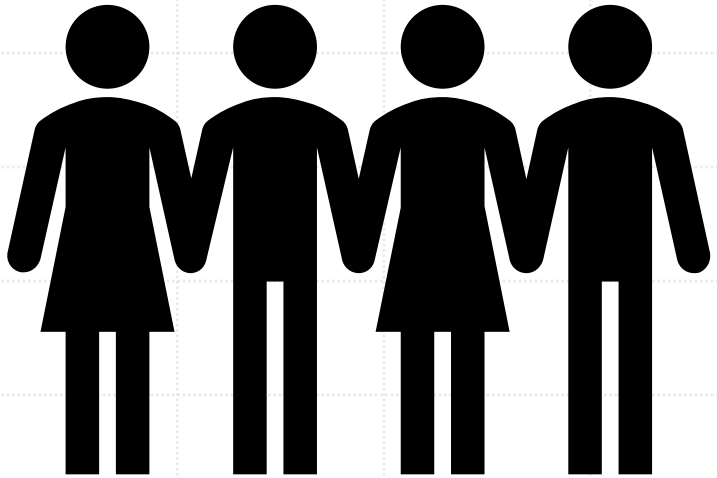
Partial Correlations Between TCA Metabolites and Fatigue Within SLE Group, Controlling for Age

	General Fatigue	Physical Fatigue	Reduced Activity	Reduced Motivation	Mental Fatigue
Citrate	.09	.22	-.11	-.42	-.25
Aconitate	.08	.20	-.05	-.37	-.12
Alpha-Ketoglutarate	.29	.45*	.33	.08	.16
Succinate	.43	.58*	.03	-.02	.09
Fumarate	-.16	.18	-.27	-.13	-.27
Malate	-.24	.16	-.27	-.10	-.28

* p < .05

Associations Between Tricarboxylic Acid Cycle Plasma Metabolites and Fatigue Phenotypes in Black Females with SLE: An Untargeted Metabolomics Analysis

L.P. Kimble, A. Khosroshahi, G. Brewster, R. Eldridge, N. Carlson (Emory Univ.) & E. J. Corwin (Columbia Univ.)



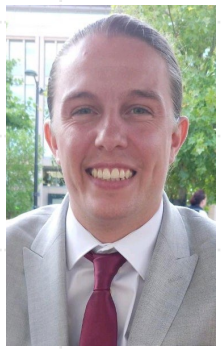
Build a Strong Team:

- Initial team very strong and committed
- Added additional team members to support work and also promote scholarship of junior faculty
- Addition of scientist with expertise in immunometabolism to team led to higher level of interpretation and insight.

Team Members:

Arezou Khosroshahi, MD
Emory School of Medicine
Dept. of Rheumatology

Elizabeth Corwin, PhD, RN
Columbia University
College of Nursing



Dylan Ryan, PhD
Postdoctoral Researcher
University of Cambridge

Glenna Brewster, PhD, RN
Emory University
School of Nursing

Nicole Carlson, PhD, CNM
Emory University
School of Nursing

Ronald Eldridge, PhD, MPH
Emory University
School of Nursing

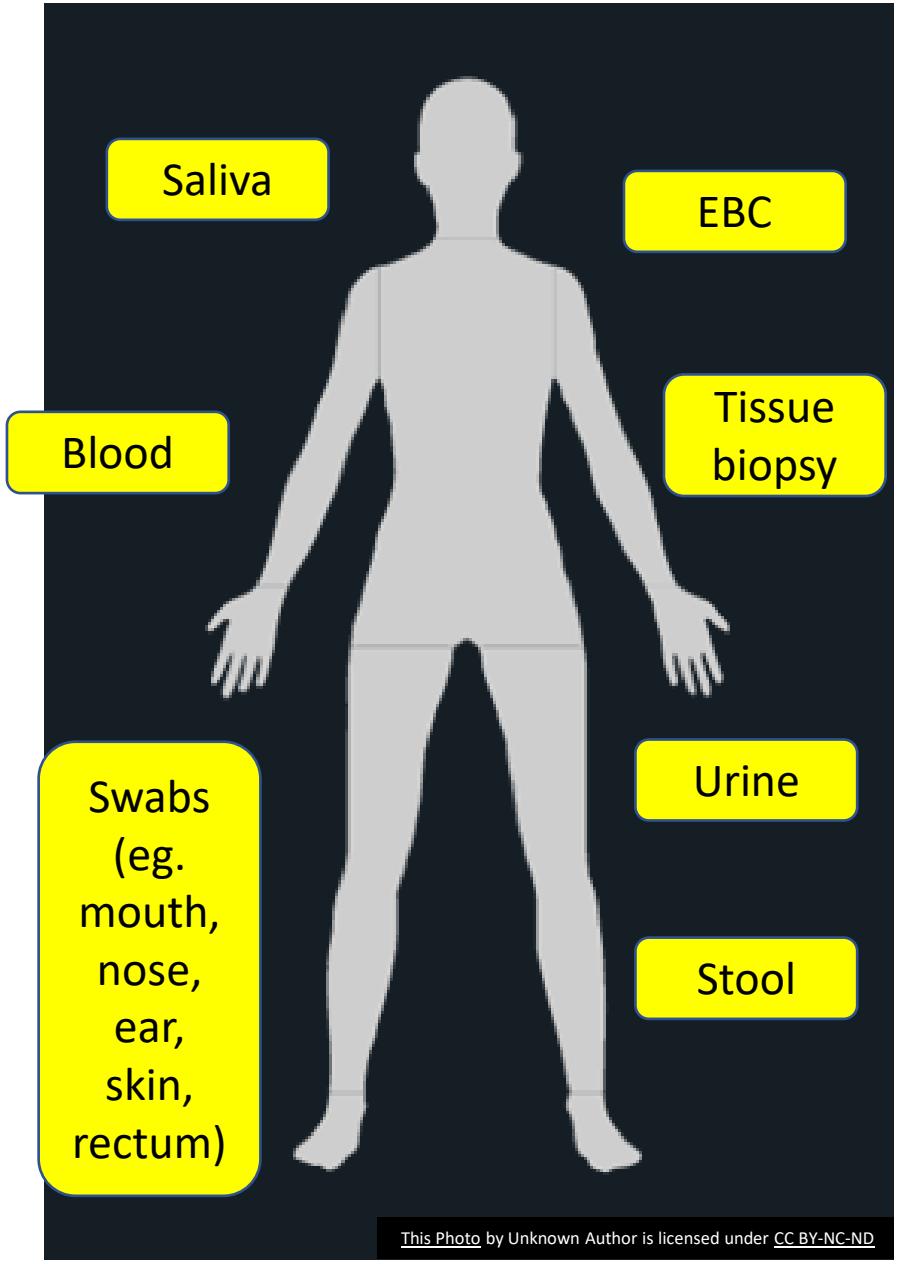
Conclusion

- With strong motivation and good team, can conduct research using omics methods even without a basic science background
- Need to rely on team science to assure research is at a high, robust level
- Work in progress, so need to consistently build knowledge
- Stay tuned– major test will be with R application

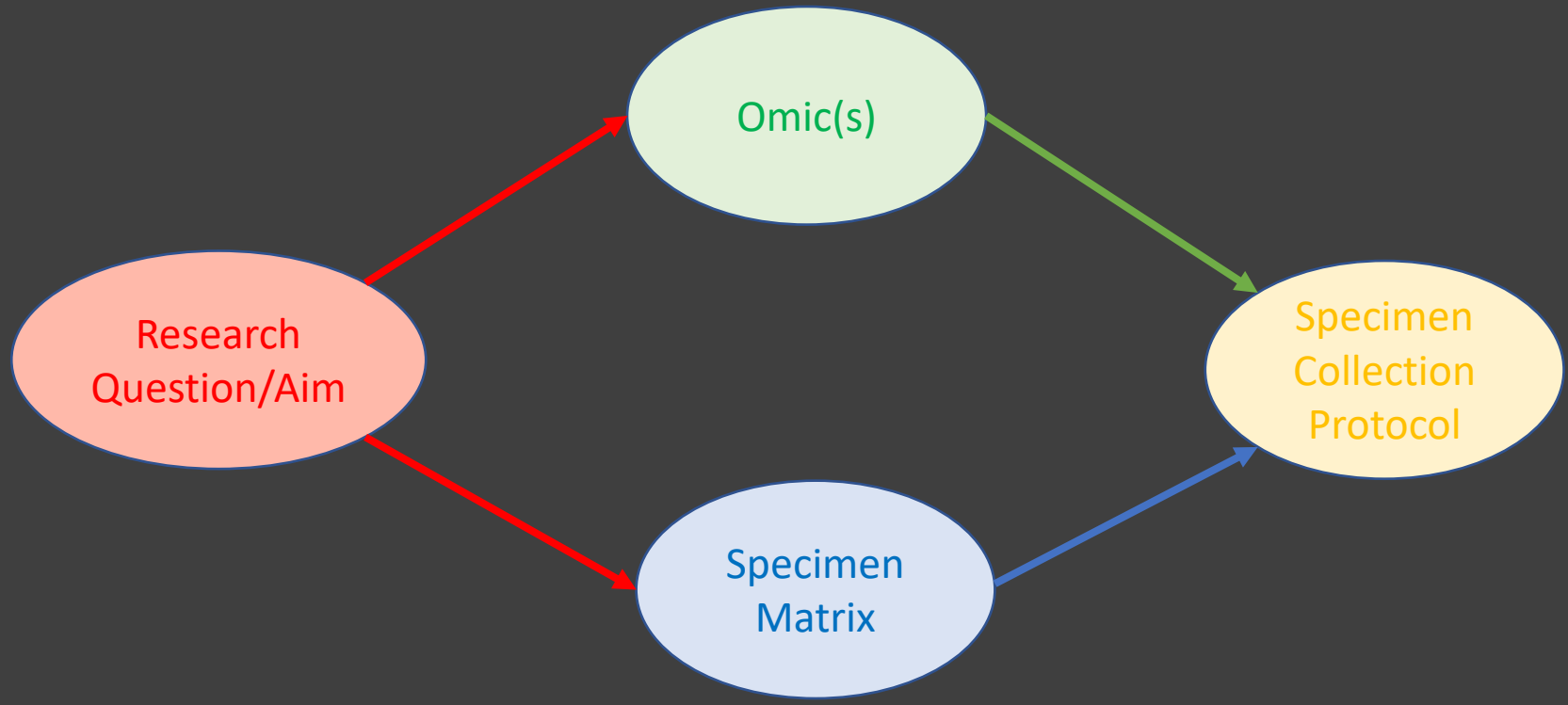
Acknowledgement of Research Funding

- Metabolites and metabolic pathways associated with symptoms among African Americans with systemic lupus erythematosus and hypertension (***L. Kimble****,Co- PI with Corwin,PI*). Research career re-entry supplement to Center for the Study of Symptom Science, Metabolomics, and Multiple Chronic Conditions (Corwin, PI). National Institute of Nursing Research. Total costs: $403,878. Funding period: 6/1/19-5/31/21. No cost extension through 5/31/2022.

Sample Collection in Omics Research



Primary Considerations



JOURNAL OF NEUROTRAUMA 33:1576–1585 (September 1, 2016)

DOI: 10.1089/neu.2015.4191

Original Articles

Genome-Wide Changes in Peripheral Gene Expression following Sports-Related Concussion

Kian Merchant-Borna,[1,*] Hyunhwa Lee,[2,*] Dan Wang,[3] Viktoria Bogner,[4] Martijn van Griensven,[5] Jessica Gill,[3] and Jeffrey J. Bazarian[1]

Abstract

We conducted a prospective study to identify genome-wide changes in peripheral gene expression before and after sports-related concussion (SRC). A total of 253 collegiate contact athletes underwent collection of peripheral blood mononuclear cells (PBMCs) before the sport season (baseline). Sixteen athletes who subsequently developed an SRC, along with 16 non-concussed teammate controls, underwent repeat collection of PBMCs within 6 h of injury (acutely). Concussed athletes

Biological Research For Nursing
OnlineFirst, January 13, 2023

https://doi-org.proxy.library.emory.edu/10.1177/10998004221149959

Report of Original Research

Saliva and Exhaled Breath Condensate Correlate With Serum in 4-12-Year-Olds Exposed to Secondhand Electronic Cigarette Vapors: A Pilot Study

Jeannie Rodriguez, PhD, RN, APRN [1], Donghai Liang, PhD, MPH [2], Rachel Tchen, MPH [3], and Irene Yang, PhD, RN [1]

Abstract

Electronic cigarette use is highest among adults of child-bearing age. Many parents that use electronic cigarettes believe that secondhand exposure of electronic cigarette vapors for their children is not dangerous and is less harmful than secondhand exposure to traditional cigarette smoke. These beliefs may prompt excessive secondhand exposure to electronic cigarette vapors for their children. Little research has been done to document exposure in children. The traditional biological method of exposure detection is through a blood draw, which is difficult and undesirable in children. The purpose of this study was to assess the feasibility of using saliva and exhaled breath condensate as non-invasive biomatrices for detecting secondhand electronic cigarette vapor exposure in children. In this cross-sectionally designed study, we recruited 22 children exposed to electronic cigarette vapors and 26 non-exposed between the ages of 4–12 years. We compared metabolic features across three biomatrices, blood, saliva, and exhaled breath condensate. We noted moderate to strong pairwise, sample-specific, and feature-specific adjusted correlations. Annotated features associated with direct and secondhand electronic cigarette exposure were noted. These results demonstrate that less invasive biomatrices may be used to detect features associated with secondhand electronic cigarette vapor exposure in children.

Skin microbiome before development of atopic dermatitis: Early colonization with commensal staphylococci at 2 months is associated with a lower risk of atopic dermatitis at 1 year

Elizabeth A. Kennedy, BS,[a] Jennifer Connolly, MSc,[b] Jonathan O'B. Hourihane, DM,[b] Padraic G. Fallon, PhD,[c,d] W. H. Irwin McLean, DSc, FRS,[e] Deirdre Murray, PhD,[b] Jay-Hyun Jo, PhD,[a] Julia A. Segre, PhD,[f] Heidi H. Kong, MD, MHSc,[a]* and Alan D. Irvine, MD, DSc[c,d,g]* *Bethesda, Md, Cork and Dublin, Ireland, and Dundee, United Kingdom*

Background: Disease flares of established atopic dermatitis (AD) are generally associated with a low-diversity skin microbiota and *Staphylococcus aureus* dominance. The temporal transition of the skin microbiome between early infancy and the dysbiosis of established AD is unknown.
Methods: We randomly selected 50 children from the Cork Babies After SCOPE: Evaluating the Longitudinal Impact Using Neurological and Nutritional Endpoints (BASELINE) longitudinal birth cohort for microbiome sampling at 3 points in the first 6 months of life at 4 skin sites relevant to AD: the antecubital and popliteal fossae, nasal tip, and cheek. We identified 10 infants with AD and compared them with 10 randomly selected control infants with no AD. We performed bacterial 16S ribosomal RNA sequencing and analysis directly from clinical samples.

Results: Bacterial community structures and diversity shifted over time, suggesting that age strongly affects the skin microbiome in infants. Unlike established AD, these patients with infantile AD did not have noticeably dysbiotic communities before or with disease and were not colonized by *S aureus*. In comparing patients and control subjects, infants who had affected skin at month 12 had statistically significant differences in bacterial communities on the antecubital fossa at month 2 compared with infants who were unaffected at month 12. In particular, commensal staphylococci were significantly less abundant in infants affected at month 12, suggesting that this genus might protect against the later development of AD.
Conclusions: This study suggests that 12-month-old infants with AD were not colonized with *S aureus* before having AD. Additional studies are needed to confirm whether colonization with commensal staphylococci modulates skin immunity and attenuates development of AD. (J Allergy Clin Immunol 2017;139:166-72.)

From [a]the Dermatology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda; [b]Paediatrics and Child Health, University College, Cork, and the Irish Centre for Fetal and Neonatal Translational (INFANT)

Further considerations about specimen matrices

Proximity to variable of interest

Received: 25 August 2021 | Revised: 21 February 2022 | Accepted: 8 March 2022
DOI: 10.1111/odi.14186

ORIGINAL ARTICLE

ORAL DISEASES WILEY

Oral microbiome of electronic cigarette users: A cross-sectiona exploration

Irene Yang[1] | Jeannie Rodriguez[1] | Christa Young Wright[2] | Yi-Juan Hu[3]

[1]Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, Georgia, USA
[2]Chemical Insights Research Institute of Underwriters Laboratories, Marietta, Georgia, USA
[3]Rollins School of Public Health, Emory University, Atlanta, Georgia, USA

Correspondence
Irene Yang, Emory University, 1520 Clifton Road NE Room 424, Atlanta, GA 30322, USA.
Email: irene.yang@emory.edu

Abstract

Objective: Electronic cigarettes have increased in popularity globally. Vaping may be associated with oral symptoms and pathologies including dental and periodontal damage, both of which have an underlying microbial etiology. The primary aim of this pilot study, therefore, was to compare the oral microbiome of vapers and non-vapers.

Subjects and Methods: This secondary data analysis had a cross-sectional comparative descriptive design and included data for 36 adults. Bacterial 16S rRNA genes were extracted and amplified from soft tissue oral swab specimens and taxonomically classified using the Human Oral Microbiome Database.

Frontiers in Cellular and Infection Microbiology

ORIGINAL RESEAF
published: 11 May 2
doi: 10.3389/fcimb.2022.873

Subgingival Microbiome in Pregnancy and a Potential Relationship to Early Term Birth

Irene Yang[1], Henry Claussen[2], Robert Adam Arthur[2], Vicki Stover Hertzberg[1], Nicolaas Geurs[3], Elizabeth J. Corwin[4] and Anne L. Dunlop[5]*

[1] Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA, United States, [2] Emory Integrated Computatio Core, Emory University, Atlanta, GA, United States, [3] Department of Periodontology, School of Dentistry, University of Alabama at Birmingham, Birmingham, AL, United States, [4] School of Nursing, Columbia University, New York, NY, United States, [5] Department of Gynecology and Obstetrics, School of Medicine, Emory University, Atlanta, GA, United Sta

Proximity versus Accessibility

Article

Biological Research for Nursing
2020, Vol. 22(2) 157-168

DOI: 10.1177/1099800419899730
journals.sagepub.com/home/brn
SAGE

Metabolic Pathways Associated With Term Labor Induction Course in African American Women

Nicole S. Carlson, PhD, CNM[1], Jennifer K. Frediani, PhD, RD, ACSM-CES[1], Elizabeth J. Corwin, PhD, RN[1,2], Anne Dunlop, MD, MPH[1,3,4], and Dean Jones, PhD[5]

Specific Collection Protocol Considerations Relevant for Genomics Research

Blood and saliva most commonly used specimens

Gene expression (mRNA) or epigenetic markers are cell-specific

Storage at -80℃ ASAP is advisable unless processing immediately to avoid DNA/RNA degradation

Szczepek, A. J., Frejo, L., Vona, B., Trpchevska, N., Cederroth, C. R., Caria, H., & Lopez-Escamez, J. A. (2019). Recommendations on collecting and storing samples for genetic studies in hearing and tinnitus research. *Ear and Hearing*, *40*(2), 219.

Specific Collection Protocol Considerations Relevant for Metabolomics Research

- Time of collection
  - Food intake
  - Circadian rhythm
- Aliquoting and storage at -80℃ ASAP
- Blood: plasma, serum, and dried whole blood
- Standardizing collection tubes

Smith, L., Villaret-Cazadamont, J., Claus, S. P., Canlet, C., Guillou, H., Cabaton, N. J., & Ellero-Simatos, S. (2020). Important considerations for sample collection in metabolomics studies with a special focus on applications to liver functions. *Metabolites*, *10*(3), 104.

Specific Collection Protocol Considerations Relevant for Microbiome Research

PREVENTING CONTAMINATION AND BIAS
Explicit instruction for self-collection and storage
Different habitats have different sampling procedures – important to consider collection protocol to maximize bacterial/organism load
-80℃ ASAP unless collected in buffer allowing for long-term stability at ambient temperatures (eg. DNA Genotek or Zymo)
Collecting relevant additional data (diet, medication, hygiene, health history)

Blood

- Genomics, epigenomics, transcriptomics, metabolomics, proteomics
- Venipuncture drawn blood remains the gold standard and is minimally invasive
- Increasing development of microsampling (eg. Tasso+) for easy, painless capillary whole blood collection

Roberts, J. L., Whiley, L., Gray, N., Gay, M., & Lawler, N. G. (2022). Advanced microsamples: Current applications and considerations for mass spectrometry-based metabolic phenotyping pipelines. *Separations*, *9*(7), 175.

Saliva

- Non-invasive and relatively easy collection
- Genomics, epigenomics, transcriptomics, proteomics, metabolomics, microbiome
- Secreted by salivary glands and also contains GCF derived from serum
- Several infectious and non-infectious diseases have identifiable changes in saliva

Cuevas-Córdoba B, Santiago-García J. Saliva: a fluid of study for OMICS. OMICS. 2014 Feb;18(2):87-97. doi: 10.1089/omi.2013.0064. Epub 2014 Jan 3. PMID: 24404837.

Urine

- Non-invasive and usually produced in large quantities
- Multiple omic biomarkers can be detected in urine
  - Gene mutation and gene expression
  - Proteomic
  - Metabolomic
  - DNA methylation
- Urine volume, flow, pH and concentration of metabolites varies greatly between and within individuals. Normalization and dilution likely necessary prior to metabolomics analysis.

Kim J, Kim WT, Kim WJ. Advances in urinary biomarker discovery in urological research. Investig Clin Urol. 2020 Feb;61(Suppl 1):S8-S22. doi: 10.4111/icu.2020.61.S1.S8. Epub 2019 Dec 31. PMID: 32055750; PMCID: PMC7004831.

Tissue

- Gold standard for molecular profiling, but
  - Highly invasive
  - Requires specialized expertise
  - Risk of pain and infection
- Development of microbiopsy tools on the horizon

Lin LL, Prow TW, Raphael AP, Harrold Iii RL, Primiero CA, Ansaldo AB, Soyer HP. Microbiopsy engineered for minimally invasive and suture-free sub-millimetre skin sampling. F1000Res. 2013 May 2;2:120. doi: 10.12688/f1000research.2-120.v2. PMID: 24627782; PMCID: PMC3907159.


Questions?

Analyzing and Presenting Data in Omics and Research

Brittany Butts and Laren Narapareddy

Data Analyses in Omics Research

- How do you analyze omics data?
- Collaborate with a biostatistician or use a biostatistics core!
- Learn through workshops or course

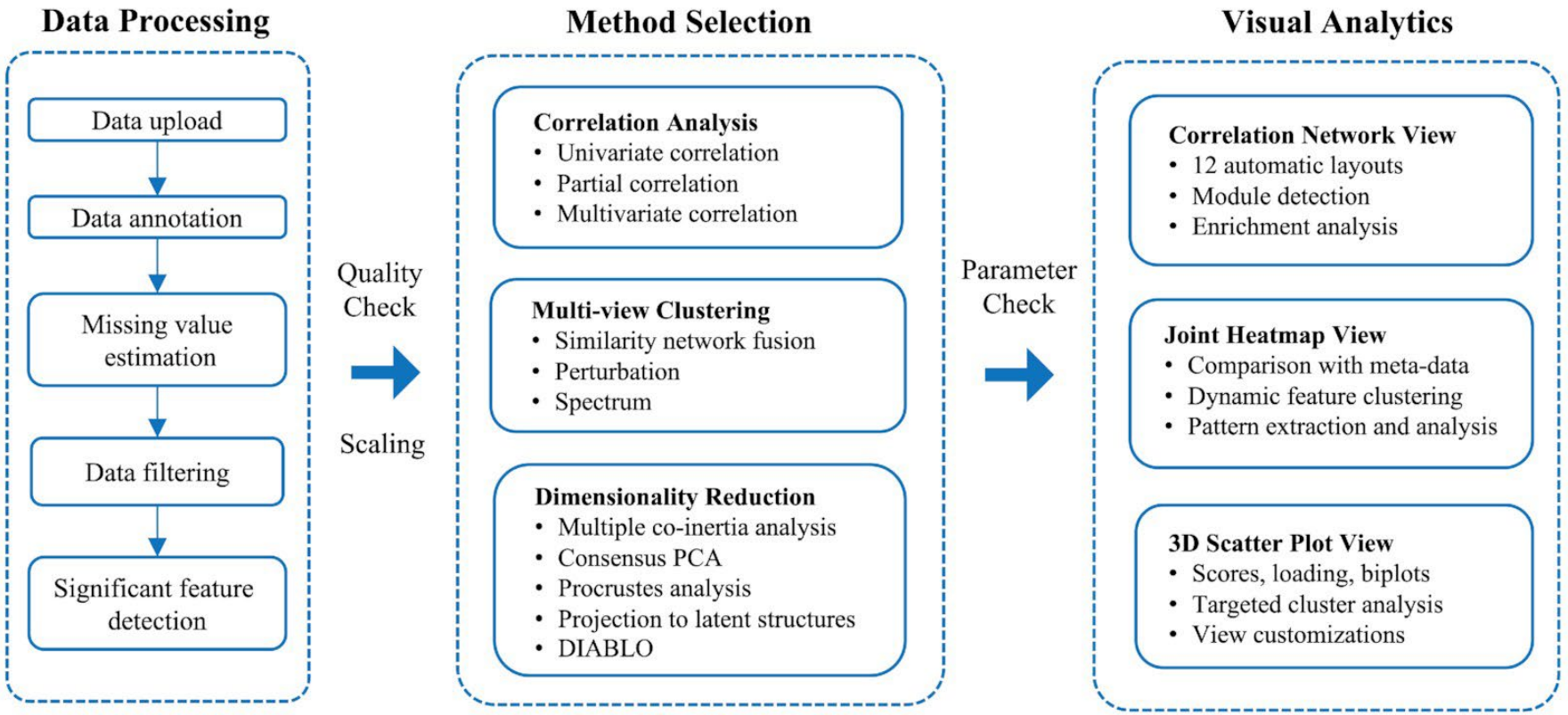
Bioinformatics for Analysis of Data Generated by Next Generation Sequencing

BIOF 521

https://education.faes.org/

Data Analyses in Omics Research

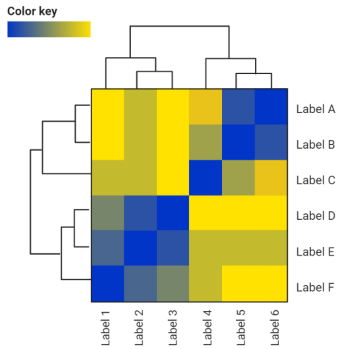
- How do you analyze omics data?



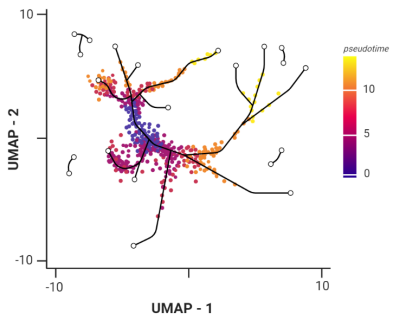
Visualizing Omics Results

How do you visualize large amounts of data?

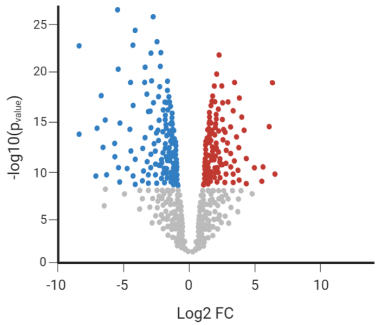
Heat Map



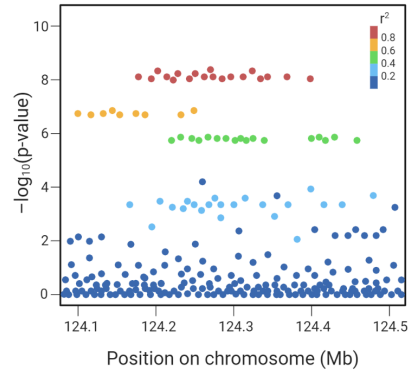
UMAP Clustering



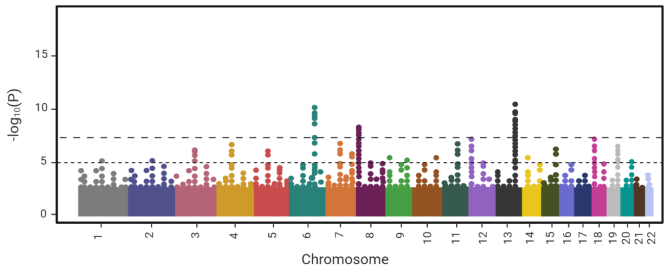
Volcano Plot



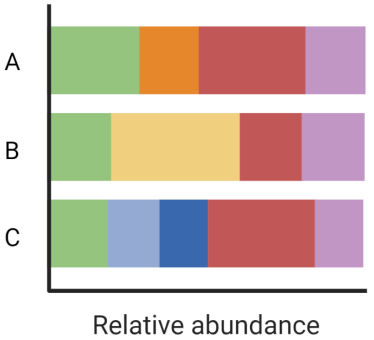
Locus Zoom Plot



Manhattan Plot



Bar Graph: Relative Abundance



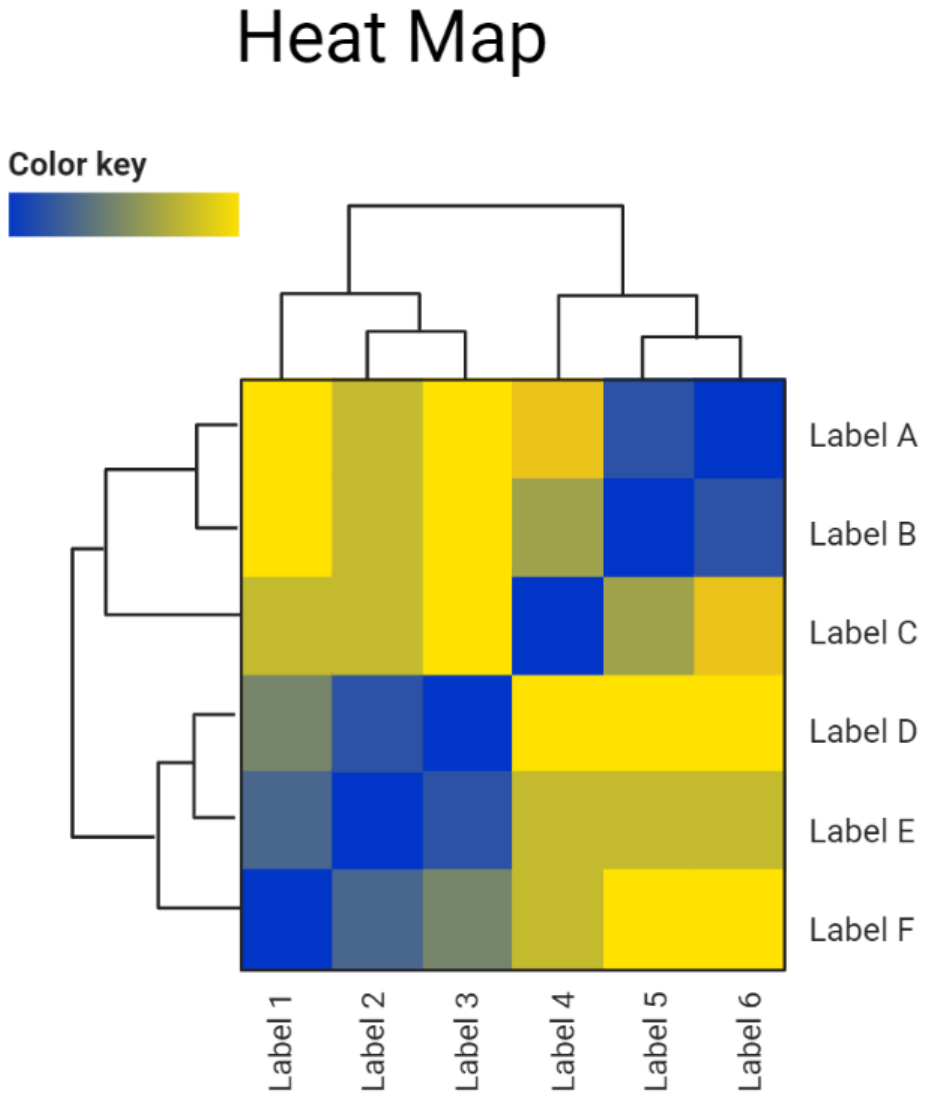
Chord Diagram

Created with BioRender.com

Visualizing Omics Results

Heat map compares groups

- Upregulation or down regulation of genes
- Abundance of molecule of interest

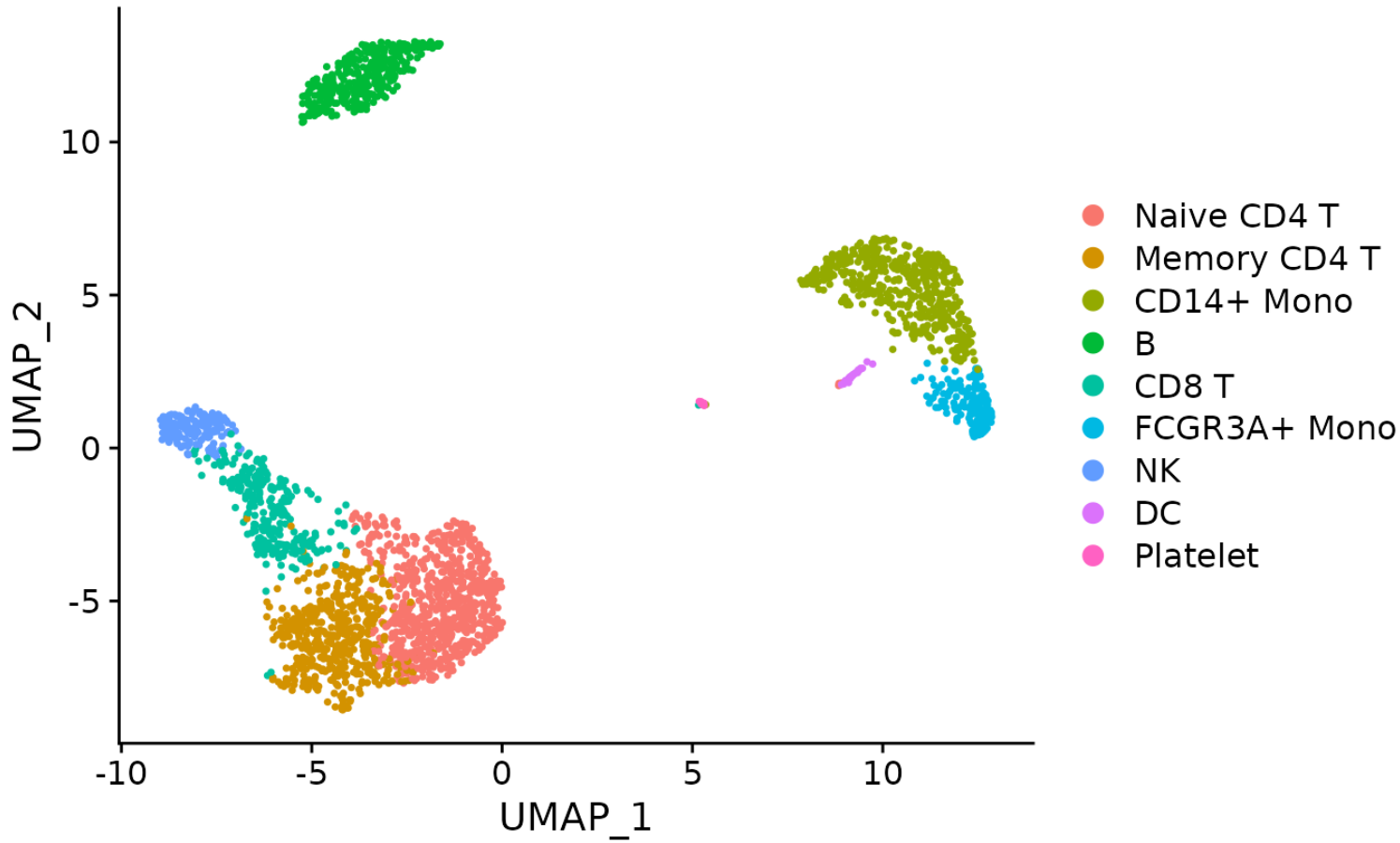


Created with BioRender.com

Visualizing Omics Results

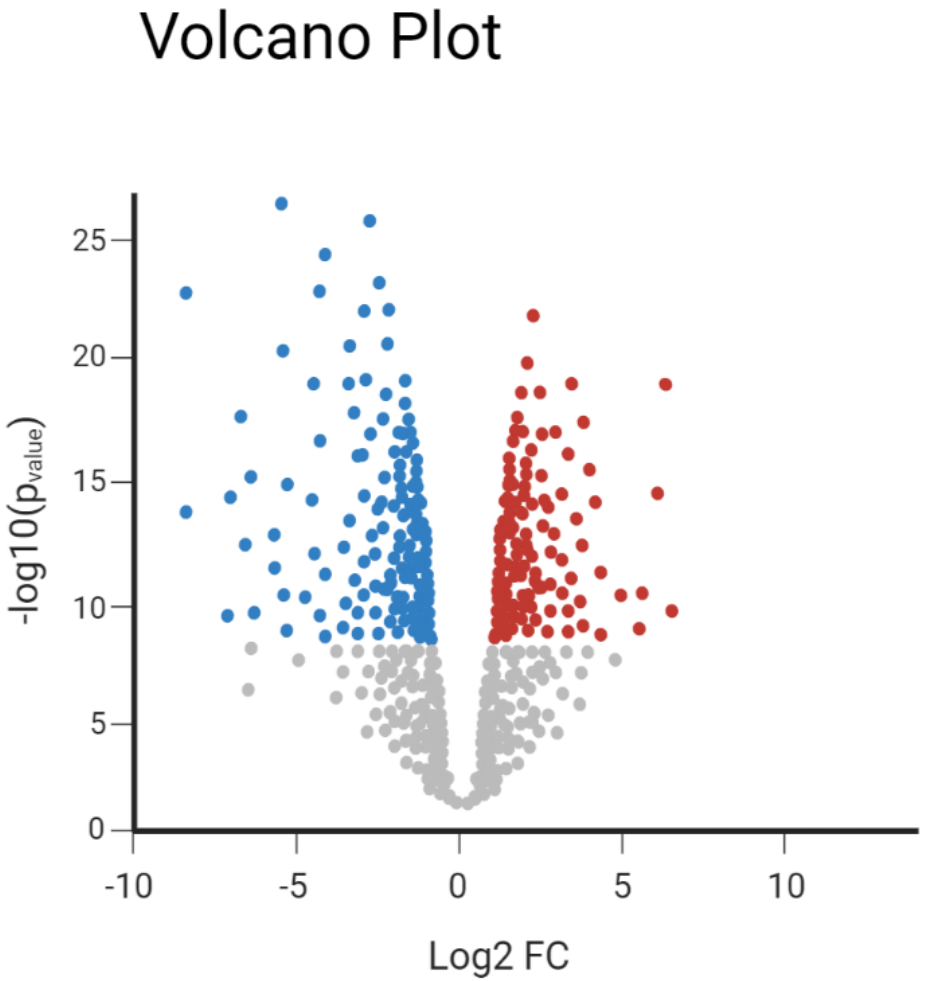
UMAP Clustering

- Mathematical way to visually cluster information to visualize data that cluster together



Visualizing Omics Results

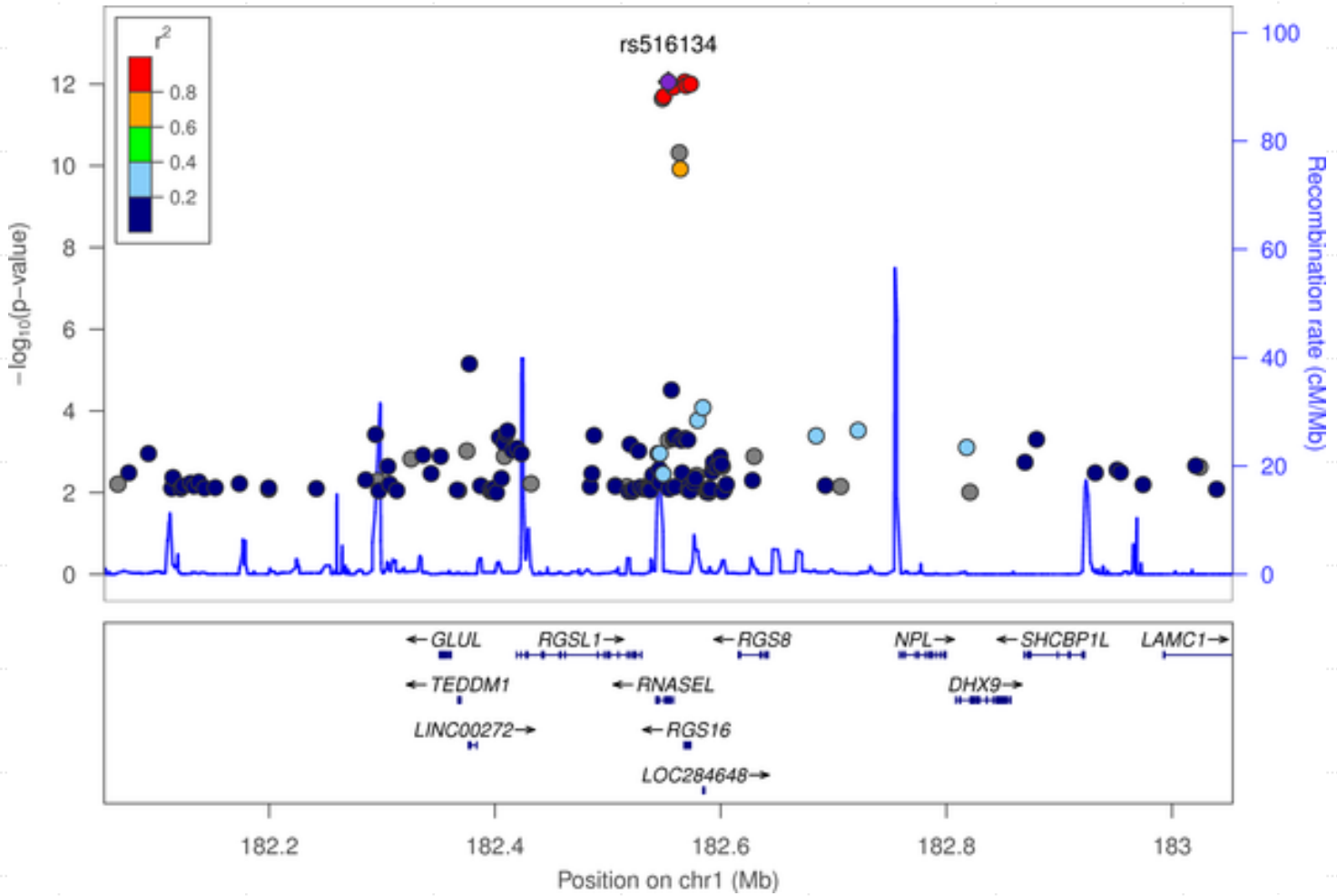
- Plots significance versus fold-change on the y and x axes.
- Enables quick visual identification of genes with large fold changes that are also statistically significant.
- These may be the most biologically significant genes



Created with BioRender.com

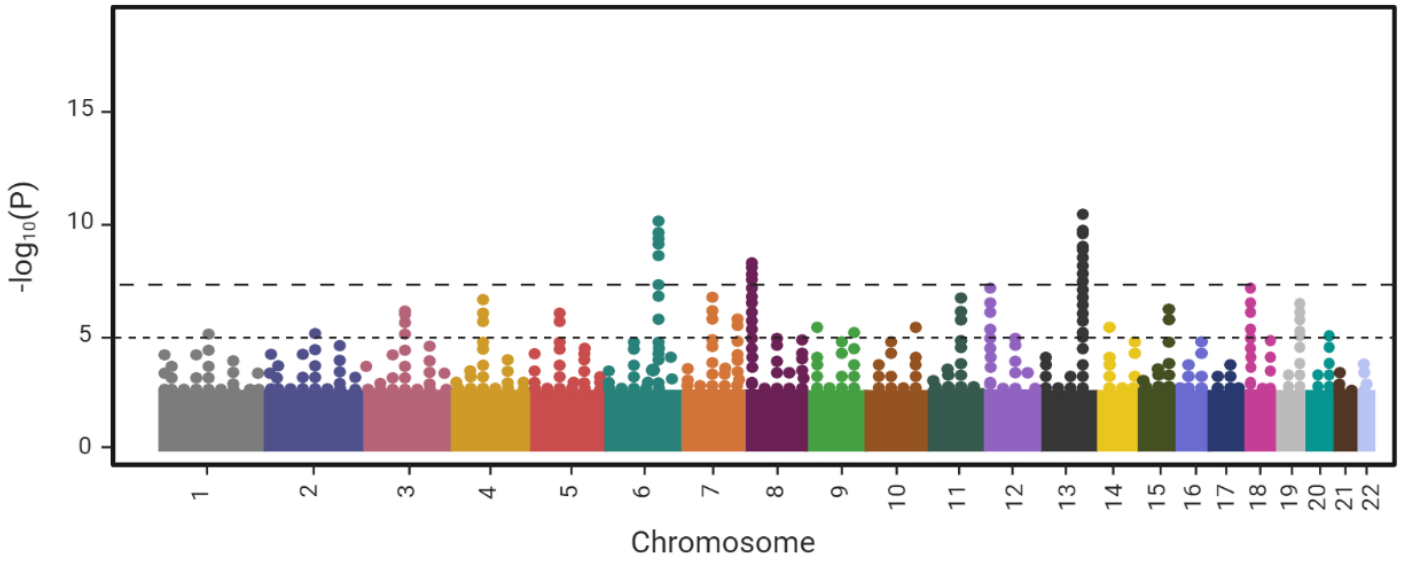
Visualizing Omics Results

LocusZoom plots visually displays regional information, such as position of genes from GWAS data.



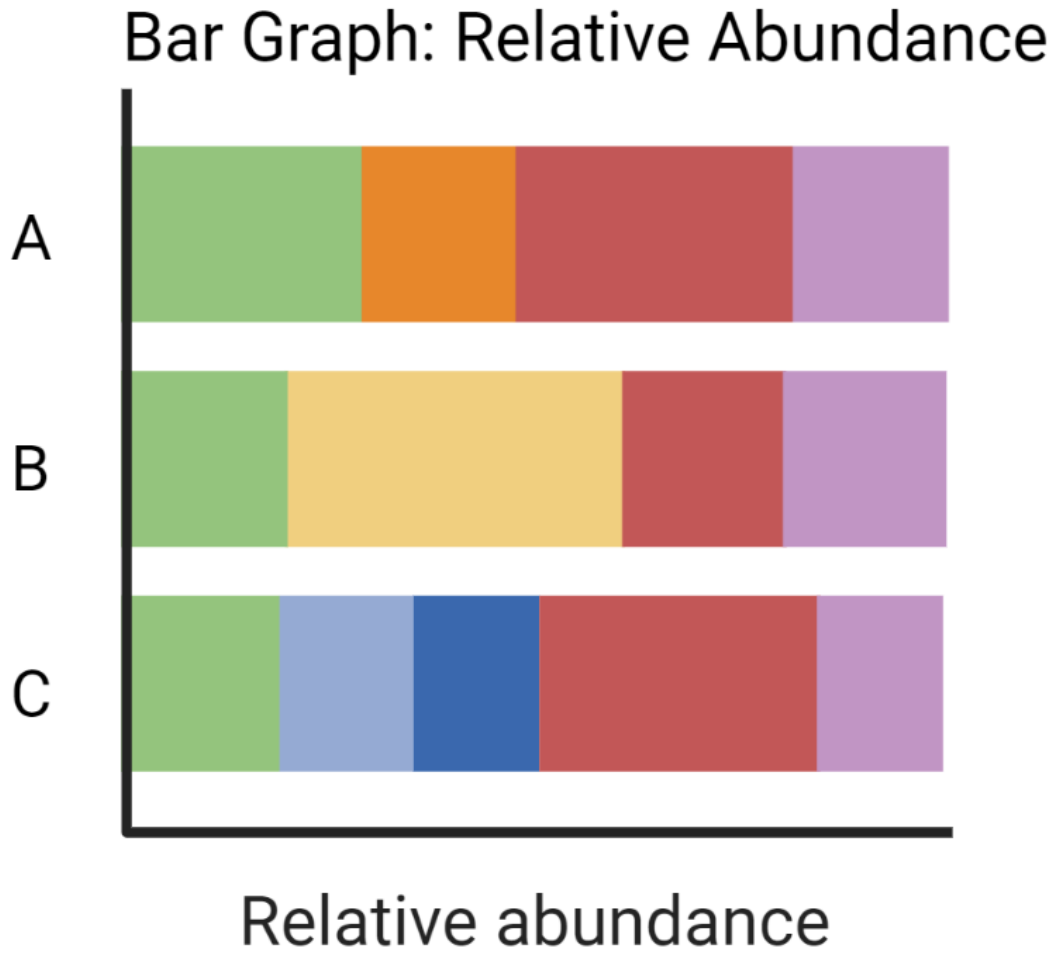
Visualizing Omics Results

Manhattan plot – often used in GWAS studies. Shows negative log p-value by chromosome position.



Visualizing Omics Results

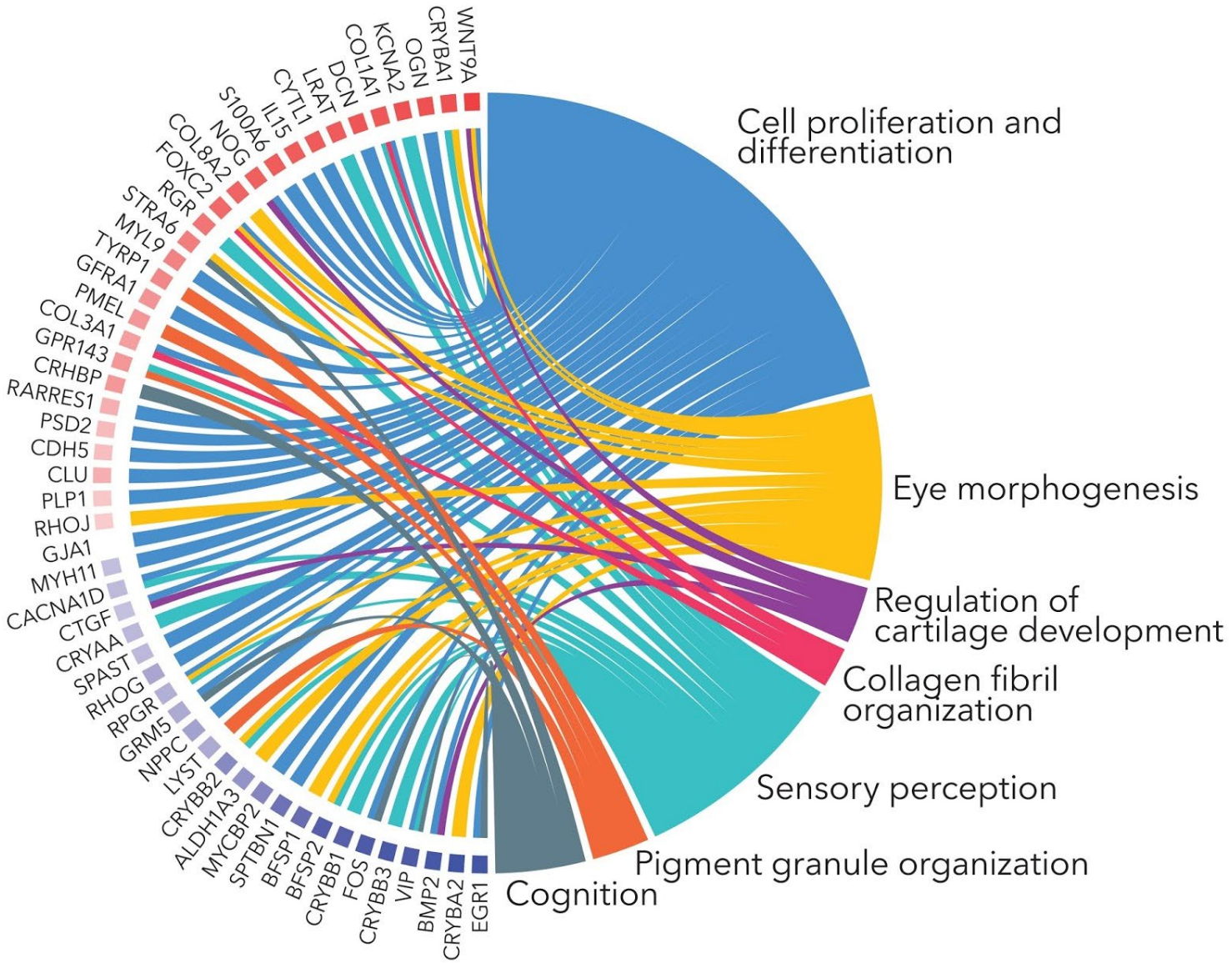
Microbiome data are often displayed as relative abundance by group or individual.



Created with BioRender.com

Visualizing Omics Results

Chord diagrams allow for visualization of linkages



Data Visualization in Research

Laren Narapareddy, PhD, RN
Nell Hodgson Woodruff School of Nursing
Emory University
laren.nara@emory.edu

Inspiration

Center for Data and Visualization Sciences at Duke University

Big thank you to **Eric Monson, PhD** for his workshops

Data visualization is anything that converts data sources into a visual representation

- Tables
- Charts
- Graphs
- Maps

Data visualization helps us identify patterns in the data

- Visual system is not great at understanding patterns by examining a lot of numerical data alone

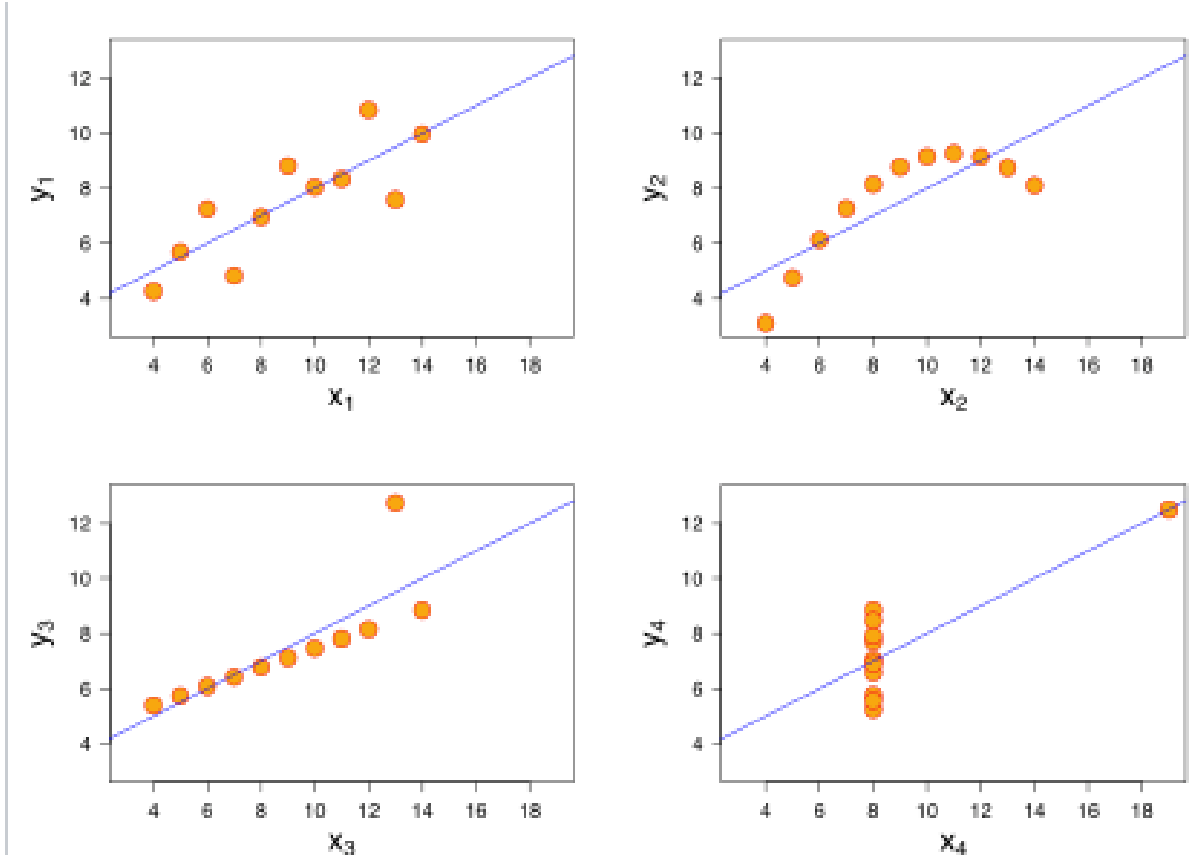
- Useful at a lot of different stages of research

  exploring → communicating

Data visualization helps us identify patterns in the data

Anscombe's quartet

I		II		III		IV	
x	*y*	*x*	*y*	*x*	*y*	*x*	*y*
10.0	8.04	10.0	9.14	10.0	7.46	8.0	6.58
8.0	6.95	8.0	8.14	8.0	6.77	8.0	5.76
13.0	7.58	13.0	8.74	13.0	12.74	8.0	7.71
9.0	8.81	9.0	8.77	9.0	7.11	8.0	8.84
11.0	8.33	11.0	9.26	11.0	7.81	8.0	8.47
14.0	9.96	14.0	8.10	14.0	8.84	8.0	7.04
6.0	7.24	6.0	6.13	6.0	6.08	8.0	5.25
4.0	4.26	4.0	3.10	4.0	5.39	19.0	12.50
12.0	10.84	12.0	9.13	12.0	8.15	8.0	5.56
7.0	4.82	7.0	7.26	7.0	6.42	8.0	7.91
5.0	5.68	5.0	4.74	5.0	5.73	8.0	6.89



https://en.wikipedia.org/wiki/Anscombe%27s_quartet

The goal of data visualization is to make it **easy** for your audience to identify the **most important patterns/comparisons**

Three main attributes of data visualization

1. **Shape** 
   - Used in most graphs
   - Commonly used to distinguish categories
   - Used alone may not be very effective
   - Don't mix too many!
2. **Spatial position**
   - Eyes are really good at making comparisons based on position on a common scale
   - Inherent in most visualizations
   - Think about axes and scales
3. **Color**
   - My favorite ☺

Best practices for **labels & titles**

- Text should be horizontal
- Shorten text, but keep it interpretable
  - Ex: Known abbreviations
- Label charts/graphs directly, rather than legend
- Order of legend should correspond to the order it appears in the visual
- ***Active*** titles tell a story

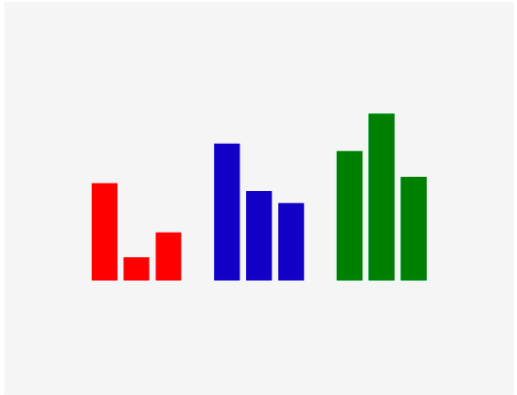
Best practices for using **color**

- **"Save color to draw attention to the story you're telling"**
  - Don't waste color
- Grayscale provides opportunity to backset data/information
- Red x green heatmaps are difficult for color deficiencies
  - Red x blue is better
- Stay consistent with what the colors mean

Best practices for using **color**

- Avoid pure saturated colors
  - some are painful to look at
  - some pop more than others, which can be misleading

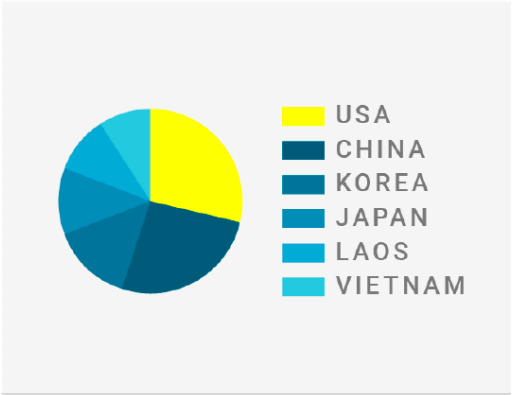
Avoid pure colors



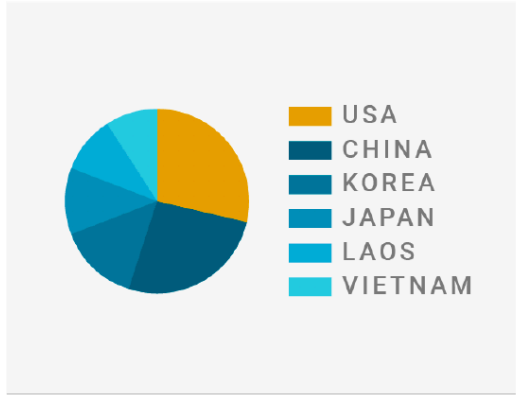
Not ideal

Better

Avoid bright, saturated colors



Not ideal



Better

https://blog.datawrapper.de/beautifulcolors/

Best practices for using **color**

- Color gradients should be saved for ordered variables
- Different hues and brightness for things that are not in order

Not ideal

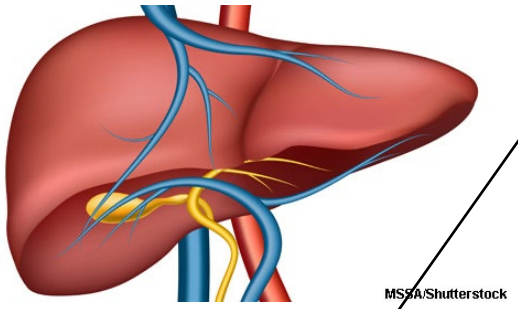
Better

https://blog.datawrapper.de/beautifulcolors/

Using **color** to distinguish group patterns

Transcriptomics
RNA Sequencing
Real-time PCR validation

Proteomics
Quantitative Mass Spectrometry (LC/MS)
Western blot validation



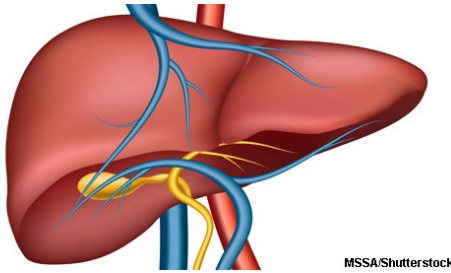
39-weeks

Genotype → DNA → RNA → Protein → Metabolite → Phenotype

IVF-females:
↑ Body weight
↑ Total cholesterol

IVF-males:
↑ Triglycerides
↑ Insulin
↑ Body fat

SREBPs = Master regulators of cholesterol & TAG synthesis



IVF-females:

↑ Body weight

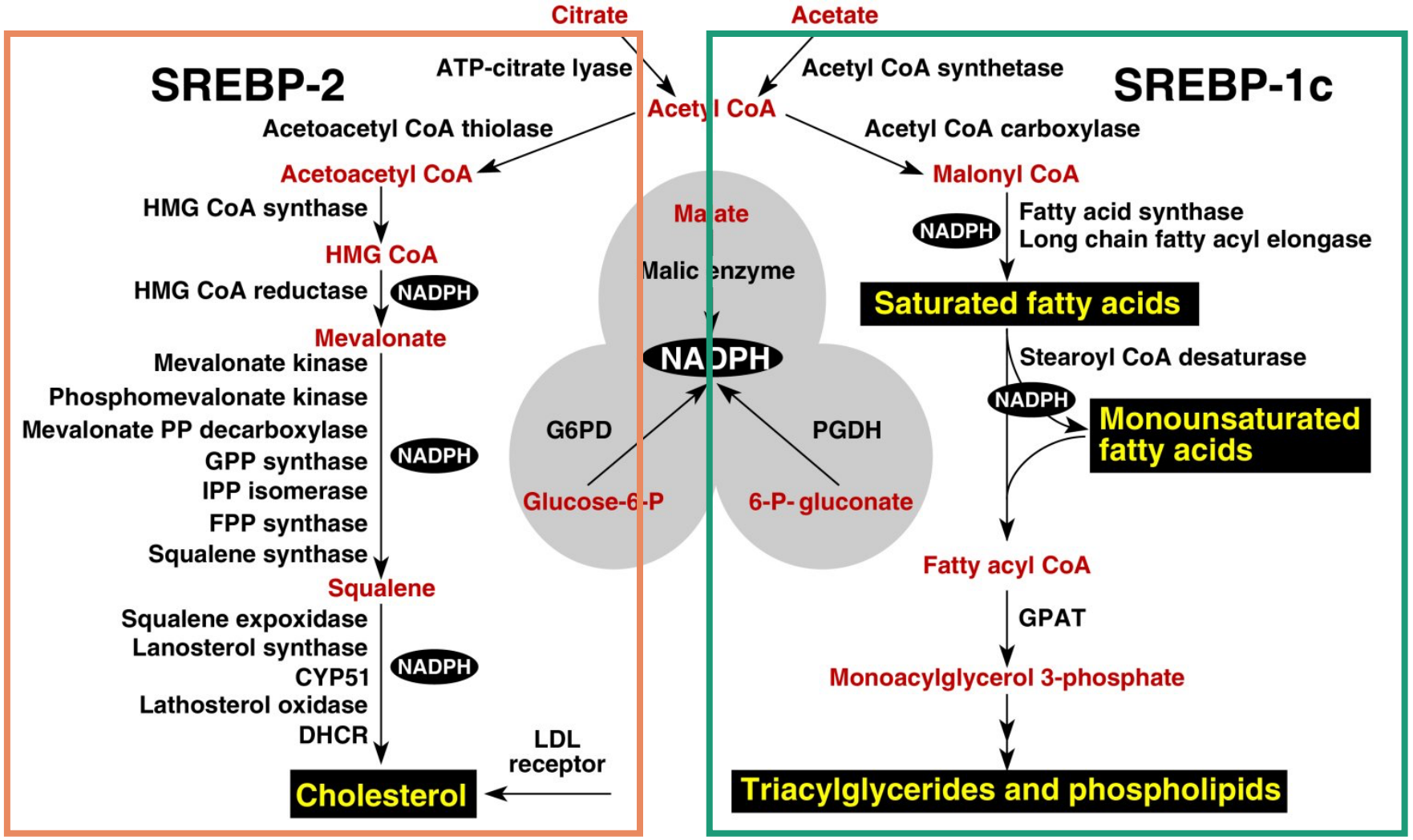
↑ Total cholesterol

IVF-males:

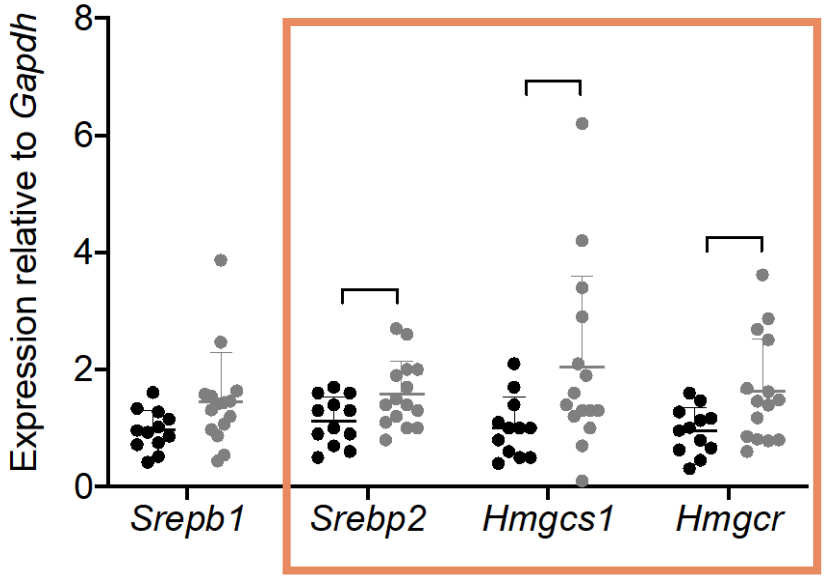
↑ Triglycerides

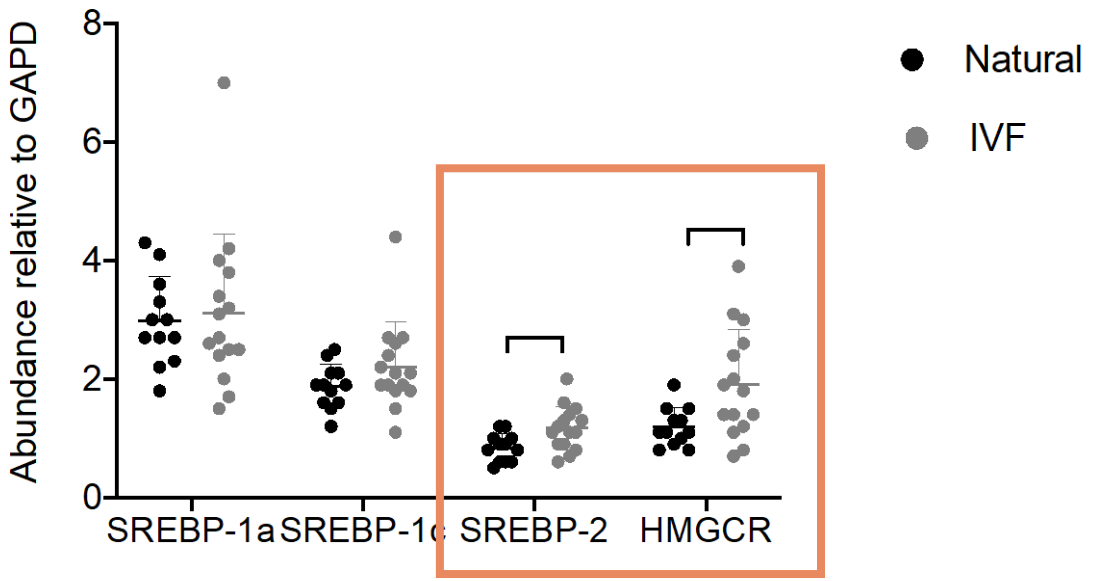
↑ Insulin

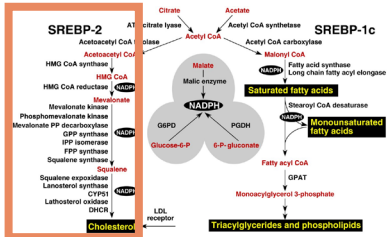
↑ Body fat



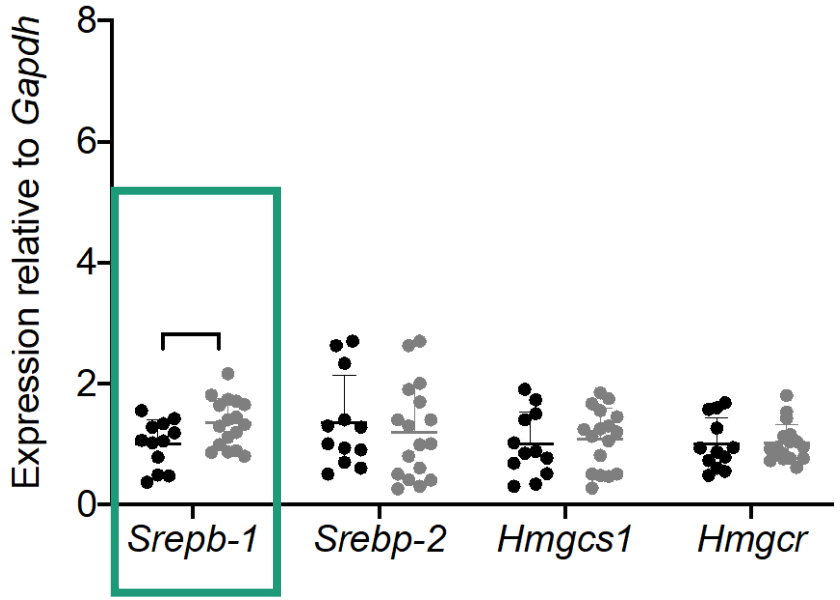
IVF-females have **significantly higher SREBP2 and HMGCR** gene expression and protein abundance

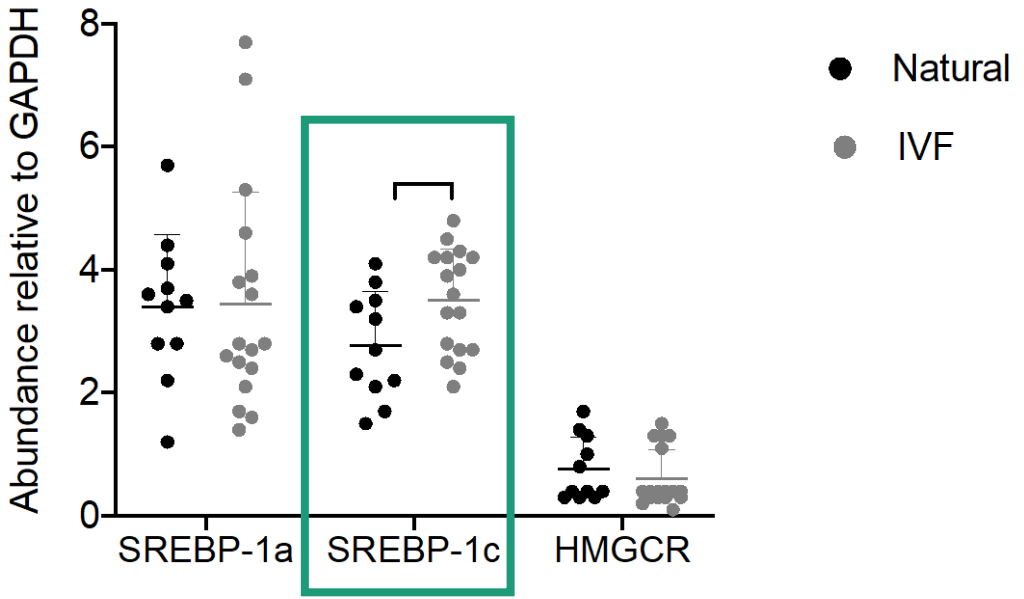


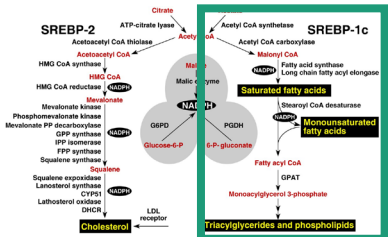




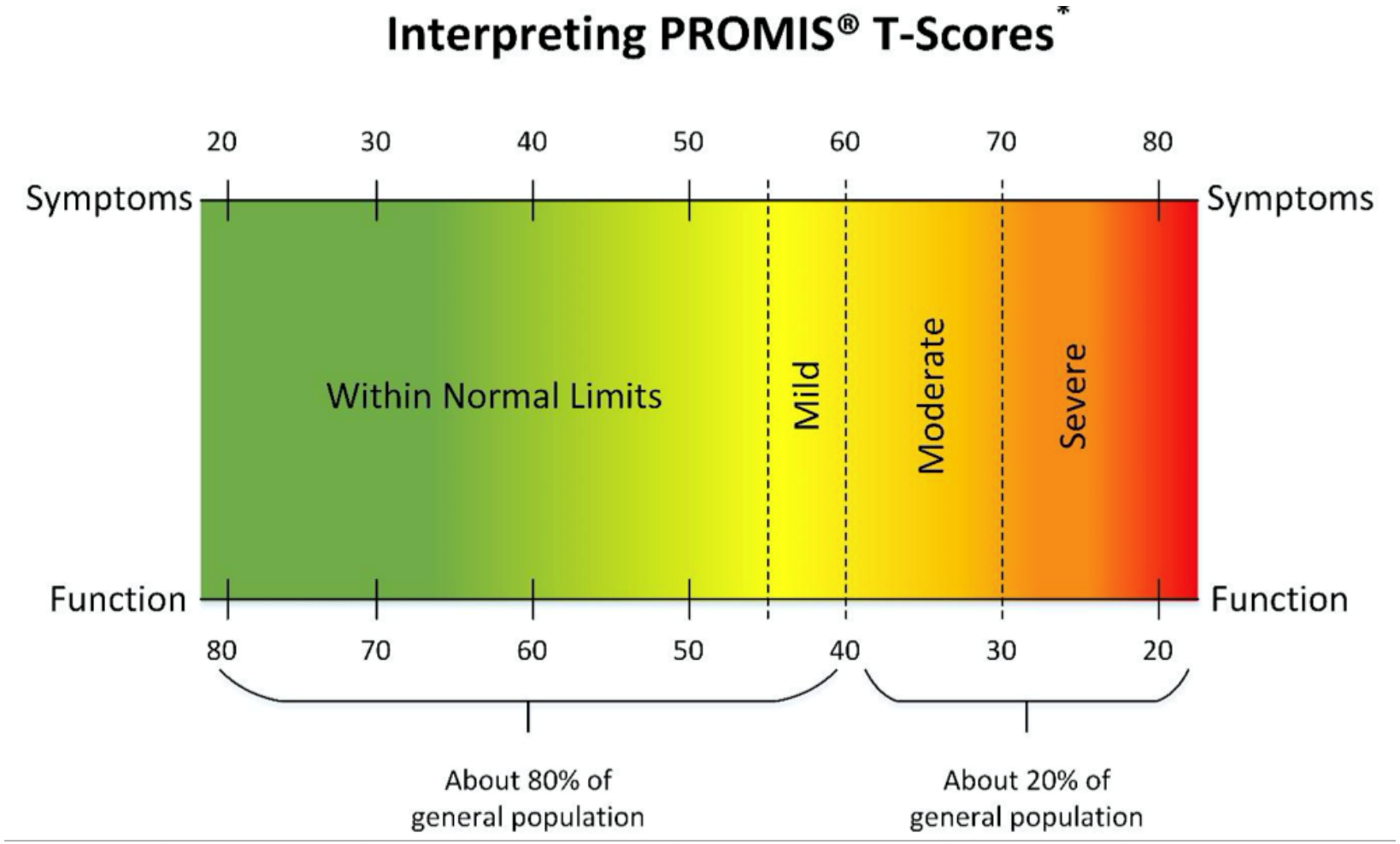
IVF-males have **significantly higher SREBP1c** gene expression and protein abundance







Using **color** to interpret findings

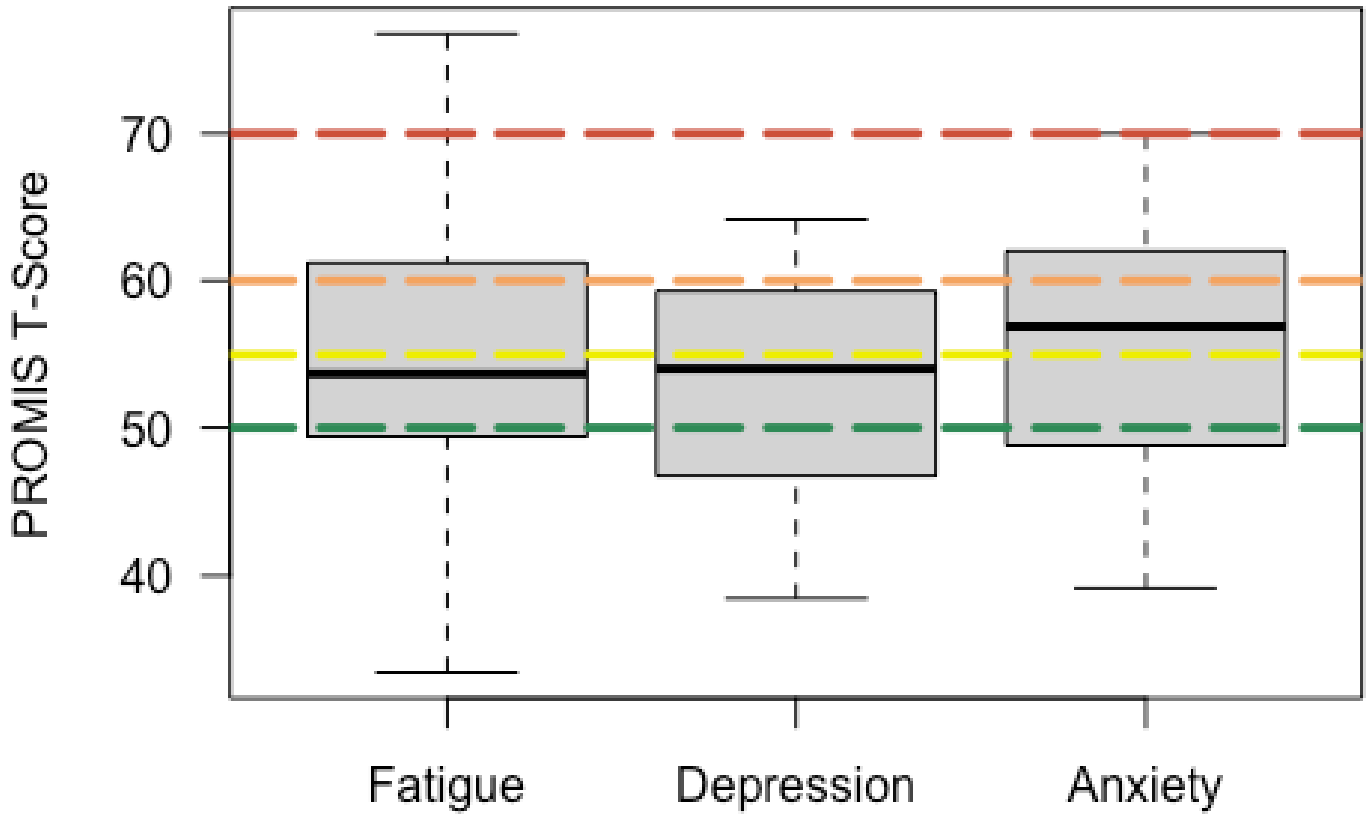


https://labs.dgsom.ucla.edu/hays/files/view/docs/psychometric/Retina_International's_November_2016_Interdisciplinary_Workshop.pdf

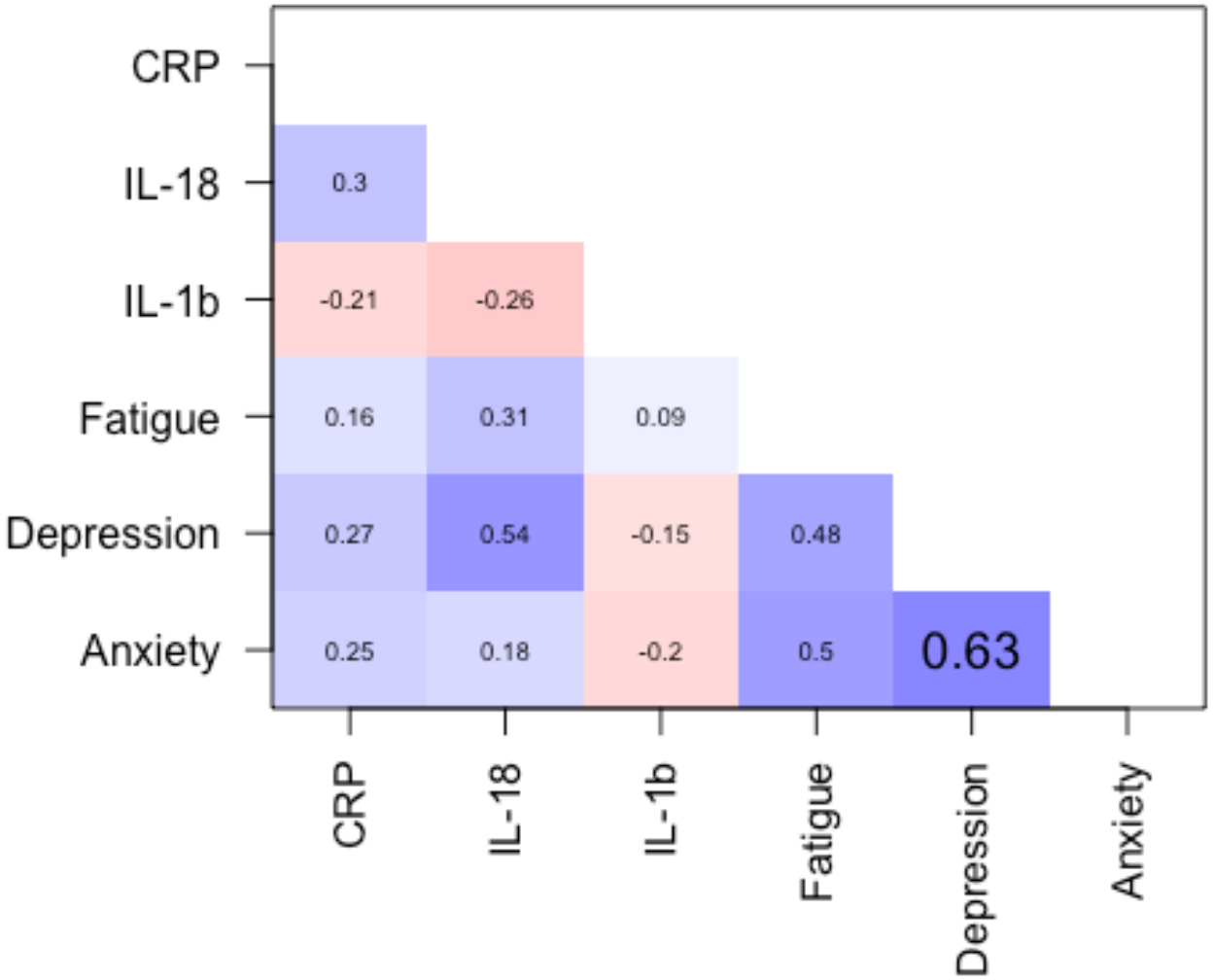
`boxplot {graphics; base r}`
Creates box and whiskers plot for specified data

`abline {graphics; base r}`
adds one or more straight lines through a current plot

Anxiety is mild to moderately severe among women with PCOS



Depression and anxiety are **moderately correlated**



`{ggplot2}`

Tutorial:
http://www.sthda.com/english/wiki/ggplot2-quick-correlation-matrix-heatmap-r-software-and-data-visualization

Best practices for **tables**

- Left align text, center okay for column labels
- Numbers can be centered or right aligned
- Highlight important values by adding bold, colors, or annotations
- Typically, not helpful to copy and paste raw output from stats program

Generating tables in R with `tbl_summary`

`tbl_summary {gtsummary}`

Calculates descriptive statistics for continuous, categorical, and dichotomous variables

Table 1. Clinical Characteristics of Sample

Characteristic	N = 51[1]
HTN Status	
PCOS	24 / 50 (48%)
PCOS + HTN	26 / 50 (52%)
Unknown	1
Age (yrs)	37.6 (6.5)
Body Mass Index	39.0 (8.5)
Waist Circ (in)	43.8 (7.5)
Unknown	3
Systolic BP (mmHg)	122.8 (12.8)
Unknown	1
Diastolic BP (mmHg)	83.5 (15.4)
Unknown	1

[1] n / N (%); Mean (SD)

Generating Tables in R with `tbl_summary`

`tbl_summary {gtsummary}`

Use **by =** argument to display summary statistics by group.

Use **add_p** to perform appropriate statistical test for comparing groups.

Tutorial: https://www.danieldsjoberg.com/gtsummary/articles/tbl_summary.html

Table 1. Clinical Characteristics by HTN Status

Characteristic	PCOS, N = 24[1]	PCOS + HTN, N = 26[1]	p-value[2]
Age (yrs)	36.0 (6.3)	39.3 (6.5)	0.082
Body Mass Index	37.7 (7.5)	39.8 (9.4)	0.5
Waist Circ (in)	41.9 (7.6)	45.6 (7.2)	0.2
Unknown	0	3	
Systolic BP (mmHg)	118.6 (11.1)	127.5 (13.0)	**0.021**
Unknown	0	1	
Diastolic BP (mmHg)	78.8 (8.4)	88.0 (19.3)	**0.007**
Unknown	0	1	

[1] Mean (SD)
[2] Wilcoxon rank sum test

Reflections on Incorporating Social Determinants of Health into Omics Research

Nicholas A. Giordano, PhD RN | Assistant Professor, Emory

Disclosures

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- This work was supported, in part, by the Center for the Study of Symptom Science, Metabolomics and Multiple Chronic Conditions (NINR P30NR018090) and the Georgia Center for Diabetes Translation Research (NIDDK P30DK111024)
- The content of this presentation reflect the views of the presenters and neither the funders nor the United States government

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  - Dean McCauley, Dr. Dunbar, Dr. Yeager, Deanna West Tankoo
- Co-Investigators
  - Nicole Carlson CNM, PhD, FACNM, FAAN & Madelyn C. Houser, PhD
- Study Staff
- Participants for their time and contributions to the science

Outline

- Social determinants of health: What are they and why are they important?
- Efforts to measure social determinants of health
- Emerging challenges to incorporating social determinants of health into research analyses
- Integrating social determinants of health with high-throughput variables

Social Determinants of Health

"Social determinants of health (SDOH) are the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks."

- US Department of Health and Human Services, Office of Disease Prevention and Promotion, Healthy People 2030

Social Determinants of Health: An Example

- Limited access to affordable grocery stores with healthy foods is linked to having suboptimal nutrition
- Over time increased risks of multiple chronic conditions that lower life expectancy
- Promoting healthy choices alone doesn’t change behavior or health outcomes
- The gut microbiome is influenced largely by environment and social factors, including diet and stress

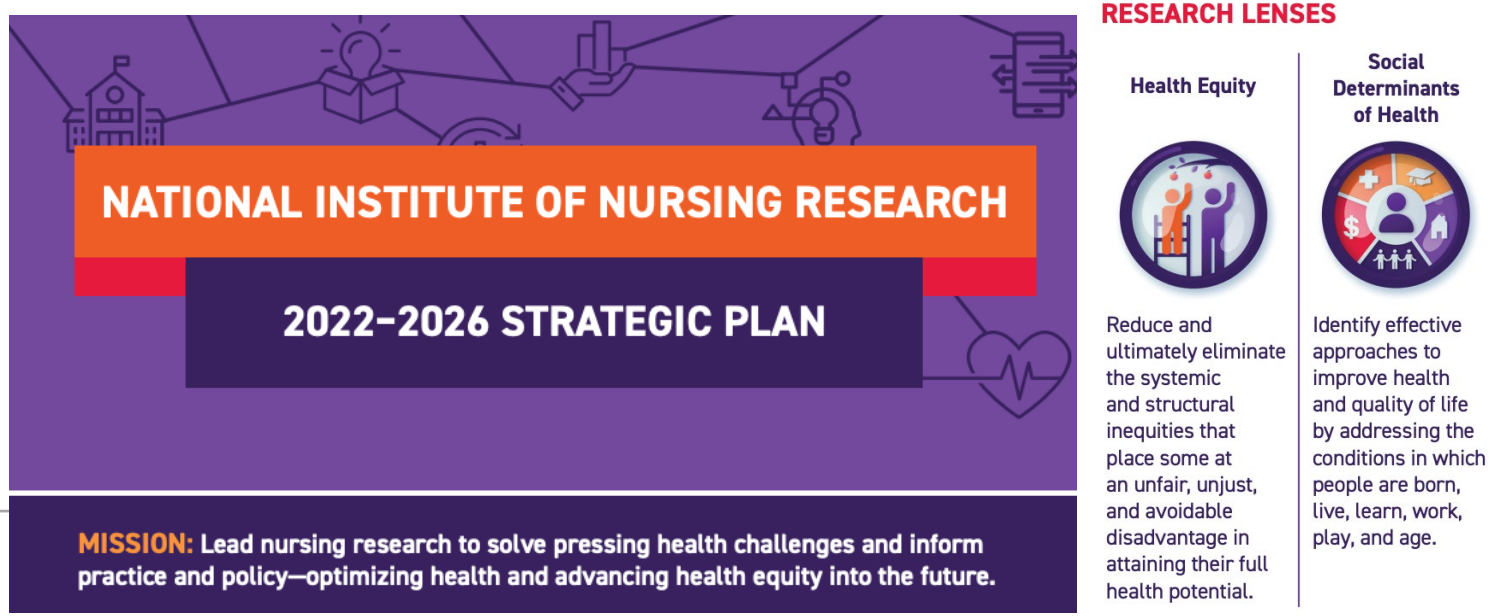
Social Determinants of Health in the Context of COVID-19

- Black and Brown people disproportionately holding essential occupations that carry higher risks of exposure to COVID-19
- Social distancing measures pose challenges and risk individuals with disabilities concentrated in congregate settings and crowded households
- Individuals with substance use disorders experienced isolation and barriers to treatment resulting in increased overdose deaths during the ongoing pandemic

Social Determinants of Health

"While inequities have plagued our health care and our governmental institutions, there is a once-in-a-generation opportunity for transformational change."

- Presidential COVID-19 Health Equity Task Force Final Report



Measuring Social Determinants of Health

- Broad definitions with opaque approaches to measurement
- Efforts to quantify the contribution of any single factor on health outcomes are often not helpful
- Need for systematically capturing contributors to health in an organized and informative manner to guide research that can ultimately improve outcomes

SDOH CORE DOMAINS

Psychological

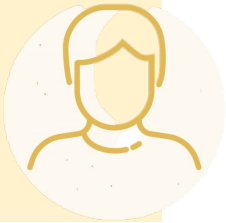
- Stress
- Negative affect / mood
  - Depression
  - Anxiety
  - Anger
- Self-efficacy / optimism
- Cognitive function
- Life satisfaction

Behavioral

- Diet
- Physical Activity
- Alcohol use
- Substance use
- Sexual practices
- Firearm exposure
- Risk taking behaviors
- Tobacco use / exposure

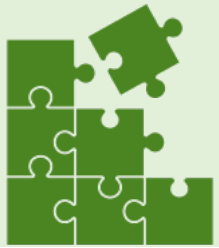
Individual Level

- Social connectedness and isolation
- Exposure to violence
- Social support
- Work conditions
- History of incarceration
- Military service
- Health decision making
- Discrimination



Sociodemographic

- Sexual orientation
- Gender identity
- Race/Ethnicity
- Country of origin
- Education
- Employment
- Food security
- Housing security
- Income
- Health Literacy



Neighborhood

- Racial/ethnic composition
- Socioeconomic composition
- Pollution and allergens
- Hazardous exposures
- Parks and open space
- Health and social services
- Educational opportunities
- Food options
- Transportation
- Job opportunities

Measuring Social Determinants of Health: Clinical Settings

# of Participant Facing Items	27	14	26
Core Domains			
Sociodemographic	+	+	+
Psychological	+	-	+
Behavioral	-	-	+
Individual	+	+	+
Neighborhood	-	+	+

Measuring Social Determinants of Health: Research

- NIH Common Data Elements (CDEs) for capturing SDOH
- NINR first developed a set of CDEs commonly collected in all symptom studies, now includes a 30 items SDOH tool
- The PhenX Toolkit (consensus measures for Phenotypes and eXposures) provides recommended standard data collection protocols for conducting biomedical research
- These collections provide a common currency for studying SDOH across research studies

NIH
National Institutes of Health

cdRNS
Common Data Repository for Nursing Science

PhenX Social Determinants of Health Assessments Collection

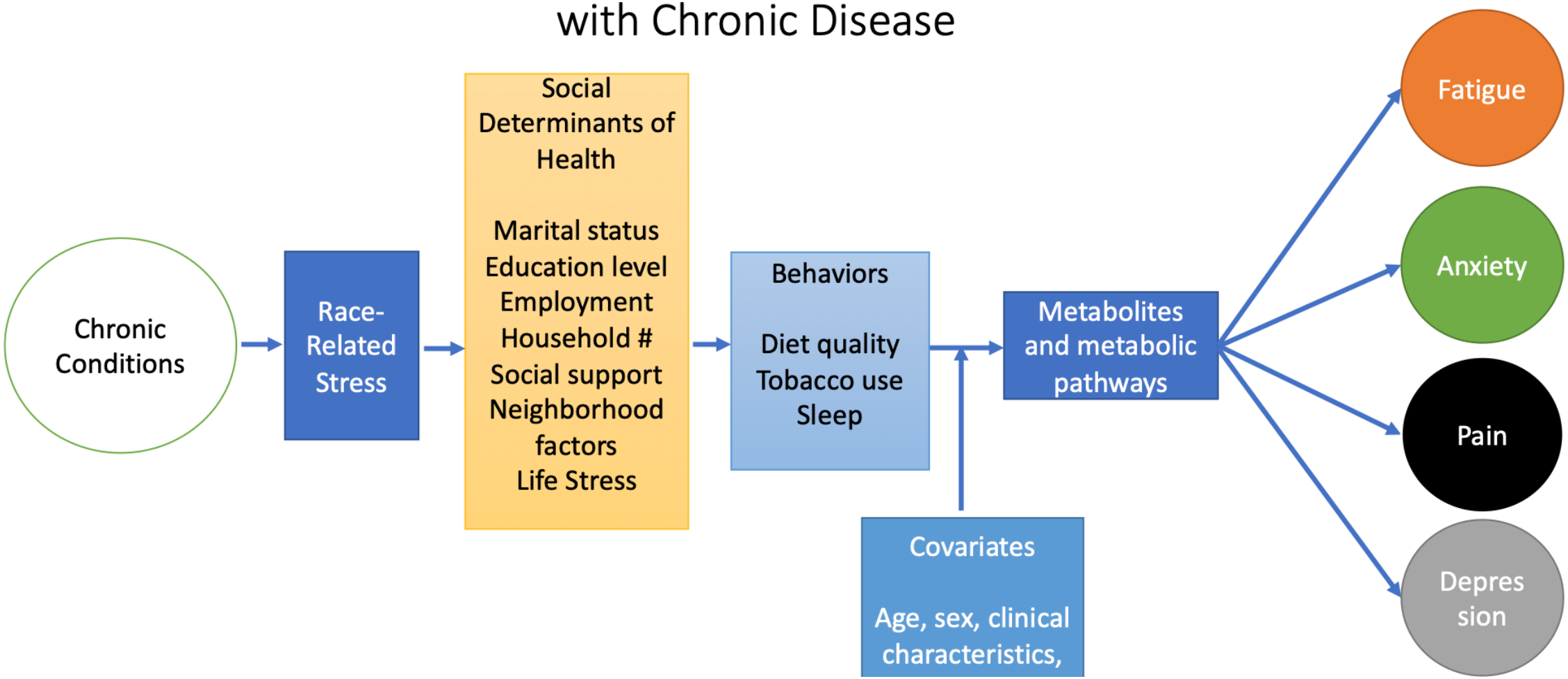
The Center for the Study of Symptom Science, Metabolomics, & Multiple Chronic Conditions

- NINR-funded P30 Award at Emory University School of Nursing
- Aim: Use metabolomics, microbiomic technologies, and big data analysis to understand symptom etiology in adult African-American people with MCC (multiple chronic conditions)
- 5 Pilot Studies
- 2 Supplemental Studies
- Shared core surveys, biological samples
- *plus* study-specific questionnaires and biomarkers

SDOH in the Emory MCC P30

- Marital status
- Education level
- Employment
- Household number
- Social support
- Neighborhood factors (zip code, address)
- Life stress
- Index of Race-Related Stress

Physiologic Markers of Racism and Social Determinants of Health Affecting the Symptom Experience of Black Adults in the Southern US with Chronic Disease

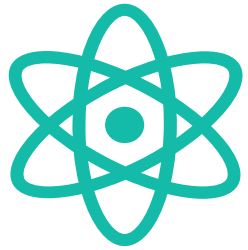


Secondary Analysis with SDOH in Several Small, Related Studies

Challenges:

Not all studies collected the same questionnaire data from all participants

Differing rates of missingness by sub-study



Opportunities:

Characterize metabolites and metabolic pathway (the internal environment) differences across people with exposure to variations in SDOH.

Incorporating SDOH in Omics Data Analysis

Challenges:
Inconsistency in SDOH data collection

- Complicates cross-study comparison

	P1 (N=30)	P2 (N=34)	P3 (N=56)	P4 (N=49)	P5 (N=20)	S1 (N=34)	S2 (N=42)	**Total (N=265)**
Health Insurance								
Private insurance	NA	NA	13 (45%)	NA	14 (74%)	NA	18 (49%)	**45 (53%)**
Medicare	NA	NA	11 (38%)	NA	1 (5%)	NA	10 (27%)	**22 (26%)**
Medicaid	NA	NA	3 (10%)	NA	3 (16%)	NA	3 (8%)	**9 (11%)**
National Health Insurance	NA	NA	NA	NA	0	NA	NA	**0**
Veterans Affairs/Military	NA	NA	NA	NA	0	NA	NA	**0**
Other	NA	NA	NA	NA	1 (5%)	NA	NA	**1 (1%)**
None	NA	NA	2 (7%)	NA	0	NA	6 (16%)	**8 (9%)**
Missing	*30*	*34*	*27*	*49*	*1*	*34*	*5*	***180***

Challenges:
Data quality

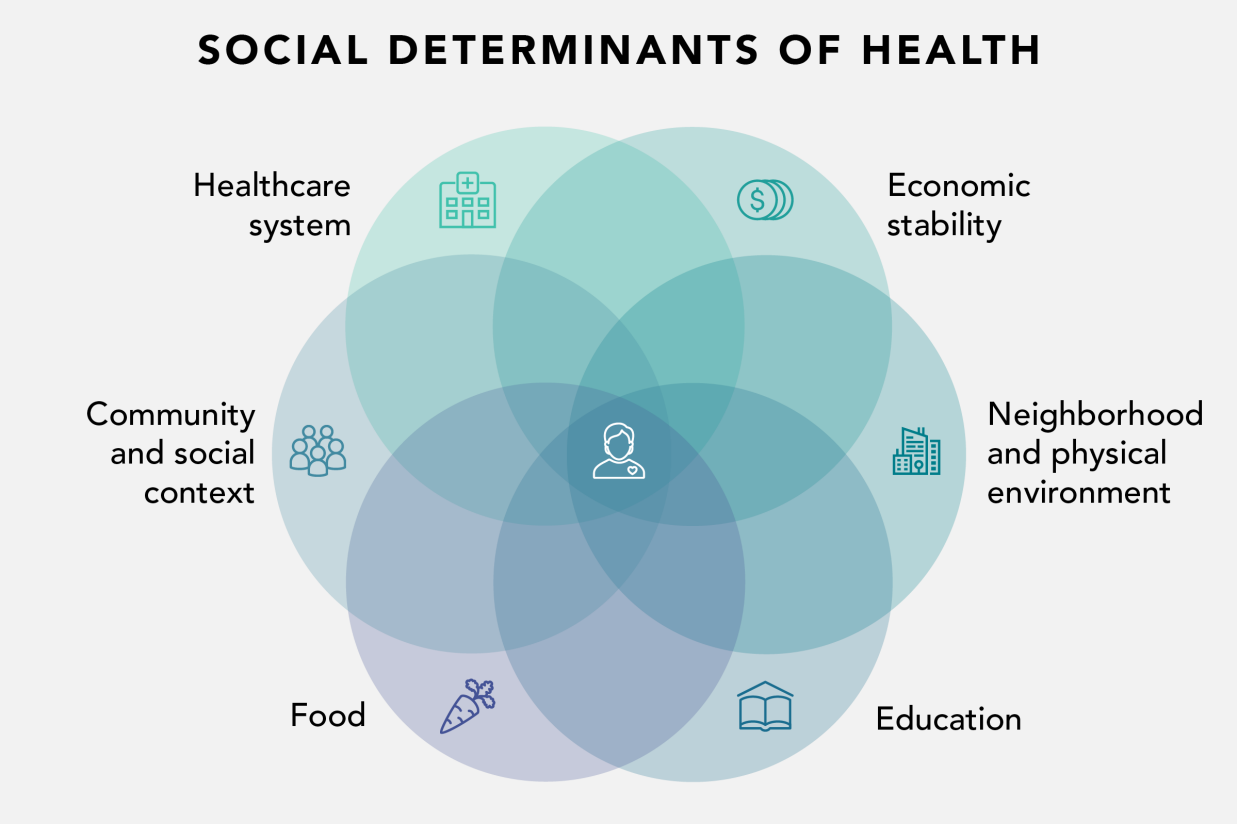
- May be more data quality issues in studies involving disadvantaged groups

MONTHLY INCOME	
MEDIAN	1850
RANGE	0 – 55000
MISSING	87

Have you ever experienced heat stroke?	
Yes	24 (80%)
No	6 (20%)

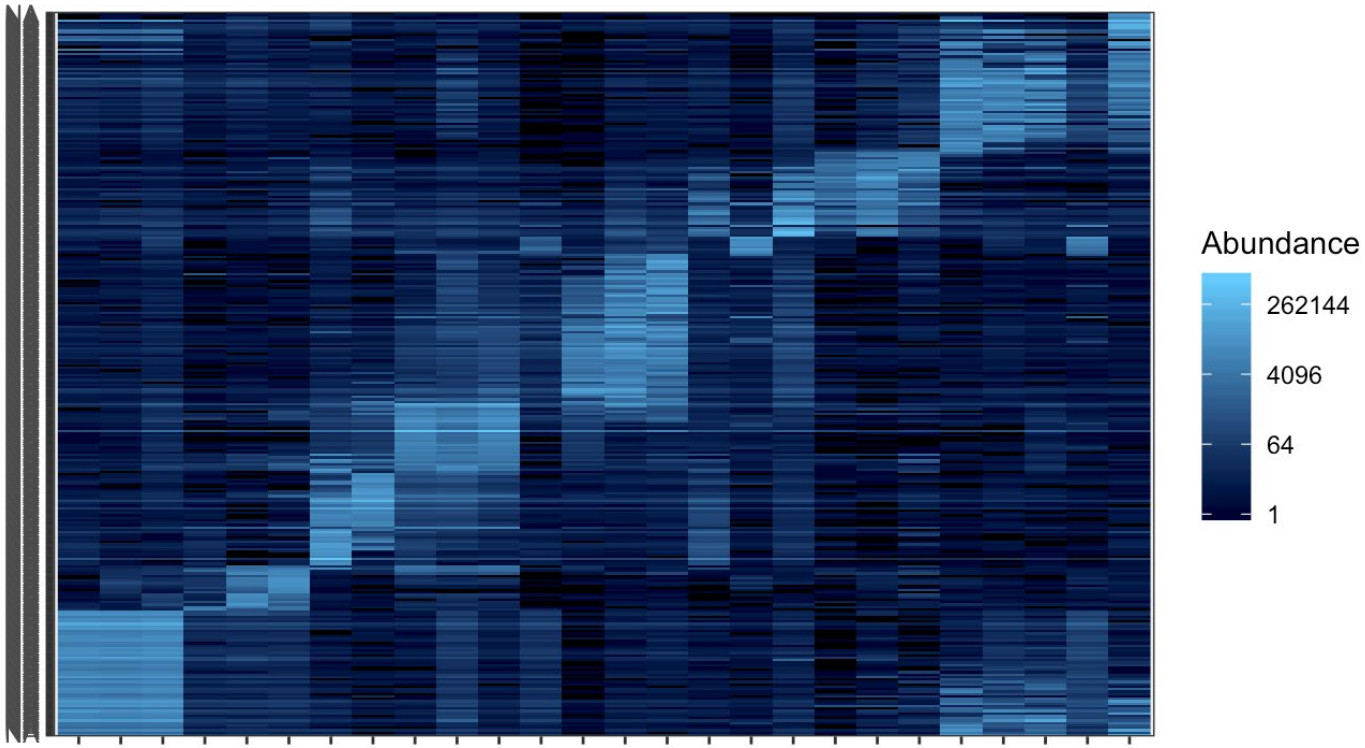
Challenges:
SDOH variable selection

- Include as many variables as possible?
  - Many SDOH variables correlate
- Include only those most relevant to the particular study?
  - May be difficult to determine



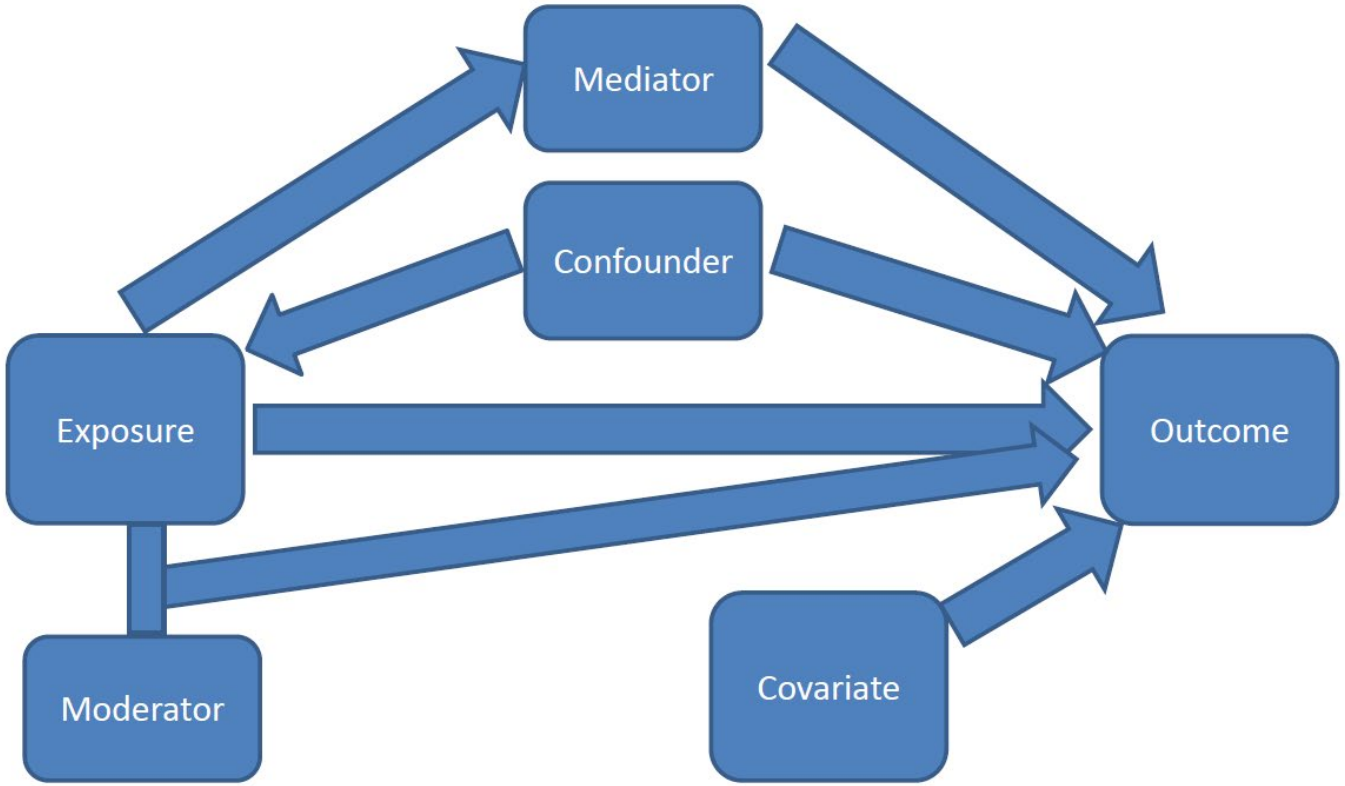
Challenges:
SDOH variable utilization

Omics studies often not powered for consideration of numerous covariates



Challenges:

SDOH variable utilization

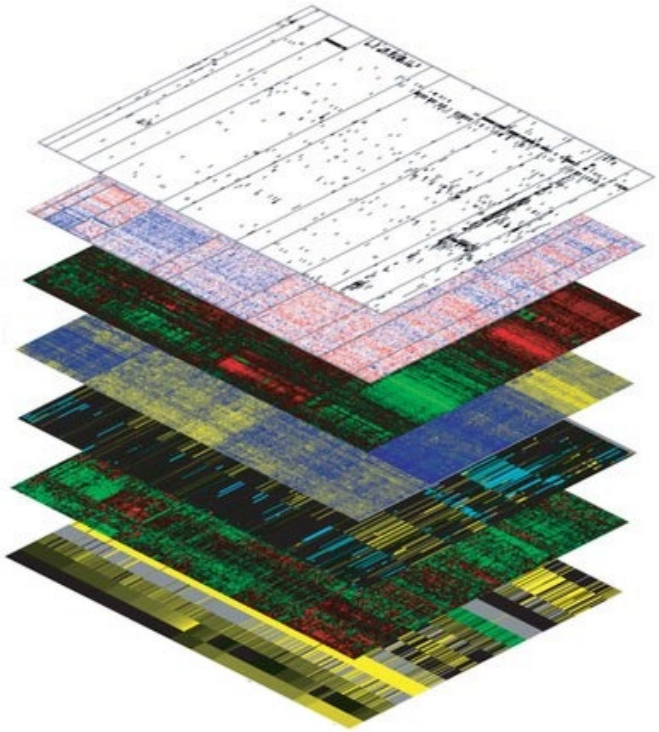


How should SDOH measures be treated in analysis?

Approaches:

Definitive approach not established

Healthy People 2030

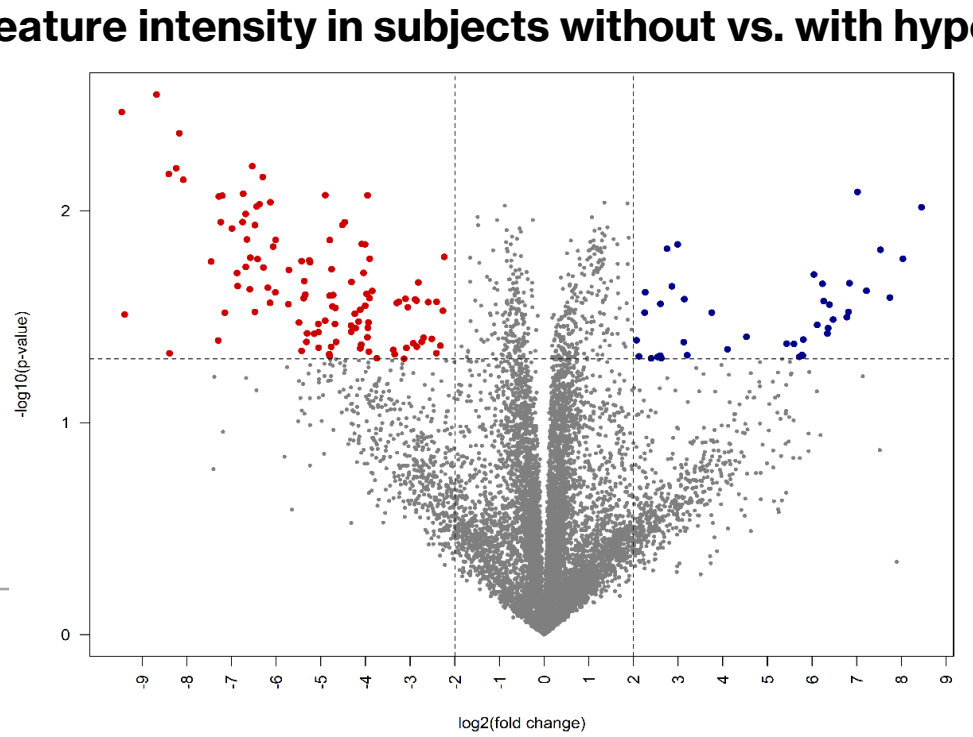


The Cancer Genome Atlas Research Network, *Nature Genetics* 2013

Approaches:

Traditional methods often lacking

Typical omics workflow: compare levels of all features by variable of interest, with or without covariate adjustment, then correct for multiple comparisons

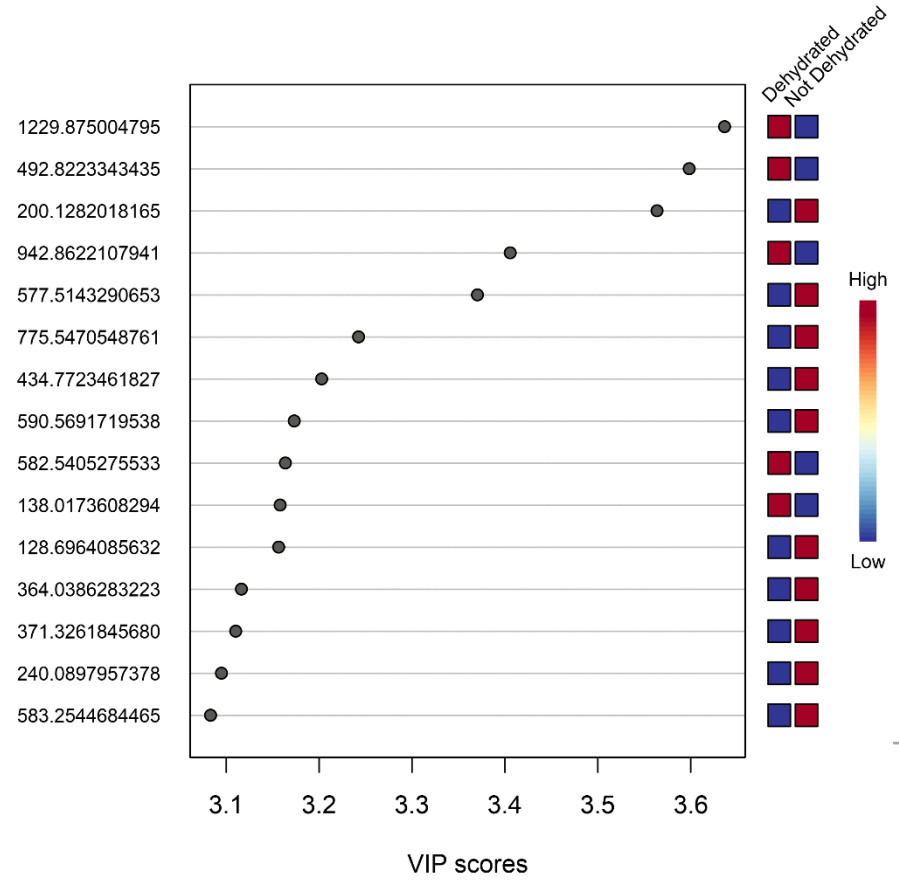


Covariate adjustment is often regression-based

Approaches:

Reduce dimensionality of omics data

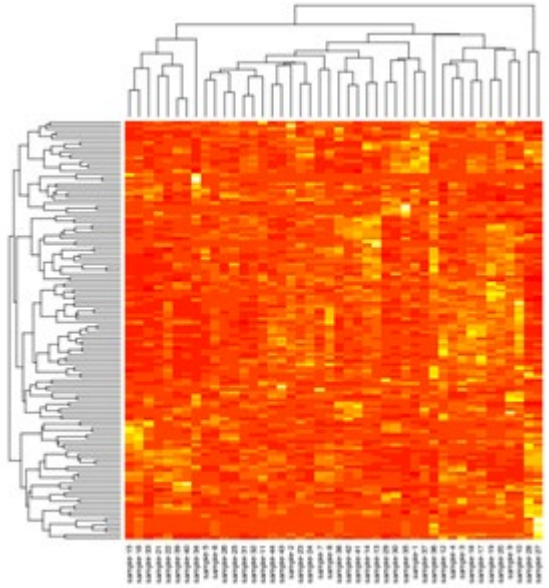
Subset omics data, then integrate SDOH measures

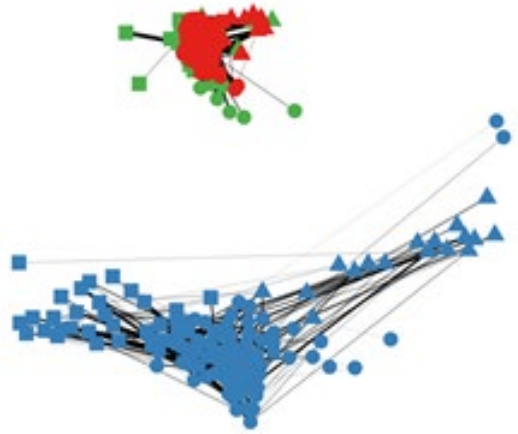


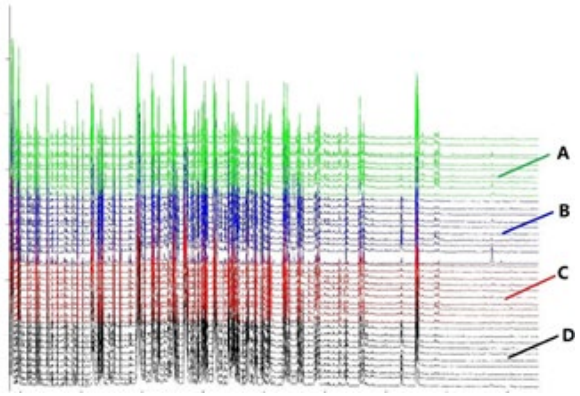
Approaches:

Beyond covariates in regressions

- Clustering, network, class analysis
- Machine learning







SDOH are critically important descriptions of people's lived circumstances

SDOH critical for researchers seeking to understand how to optimize health

SDOH + Omics has potential to reveal etiologies by which a person's lived experience manifests in their body and changes health

Challenges exist: selecting SDOH for a study, participant burden, analysis with multiple SDOH, how to consider SDOH with Omic analyses

Solutions to these problems are being tested: mixed methods techniques to better understand how SDOH influence health, theoretical models to guide SDOH selection, dimensionality reduction

My First Omics Research: Lessons Learned

My First Omics Research: Lessons learned

- Specimen collection in the field (i.e. in participant homes or in clinical exam rooms) a LOT harder than I anticipated.
- Saliva is non-invasive, but surprisingly more time consuming than I thought to collect.
- Lipstick turns the saliva pretty colors
- Aliquoting saliva makes me gag sometimes
- Needed support for both the bioinformatics pipeline AND biostatistical analysis.

Lessons learned in omics research

https://www.shutterstock.com/search/collaboration

Omics lessons learned

1. Collection → analyses can take a long time

2. Dependent on collaborators or outside laboratories for analyses

3. Opportunities for new collaborations

Discussion

https://www.brittanybutts.com/omics-workshop-snrs-2023.html