

people's physical activity, sedentary behavior, and sleep (in the lab and at home). As a clinical investigator, I focus on cold-induced thermogenesis, brown adipose tissue, muscle activities, heart rate and heart-rate variability, and body and skin temperature in response to subtle changes in environmental temperature. We are quantifying the capacity of cold-induced thermogenesis (how many extra calories are burned during tolerable cold exposures) to see what the differences are between lean and obese subjects, men and women, and young and old, and among different races. We are also quantifying, in humans, the amount, activity, and distribution of brown adipose tissue, which will allow us to better understand how it regulates body temperature and metabolism.

Our three custom-made metabolic chambers measure minute-by-minute energy expenditure for several hours to several days. In this well-controlled environment, we can also simultaneously measure movement and physiological parameters to determine the impacts of physical activity, diet, medications, and other stimuli on energy metabolism, heart rate, and hormonal responses. In addition, we can use a variety of techniques to quantify people's body composition.

Currently, we are working with intramural and extramural investigators to study energy balance in different populations such as people with diabetes, lipodystrophy, nonalcoholic fatty liver disease, inborn errors in metabolism, overgrowth, chronic fatigue syndrome, and certain cancers, as well as in a range of healthy volunteers (different ages and weights and in different geographic locations). We are also studying the effects of medications and dietary interventions on metabolism.

YAMINI DALAL, PH.D., NCI-CCR

Senior Investigator and Group Director, Laboratory of Receptor Biology and Gene Expression, Center for Cancer Research, National Cancer Institute

Education: St. Xavier's College, Mumbai, India (B.Sc. in biochemistry and life sciences); Purdue University, West Lafayette, Indiana (Ph.D. in cell and molecular



biology)

Training: Postdoctoral fellow at Fred Hutchinson Cancer Research Center, Seattle

Before coming to NIH: Postdoctoral research associate, Fred Hutchinson Cancer Research Center, Seattle

Came to NIH: In September 2008

Selected professional activities: Affiliate professor, Department of Biological Sciences, University of Maryland (College Park, Maryland); Faculty of 1000 since 2010; editorial boards for *Public Library of Science*, *F1000 Research*, *Chromosoma*, and *Scientific Reports*

Outside interests: Reading historical fiction, science fiction, and popular science; appreciating archaeology and ancient languages; enjoying folk and Americana music; biking; hiking; spending time with family and friends

Website: <https://irp.nih.gov/pi/yamini-dalal> (<https://irp.nih.gov/pi/yamini-dalal>)

Research interests: My research focuses on centromeres, which are essential for chromosome segregation during cell division. My lab studies proteins called histones, the main protein components of chromatin (made up of DNA and protein), which packages and orders DNA into nucleosomes (the building blocks that make up chromosomes). In cancer cells, certain chromatin regions are fragile and prone to chromosomal rearrangements. We use an interdisciplinary approach—combining chromatin biochemistry, computational modeling, single-molecule microscopy, genetics, genomics, and cell biology—to determine how specialized chromatin structures contribute mechanically and epigenetically to centromere function.

The principle challenges we have addressed in recent years are how the essential centromeric histone variant called centromere protein (CENP) A (CENP-A) determines where the centromere is located every cell cycle; whether CENP-A and its complexes physically alter the chromatin fiber to support the mechanical stresses of mitosis; and whether such states can be inherited over several cell cycles.

In previous work, we documented that CENP-A nucleosomal and pre-soluble assembly structures are diverse and possess unique modifications and

dynamics that make them intrinsically distinct from histone H3 (one of the five main histones involved in chromatin structure).

In a recent breakthrough, we used an adaptation of a very-high-resolution microscopy technique, called atomic force microscopy, to make nanoscale elasticity measurements of CENP-A nucleosomes and compare them with nucleosomes that have different histone compositions. We found that CENP-A nucleosomes were surprisingly elastic, or “squishy,” but adding kinetochore proteins made them rigid. (Kinetochores are where the microtubules attach during cell division.) Overexpression of CENP-C in human cells showed that a higher CENP-C/CENP-A ratio decreases the elasticity of the nucleosome and “closes” the chromatin fiber.

We speculate that the plasticity of CENP-A might be the key inherited feature conserved across the CENP-A of all species, and it is this feature that is uniquely recognized by centromere-binding proteins.

In our second project, we are focusing on the regulation and deposition of histone variants in normal and cancer cells. We were the first to report that in embryonic stem cells, naturally excess CENP-A is involved in chromatin repair and that error-free CENP-A assembly to human centromeres requires targeted and cell-cycle specific transcription.

We were also the first to demonstrate that in human colon-cancer cell lines and tumors, CENP-A invades transcriptionally coupled H3.3 (a histone variant that is structurally much like histone H3) pathways to deposit hybrid CENP-A:H3 nucleosomes at non-centromeric regions.

A significant question remains: How does non-centromeric CENP-A drive cancer progression? In recent work, we have shown that CENP-A can drive chromosome instability by seeding large fragile domains outside of native centromeres. We have proposed that targeting cancer-specific CENP-A mis-interactions can potentially serve as a therapeutic target. To test these ideas, we have worked on H3.3 pathways that are invaded by CENP-A, and recently we developed high-precision computational-prediction approaches to block these interactions.

[RESEARCH SECTION WRITTEN BY MOHOR SENGUPTA, NEI]

I am the principal investigator of the B-WELL-Mom study (Breathe- Wellbeing, Environment, Lifestyle, and Lung Function (B-WELL-Mom) study. B-WELL-Mom examines changes in asthma symptoms and control of asthma over the course of pregnancy and during the postpartum period. The study also compares lung function and immune markers for asthmatic and non-asthmatic women in relation to air pollution, dietary antioxidants, and allergies. Our research 1) assesses whether atopy (predisposition to allergic hypersensitivity) status—measured by total immunoglobulin E at the time a person enrolls in the study—predicts variability in asthma control during pregnancy; 2) evaluates whether atopy status is associated with additional decrements in lung function and increased inflammation in pregnancy among women with asthma; 3) evaluates the impact of regulatory T-cell concentrations on asthma control variability during pregnancy; and 4) evaluates changes in lung function and inflammation in all women exposed to poor ambient air quality (traffic, commuting, and ambient measures) and potential mediation by dietary antioxidants.

GWENYTH REID WALLEN, R.N., PH.D., CC

*Senior Investigator and Clinical Nurse Scientist;
Chief Nurse Officer; and Chief of Nursing Research
and Translational Science, NIH Clinical Center*



Education: University of Maryland, Baltimore (B.S.N. in nursing); Central Michigan University, Mt. Pleasant, Michigan (M.A. in management and supervision/business management); University of Maryland, College Park, Maryland (Ph.D. in public health/health education)

Training: Postdoctoral research associate, Department of Family Studies, University of Maryland (College Park, Maryland); Bravewell Fellow in Integrative Medicine, University of Arizona (Tucson, Arizona)

Before coming to NIH: Clinical nurse specialist, Neonatology, Washington Hospital Center (Washington, D.C.)

Came to NIH: In 2001 as section chief, Office of Research and Outcomes Management, Nursing and Patient Care Services, NIH Clinical Center; chief of the Research and Practice Development Service, NIH CC (2005–2009); and chief, Nursing Research and Translational Science, NIH CC (2010 to present)

Selected professional activities: Adjunct associate professor, Behavioral and Community Health, University of Maryland, School of Public Health (College Park, Maryland); adjunct assistant professor, Graduate School of Nursing, Uniformed Services University of the Health Sciences (Bethesda, Maryland); reviewer for several journals; vice chair and member of the National Institute of Child Health and Human Development's institutional review board since 2001; collaborating with nursing colleagues in England and China to define the role of the nurse in clinical research as well as the role of the clinical nurse-scientist

Outside interests: Travelling; gardening; swimming; kayaking; boating; snorkeling

Website:

https://clinicalcenter.nih.gov/about/SeniorStaff/gwenyth_wallen.html (https://clinicalcenter.nih.gov/about/SeniorStaff/gwenyth_wallen.html)

Research interests: My clinical research focuses on health behaviors and health disparities—inequities in access to health-care services among minorities. My team and I are especially interested in the methodology and measurement in end-of-life care, integrative health, and vulnerable populations. We are testing the feasibility of health-behavior-change interventions that improve sleep quality, physical activity, and nutrition, particularly in patients with chronic diseases.

One of my earliest projects was with the NIH Clinical Center's Pain and Palliative Care Service, studying how to provide the best possible care to cancer patients at the end of life. I am interested in working further with **Ann Berger**, chief of the service, who plans to open the Clinical Center's very first Comfort Care Suite.

In a collaborative study with National Institute of Arthritis and Musculoskeletal and Skin Disease researchers, I worked with an urban community clinic that helps people with arthritis, lupus, and other rheumatic diseases. We determined that, for Hispanic patients, involving family members and spouses in the plan of care could facilitate health promotion and chronic disease management. (*Clin Med Insights Arthritis Musculoskeletal Disord* **7**:21-26, 2014; DOI:10.4137/CMAMD.S13849 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3972077/>))

I have a strong collaboration with **Tiffany Powell-Wiley** at the National Heart, Lung, and Blood Institute. We are examining cardiovascular risk assessment in people from under-resourced communities. My expertise in qualitative and mixed-methods study designs provides a unique opportunity to understand the experience of at-risk individuals in their communities.

In a recently completed project, my team explored the effect of severe alcohol-use disorder (AUD) on sleep. AUDs are often accompanied by comorbid physiologic and psychosocial conditions such as anxiety, depression, post-traumatic stress disorder (PTSD), and sleep disturbances, which are associated with an increased risk of relapse to drinking after detoxification and rehabilitation.

In following up with patients who had undergone inpatient alcohol rehabilitation, we used a statistical method called latent class analysis (LCA) to see whether any group was at a higher risk of sleep disturbances. For example, we found that women with highest alcohol-withdrawal symptoms and sleep disturbances also had PTSD and higher levels of anxiety and depression. Our study showed that LCA may provide clinicians with insight into the integrative tailoring of interventions that meet the varied needs of individuals with AUDs, accompanying comorbidities, and sleep disturbances. (*Behav Sleep Med*, DOI:10.1080/15402002.2018.1425867; 2018 (<https://doi.org/10.1080/15402002.2018.1425867>)).

I am also mentoring a postdoctoral fellow who is designing a collaborative study with the culinary medicine program of Tulane University (New Orleans) in which individuals are taught cooking skills and dietary practices based on the Mediterranean Diet. Evidence suggests that health behaviors improve when people participate in joint activities, such as cooking.

In addition to doing my own research, I am helping to provide more formalized fellowship opportunities for scientists from diverse backgrounds to enter and

stay in the field of health-disparities research.

[RESEARCH SECTION WRITTEN BY MOHOR SENGUPTA, NEI]