Towards a coherent understanding of the influence of sex and age on the genetic basis of human physiology and disease

Research: In spite of decades of biomedical research, we lack a fundamental understanding of why and how most diseases vary in prevalence and impact between females/males and between individuals at different life stages. For instance, why is arthritis more common in females than males when they reach about 40 years of age? Why is autism five times more common in boys than girls? Age and, especially, sex have been largely ignored in basic/preclinical studies and in translating findings to clinical research and medical interventions. To uniformly address questions about female/male tissue biology across all age intervals (e.g., childhood, adolescence, or old age), we need to reanalyze hundreds of thousands of human genomic profiles that are already available, in addition to analyzing rapidly-accumulating new data on sex-specific and aging-associated data. Our research group at MSU develops computational approaches that can integrate massive collections of genetic and molecular data to build predictive models about the roles genes might play in various complex diseases. As part of the AAP African Futures Research Leadership Program, the visiting researcher will work with mentors Dr. Arjun Krishnan and Dr. Amy Ralston to participate in our ongoing project on developing new data-driven computational methods to delineate the genomic basis of differences in tissue physiology and disease between sexes and across ages. This research project falls under the **"Health & Nutrition" AAP priority area** and, in the long term, the findings from this work will be crucial for advancing disease diagnosis and intervention.

Research activities: The researcher will closely collaborate with an exceptional graduate student, Kayla Johnson, and contribute to this project by heling develop new computational approaches to 1) make all human genomic profiles available for analysis by predicting their age, sex, and tissue, and 2) characterize age- and sex-specific molecular signatures and networks of human tissues/cell-types. We expect to communicate the methods and discoveries openly to the broader biomedical/clinical community through high impact manuscripts on which the visiting researcher will be a contributing author. Given the increasing need for biologists who write code and programmers who "speak biology," this work will provide the visiting researcher a unique and timely training opportunity in a number of advanced skills in computational biology and bioinformatics, including downloading and processing high-dimensional datasets, writing code implementing several statistical techniques, setting-up computational evaluations, and using the high-performance computing cluster.

Mentoring & professional-development: Both Krishnan and Ralston are NIH-funded PIs who offer complementary scientific expertise and have strong track records in mentoring and career development. The researcher will work with the Krishnan Lab in the Department of Computational Mathematics, Science and Engineering (CMSE), and will also regularly interact with the Ralston Lab via weekly group meetings and events in the Department of Biochemistry and Molecular Biology (BMB). The PIs will jointly meet with the researcher at least four times during the visit. Mentoring will include opportunities to explore career opportunities in academia and the private sector through interactions with speakers at the BMB & CMSE seminar series. Participation in The Exchange, a new departmental weekly meeting for career development will also offer the researcher opportunities for exploration of issues in diversity in the workforce. The researcher will also get opportunities to mentor junior students, give class lectures, and participate in peer-review and grant-writing.