Specific Aims

The United States (U.S.) is a world leader in advanced medical technologies and practice, spending almost twice as much on health care as citizens of the Organization for Economic Cooperation and Development countries\(^1\). Yet, the U.S. is not a healthy country. Americans live shorter lives and experience more chronic diseases than people in other high-income countries. The U.S. ranks 27th in life expectancy, 31st in infant mortality, and first in the incidence of adult obesity (BMI≥30 kg/m\(^2\)) out of the 34 OECD countries\(^1\).

We propose to establish the Johns Hopkins University **Center for Precision Medicine and Health Equity** (CPMHE) in partnership with George Washington University and Drexel University. The CPMHE will develop precision medicine tools that integrate individual variability in genes, environment, and behavior into composite scores, which track individual health and disease throughout the life course. Our vision is driven by a finding that has been replicated in several social science studies. When black and white Americans live together, their health outcomes are similar\(^2\)\(^-\)\(^6\). We intend to show the molecular underpinnings of this socio economic reality and develop tools that can monitor the multi-level interventions needed to improve the health of this country and achieve health equity for all Americans. The **overall hypothesis** of this research program is: **People living under similar social and environmental conditions, regardless of race or ethnicity, will have similar profiles of molecular and clinical indicators linked to obesity co-morbidities, which can be identified and tracked with precision medicine tools** designed to **advance health equity, improve health care quality and reduce health care costs**. The Specific Aims that will be carried out to examine this hypothesis are:

**Aim 1** To develop precision medicine tools to advance health equity using a Learning Health Care System approach.

**Aim 1a** To integrate and analyze complex, multilevel data and condense them into composite precision medicine scores, which will be used in patient risk stratification strategies.

**Aim 1b** To develop and test interpretable precision medicine models, tools and applications focused on improving health care quality and reducing health care cost.

**Aim 1c** To develop methodologies that minimize technological biases in genomics and transcriptomics due to current Eurocentric-only standard references.

**Aim 1d** To develop a Web-based computational platform that will enable data integration harmonization, joint analysis across large numbers of genetic/genomic datasets and associated phenotype data, and publishing of data back to public databases.

**Aim 1e** To develop methods that integrate electronic medical records with environmental hazards and community stresses.

**Aim 2** To identify contextual determinants of genome-phenome interactions linked to obesity related co-morbidities

**Aim 2a** To identify the psychosocial determinants of genome-phenome interactions linked to obesity related hypertension and diabetes in black, white and latino adults living under similar social and environmental conditions.

**Aim 2b** To examine the contextual determinants of genome-epigenome interactions associated with pre-term birth in white and black newborns living under similar social and environmental conditions.

**Aim 2c** To identify psychosocial and molecular determinants of successful participation in a remote weight reduction intervention for Breast Cancer Survivors.

**Aim 3** To identify potential facilitators and barriers to implementation and adoption of precision medicine approaches in multiracial and culturally diverse populations

**Aim 3a** To convene a multi-disciplinary expert group to provide recommendations for individual, community and multi-level precision medicine approaches to risk reduction and consequent implications for health equity

**Aim 3b** To explore the ethics of using precision medicine tools in diverse populations with community based participatory research (CBPR) strategies at multiple levels, including individual interviews and focus groups with policy makers, institutional stakeholders, physicians and patients.

**Aim 3c** To conduct a randomized trial contrasting two methods of conveying individualized precision medicine risks and actionable recommendations for breast cancer recurrence on patient understanding, perceived utility, behavioral intentions and motivation for lifestyle modification and weight loss.

**Impact:** The successful completion of these aims will advance health equity, improve health care quality and reduce health care cost. Our tools will identify people most at risk, earlier; enabling an increase in treatment choices and a decrease in long-term treatment costs for all, regardless of race, ethnicity or social status.