Twin Matters
A Family Newsletter from the Mid-Atlantic Twin Registry

Summary of Published Results from the Genetics & Epigenetics of Healthy Aging in Twins (GHA) Study

MATR twins that have participated in research studies are often curious about knowing what a study “discovers,” so, we are always pleased to share updates on study results! From approximately 2013 to 2015, the MATR helped recruit full pairs of same-sex twins 65 years or older into the Genetics & Epigenetics of Healthy Aging in Twins (GHA) study, which aimed to identify why some individuals seem to age “better” than others. Researchers know that, generally, much of the variation seen in aging characteristics is based less on inherited genetic factors and more on environmental factors influencing non-inherited gene changes called epigenetic changes. The GHA study was particularly interested in the impact these epigenetic changes have on the aging process. Twin participants were crucial to helping the research team understand how some of these epigenetic changes may influence aging.

Epigenetic changes are chemical changes that happen to the DNA that makes up our genes. In simplest terms, these changes often act to turn “on” or “off” certain genes. Though epigenetic changes are part of the normal and necessary chemical interactions in our cells, they can be influenced by a variety of factors, including what we are exposed to throughout our lives, such as pollution, medicines, and other chemicals, as well as by illnesses and even how much sleep we get! For example, someone that is a lifetime smoker will often have epigenetic changes that might make that person look like they have “aged quicker.” This is why you may encounter a pair of (genetically) identical twins and the one that was a lifetime smoker sometimes looks older than the one that did not smoke.

For the GHA study, the epigenetic change of interest is called DNA methylation. DNA methylation involves a chemical group, called methyl, bonding to sections of DNA that might “turn on or off” another gene. In this case, the study observed how the methyl groups would associate with biological age. Biological age is a bit different from chronological age. You may be a certain age in years (chronological age) but your biological chemical-markers and related health measures may indicate that you are younger- or older-seeming than your actual age in years.

Since biological age is determined by a variety of factors, including scaled answers to health questionnaires, the presence or absence of certain health conditions, and other variables, it can be difficult to treat biological age as a discrete measure. This makes it challenging to use in analysis so researchers will often develop a score, called a frailty index, to represent biological age. A lower frailty index is generally an indicator of “healthier” aging or “younger” biological age. Once the GHA study team established the frailty index for this study, they could then begin to look at this measure and the concentration of methyl groups at various DNA sites to see if there were any predictable relationships between the frailty index and DNA methylation patterns.

Through its analysis, the study found that higher levels of DNA methylation were associated with decreases in the activity of the PCDHGA3 gene, which in turn seemed to lead to a change (typically higher) in the frailty scores. This suggests a possible relationship between PCDHGA3 gene-activity, DNA methylation, and biological age. Ultimately, this will help shed light on whether this is one of the potential pathways that influences “healthy” vs. “unhealthy” aging patterns. While this sounds very technical and gene-specific, having these “molecular details” are what is needed to truly understand variation in aging. It is from this type of methodical improved understanding that the GHA researchers seek to find ways to help offset age-related health declines.

The full article, DNA methylation associated with healthy aging of elderly twins, by Sangkyu Kim and others, can be found in the August 2018 edition of GeroScience. This article illustrates the complexity of answering seemingly straightforward scientific questions! It also demonstrates the level of care and quality control the researchers took in making sure their results were as reliable as possible. We will link to this article on our website once it becomes publicly available. We thank the MATR twins who took part in this research study for furthering knowledge of the human aging process!
Dr. Thomas Mack

We are pleased to start a collaboration, looking into breast cancer risk factors, with Dr. Thomas Mack—Professor of Preventive Medicine & Pathology at the University of Southern California. This partnership represents a full circle in Dr. Mack’s career. A career, which spans impressive medical training at Columbia University, the Centers for Disease Control, National Institute of Health, and includes work on smallpox eradication, certain cancers, and Hodgkin’s disease. Much of Dr. Mack’s research, including his current work incorporating the MATR, has its footing in a chance meeting from a couple of decades ago. While serving on a National Institutes of Health committee evaluating grants, he happened to be seated next to Dr. Walter Nance. Many of our longtime MATR members will remember Dr. Nance because his work in pediatric twin studies at VCU helped lay the foundation for the Mid-Atlantic Twin Registry. Through their discussions about twin research, Dr. Mack saw the exciting potential for helping to overcome some of the challenges he faced in studying chronic disease. He realized that adult twin subjects could help him sort out the genetic, cultural, and lifestyle factors that play an all-encompassing role in the development of chronic diseases, like cancer. From that happenstance meeting, Dr. Mack went on to establish twin studies and registries that have helped solidify our understanding of certain chronic diseases. For example, twin participation in his research has helped his team learn that Hodgkin’s lymphoma has a strong heritable component and shares features with autoimmune diseases; that childhood exposure to sunlight (thus Vitamin D) seems to help protect against multiple sclerosis; and, that both genes and environment play a role in the development of malignant melanoma. Now Dr. Mack is seeking continued help from twins on his search for a clearer understanding of just how the factors that influence breast cancer risk (genes, environment, lifestyle choices, etc.) impact the likelihood of breast cancer development. As you can tell from just a few highlights of his impressive career, Dr. Mack is passionate about improving health outcomes. Both he and the MATR hope that MATR twins that are eligible for the study are equally passionate in supporting these efforts. See the Twin Breast Cancer Study advertisement in this newsletter and visit: go.vcu.edu/learnmore to sign up for more information.

Adolescent Behavior Cognitive Development (ABCD) Study Update

The first benchmark in the ABCD study has been reached with approximately 430 twins (215 pairs) completing the ABCD baseline study measures! This is an ambitious, groundbreaking research effort, with multiple university partners across the United States. The ABCD study will use this first set of data provided by participants as a baseline and then hopes to follow those same participants for up to ten years. By doing so, this research will create an impression of deep data about brain and cognitive development.

Since the ABCD study hopes to follow-up with participants, they will continue to contact families that agreed to hear from the study for some time to come. Families that are enrolled in the study are encouraged to keep in touch with the study staff for some time to come. Participants that are no longer interested in learning more about any of these studies, please let us know and make sure we have your current contact information by completing the online form found here: go.vcu.edu/learnmore.

Informed consent: A condition due to overactive parathyroid gland(s). The four parathyroid glands sit behind the thyroid and hyperparathyroidism is a different health condition.

NEW STUDY OPPORTUNITIES FOR ADULT TWIN PAIRS…

Role of the Microbiome in Monozygotic Twins with Psoriasis & Psoriatic Arthritis

(a.k.a., Psoriasis & Psoriatic Arthritis Twin Study – PATS)

The Psoriatic Arthritis Center and the New York University Department of Rheumatology are providing funding to investigate potential causes of psoriasis and psoriatic arthritis. They are partnering with the MATR to invite twins to participate.

Participants the study will need include:
- FullPairs of Same-sex twins
- Adult twin pairs (18 and up)
- Identical (or unknown/unsure zygosity)

Study participation involves:
- Completing the MATR invitation to “sign-up.”
- Providing your consent and possibly medical authorization to access medical records related to psoriasis/psoriatic arthritis to the study.
- Providing answers to questionnaires as well as stool, blood/DNA, and skin swab samples to the study – participants will be provided the opportunity to complete the study at New York University (travel costs provided by study) or at home.
- Compensation ($) is provided

Twin Breast Cancer Study

The National Institutes of Health (NIH) has provided funding to Dr. Thomas Mack of the University of California to study breast cancer risk factors in twins. Dr. Mack is partnering with the MATR to invite twins to participate.

Participants the study will need include:
- Female identical or fraternal twins with a history of breast cancer in one or both twins
- Ages 18+
- Full pairs are ideal but NOT required for participation

After completing the MATR invitation to “sign-up” to learn more:

Study participation involves:
- Providing the study with your consent and possibly medical authorization to access medical records related to breast cancer.
- Providing answers to questionnaires as well as a saliva sample for obtaining DNA.

For the past few years, our collaborators have focused their research on human behaviors and mental health. Recently, researchers have been in contact with us to see if it would be feasible to generate enough twin participants for research on physical health conditions. We are excited to get started on two new studies—one that wants to better understand psoriasis and psoriatic arthritis and another that will investigate breast cancer risk (see below for more). Lastly, there may be the opportunity to be a ticket to the event or a gift card for a modest dollar amount. Recipients are chosen by random periodic drawings, so please keep those updates, stories, and photos coming our way—even the next recipient of those one tickets! Read what some of our lucky members had to say below about being in the MATR:

We are pleased to introduce another collaboration between the MATR and the University of Southern California. This partnership represents a full circle in Dr. Mack’s career. A career, which spans impressive medical training at Columbia University, the Centers for Disease Control, National Institute of Health, and includes work on smallpox eradication, certain cancers, and Hodgkin’s disease. Much of Dr. Mack’s research, including his current work incorporating the MATR, has its footing in a chance meeting from a couple of decades ago. While serving on a National Institutes of Health committee evaluating grants, he happened to be seated next to Dr. Walter Nance. Many of our longtime MATR members will remember Dr. Nance because his work in pediatric twin studies at VCU helped lay the foundation for the Mid-Atlantic Twin Registry. Through their discussions about twin research, Dr. Mack saw the exciting potential for helping to overcome some of the challenges he faced in studying chronic disease. He realized that adult twin subjects could help him sort out the genetic, cultural, and lifestyle factors that play an all-encompassing role in the development of chronic diseases, like cancer. From that happenstance meeting, Dr. Mack went on to establish twin studies and registries that have helped solidify our understanding of certain chronic diseases. For example, twin participation in his research has helped his team learn that Hodgkin’s lymphoma has a strong heritable component and shares features with autoimmune diseases; that childhood exposure to sunlight (thus Vitamin D) seems to help protect against multiple sclerosis; and, that both genes and environment play a role in the development of malignant melanoma. Now Dr. Mack is seeking continued help from twins on his search for a clearer understanding of just how the factors that influence breast cancer risk (genes, environment, lifestyle choices, etc.) impact the likelihood of breast cancer development. As you can tell from just a few highlights of his impressive career, Dr. Mack is passionate about improving health outcomes. Both he and the MATR hope that MATR twins that are eligible for the study are equally passionate in supporting these efforts. See the Twin Breast Cancer Study advertisement in this newsletter and visit: go.vcu.edu/learnmore to sign up for more information.