Environmental Polymorphisms Registry NEWSLETTER

A Message From the Director

We want to thank you once again for your generous support and interest in the EPR. We will soon be entering our 6th year of study enrollment and are getting closer to our goal of 20,000 participants. We are also pleased that so many of you have been diligently returning your information update cards. That helps us tremendously in contacting you about future studies.

We also want to thank those of you who have participated in the Glucocorticoid Receptor Study. In this effort, we have reached about 45% of our recruitment goal. Furthermore, preliminary results from this study will be presented at the National Endocrine Society conference to be held in Houston, Texas later this year.

Please read on to find out about several new EPR studies that will be initiated this year, as well as an update on our EPR Health and Exposures Survey. Also, in our Educational Corner, we have written an article that provides examples of "gene-by-environment interactions," and discuss how these can impact our health. Some of the examples will be the focus of future EPR research. At the National Institute of Environmental Health Sciences, our primary mission is to reduce the burden of human illness by understanding how the environment influences the development and progression of disease. As an EPR participant, you will be contributing to this very exciting area of health research.

Finally, I want to let you all know that I am leaving the National Institutes of Health and will step down as Director of the EPR. I very much enjoyed working on this project and will miss interacting with all of you – but please keep up the good work. The EPR is a great resource for scientists that would not be possible without your help and dedication. Thank you again.

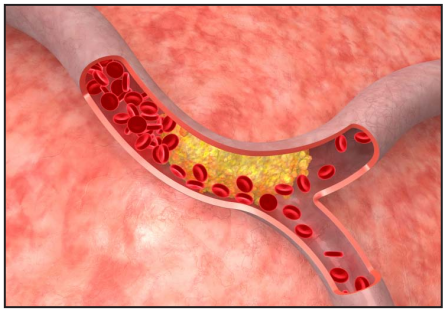
Sincerely,

Patricia C. Chulada

Pat Chulada, Ph.D., M.H.S.
EPR Director

COMING SOON: Go Green & Update Your Contact Information by E-mail

In the near future, EPR participants will have the option of updating their contact and demographic information electronically. If you have provided us with a valid e-mail address, we will send your annual contact letters and information update cards to that address. The e-mail we send you (from epr@sra.com) will be through a secure link. When you open the email, you will be channeled through to a secure website and then given instructions on how to use it for updating your information. Watch for this e-mail in the coming months, and help support our efforts to *"go green!"*



New and Ongoing EPR Studies

The Blood Vessel Study

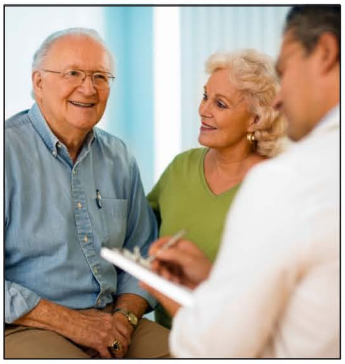
In this study, we will examine how two genes (CYP2J2 and EPHX2) affect blood vessel function and if they play a role in cardiovascular disease. The main components of our circulatory system are the heart, lungs, blood vessels and blood. The heart is a large muscle that pumps oxygen-poor blood to our lungs and oxygen-rich blood to other parts our body. The blood vessels provide the pathways through which the blood travels. There are two types of blood vessels – arteries which carry oxygenate-rich blood to our cells and tissues, and veins which carry oxygen-poor blood to the lungs.

In cardiovascular disease, fat, cholesterol, and other substances build up in the walls of our arteries and form hard structures called plaques. Over time,

as these plaques build up, they can block our arteries and make them stiff so the heart has to work harder at pumping blood. Inflammation speeds up the process of plaque buildup and stiffening, and contributes to the cardiovascular disease. The two genes being examined in this study, CYP2J2 and EPHX2, are important for maintaining the interior walls of our arteries. Polymorphisms (variations in gene sequence) that reduce the function of these genes, might contribute to cardiovascular disease.

In the Blood Vessel Study, Dr. Darryl Zeldin and other scientists at NIEHS and UNC will examine if having certain polymorphisms in CYP2J2 and EPHX2 affect the function of the genes, and in turn, examine whether that affects blood vessel function. They also will examine whether environmental factors such as diet, obesity, smoking, and living a sedentary lifestyle interact with CYP2J2 and EPHX2 in contributing to cardiovascular disease.

If you are asked to participate in the Blood Vessel Study, you will be required to visit our clinic for about 2 hours. During the visit, we will collect your blood and urine to measure



levels of lipids, inflammatory metabolites, and other analytes. You will also have an electrocardiogram (EKG) to test your heart function and a special test called flow-mediated dilation or FMD. FMD is a noninvasive test that uses ultrasound waves to test how well the blood is flowing through your arteries. For this test, a cuff (similar to a blood pressure cuff) will be placed on your arm and measure the blood flow in your brachial artery (main artery in your arm). We will take two FMD measurements, one before and after you take a short acting medication that relaxes your blood vessels. The ability of the brachial artery to relax is closely related to the ability of the heart arteries to relax, and can predict the risk for future heart and blood vessel disease. ■

EPR Health and Exposures Survey

In our last newsletter, we let you know about the EPR Health and Exposures Survey. We are pleased to announce that we have finished developing the Survey and it now under review by our ethics board. The Survey will be mailed out to EPR participants in phases, so some of you might see it in your mailboxes this spring. When you receive it, we hope that you will complete it and send it back to us.

The Survey will come in the form of a packet. The packet will contain the Survey booklet itself, step by step instructions on how to complete it, and a pre-stamped pre-addressed envelope for you to return it to us in (no postage is needed). You can take the Survey at your convenience. We find that it takes most people about 20 to 30 minutes to complete. When you are done, return the Survey in the envelope provided. Once we have your completed Survey, we will send you a $40 gift card. If you do not send us back the Survey, we will contact you and give you other options for taking it.

The information you provide is very important for the future of EPR research. It will help our scientists design future studies and select appropriate subjects for these studies. There are more exciting EPR studies on the horizon. Many of these studies are aimed at examining how our genes and environment interact, and how this can impact our health, but there will be other types of studies as well. In our Educational Corner, we describe several gene x environment interactions, that might come up for study in the next few years.

Have questions? Please feel free to call the Toll-Free Survey help line at 1-855-447-8374 or email us at EPRHealthSurvey@sra.com. The success of this Survey depends on you. We hope that you will find the time to take the Survey and return it to us.

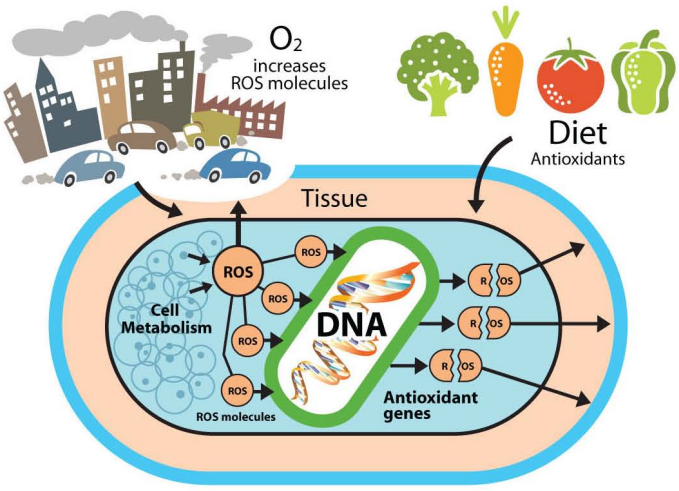
Educational Corner

Genes and Our Environment

Almost all human diseases result from a complex interaction between an individual's genetic make-up and their environments. Subtle differences in genetic sequences (called polymorphisms) cause individuals to respond differently to the same environmental exposure. This explains why some individuals have a fairly low risk of developing a disease as a result of an environmental insult, while others are much more vulnerable. As scientists learn more about how genetics and environmental factors work together, they can develop new strategies for the prevention and treatment of many diseases. In the past, most research has focused on unraveling the genetic components of disease, while ignoring the effects of environmental stimuli. At the National Institute of Environmental Health Sciences, we focus on both components of disease, and the EPR was developed as a special resource to help scientists achieve these goals.

When we refer to environmental factors in the context of contributing to human disease, most people think about toxic chemicals we are exposed to in our workplaces or at home, or in the air and water. But other types of environmental factors contribute to disease development as well. These can include the food we eat, cosmetics we use, and medications that our doctors prescribe. They also can include our habits such as alcohol consumption and recreational drug use, or leading a sedentary life style. Stress is a very important environmental factor and has been linked to cardiovascular disease, the progression of AIDS, and some forms of cancer. Research on gene-environment interactions show that children who experience highly stressful environments are more likely to become depressed as adults if they have a particular form of a gene that influences the level of the brain chemical, called serotonin.

One major focus of EPR research is the interactions between various genes and air pollution, and how these interactions might put us at higher risk for respiratory diseases like asthma, cardiovascular disease, and lung cancer. In these studies, we are looking at two groups of genes — the oxidative stress genes and the immune response genes. In this and previous newsletters, you have learned much about immune response genes but not the oxidative stress genes. These genes encode for proteins that remove reactive oxygen species (ROS) (superoxide, hydrogen peroxide, nitric oxide and others) from our bodies. Reactive oxygen



species are normal byproducts of cell metabolism but air pollution is another source of reactive oxidant species as well. If our oxidative stress genes are not functioning, oxygen radicals from our own metabolism and from environmental sources like air pollution can build up in our body and cause cell damage. Diet is another environmental factor that contributes to this process — antioxidants we get from our diet (vitamins C, E, selenium, carotenoids, and many others) are important compounds that help remove the reactive oxygen species. If we do not get enough of these antioxidants in our diet, this contributes even more to the damage to our cells caused by the reactive oxygen species.

In these efforts, one way we will estimate the amount of air pollution people are exposed to, is by measuring how close they live to a major roadway using geographical information systems (GIS) technology. Based on your address, GIS can pin point how close you live to a major road. The closer people live, the more they are exposed to higher levels of carbon dioxide and carbon monoxide, fossil fuel combustion products (benzene, formaldehyde, lead, many others), particulate matter, ozone and a host of other compounds. This might put them at higher risk for respiratory illnesses if they carry specific forms of the immune or oxidative stress genes. Also, we will determine air pollution exposures through the Environmental Protection Agency's (EPA) Air Quality System (AQS) and other databases. AQS is a database developed and maintained by the EPA – it monitors and tracks many different types of air pollutants across the state. With this database and with GIS, we can even look at your cumulative exposures over time. Stay tuned for more examples of "gene-by-environment interactions" in our next EPR newsletter. ■

Updating Your Contact Information

The success of the EPR depends on us being able to contact you for future studies. Therefore, it is very important that we have your current address, telephone numbers, and e-mail. This is why we send you letters and information update cards each year, asking you to confirm or correct what we have in our database. When you receive your information update card, please follow the instructions and return it to us by mail using the pre-stamped, pre-addressed envelope provided with it. Please send us back the card even if your contact information has not changed. If you prefer, you may update your information by phone(**1-866-809-1261**) or email (**epr@sra.com**).

Have Questions?

If you have questions about the EPR, or would like to contact us for any reason, we would love to hear from you!

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Environmental Polymorphisms Registry NEWSLETTER

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