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The Genetics & Pre-Eclampsia Study Turtle Mountain Community College

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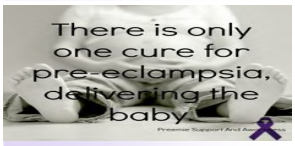
Special Points of Interest:

- Our genes are remarkably similar to those of other life forms. For example, we share 98% of our genes with chimpanzees, 90% with mice, 85% with zebra fish, and 7% with a simple bacterium such as E. Coli.
- If the genome was a book, it would be equivalent of 800 dictionaries. It would take a person typing 60 words per minute, eight hours a day, around 50 years to type the human genome.



Inside this issue:

My story about pre-eclampsia...

I was 15 years old when I was pregnant with my first baby. I started my prenatal appointments late. Everything was normal when I went in at 6 months. They noticed protein in my urine at the doctor's office shortly after that. Then, they wanted to see me every few weeks. Then, my blood pressure started to get high. I started to swell with edema. The doctors were worried and wanted me on bedrest when I was 7 months along. They gave me medication (atenolol) for my blood pressure. They told me my baby would not be born full term. After one of my prenatal appointments they called me at home and wanted me to go to the ER. I was in the hospital at Belcourt for two days at 36 weeks. Then they sent me to Minot to be induced. They gave me pitocin to induce labor and magnesium sulfate so that I wouldn't seizure during delivery. My first baby was 5lbs. 10oz.

With my second baby I started a low sodium diet right away to try to not have high blood pressure. *Editors note: low sodium diets are not generally recommended* Everything seemed to go well until I was 31 weeks. Then, the labs started to come back badly. I had to go in for appointments all the time. My blood pressure was really high, and they induced me again at 34 weeks. My second baby was 6lbs. 7oz.

With my daughter (my last baby), my first prenatal was fine, but by the second prenatal at 7 weeks my blood pressure was really high. I got sick really fast. They put me on bedrest right away. I had to go in for appointments all the time. They gave me shots for my high blood pressure. I was in and out of the hospital for the whole pregnancy. Once when I was in the hospital they gave me medication to make my blood pressure go down, but they gave me too much. My blood pressure dropped so much from the medication that I passed out. My mother told me that they were calling for more nurses and it was an emergency. They gave me steroids to get my daughter ready to be born early. They induced me in Rolla at 32 weeks. When we started the induction they told me that the hospital might not be able to handle the baby because she was so early and her lungs might not be ready. They had Trinity in Minot on standby if needed. My daughter was born in Rolla at 4lb. 1oz. She came out breathing. We were in the hospital for a week and then they let us go home. I decided to get my tubes tied because I didn't want to

"DNA is a blueprint of life"

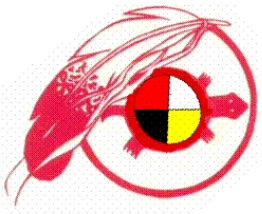
Teamwork

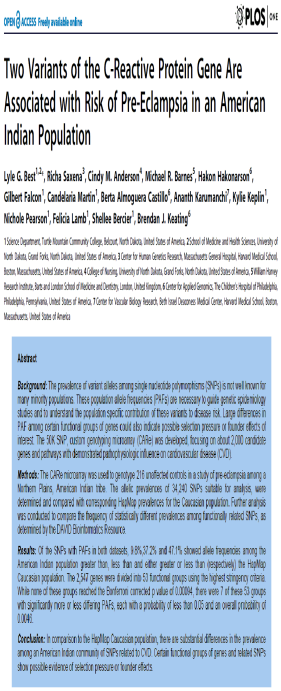
Most advances and discoveries these days are made by teams of scientists. Our genetics and Pre-eclampsia Study is no exception. From the start we have been funded and assisted by the University of North Dakota and faculty there. Besides all the help from the TMCC students (over 30 now) that have worked on this project; Drs. Gilbert Falcon and Candelaria Martin (at Devils Lake) have assisted with recruiting participants in the study and in other ways. Dr. Laramie Lunday analyzed and collected data for an article that will be published soon. Dr. Cindy Anderson was on the Nursing faculty at UND until moving to Ohio State University (see the section on CRP for details about her important contributions). As mentioned in the "publications" section, we worked with a number of other scientists on the East Coast to help confirm our initial results about the CRP gene. Drs. Shelley Cole and Karin Haack at the Texas Biomedical Research Institute have assisted in doing specialized tests on the CRP gene from about 95 of those with PE to see if there are other small DNA changes from Turtle Mountain people that haven't been found anywhere before (we found 4 so far). We hope to be working with tribes and their medical staffs in Oklahoma in the near future.

Even though it is sometimes necessary to share samples and information from our study, we are always careful to make sure that no one outside of the TMCC study has any identifying information. We are also careful to make sure that outside partners will not use any DNA or information for studies that are not about pre-eclampsia. The Tribal Nations Research Group at Belcourt also reviews

Published Papers

Since our last newsletter our study has published two reports of our results in a well-recognized journal called "Public Library of Science, One" or more commonly abbreviated as "PLoS 1". The most important was a more detailed analysis of changes in the CRP gene; and other authors from the University of Pennsylvania and Harvard that cooperated with us found similar results in a separate group of non-Indian, pre-eclampsia patients from the East coast. You will notice that there are many TMCC students and local doctors that have contributed and are listed as authors.





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Two Variants of the C-Reactive Protein Gene Are Associated with Risk of Pre-Eclampsia in an American Indian Population

Lyle G. Best[1,2], Richa Saxena[3], Cindy M. Anderson[4], Michael R. Barnes[5], Hakon Hakonarson[6], Gilbert Falcon[1], Candelaria Martin[1], Berta Almoguera Castillo[6], Ananth Karumanchi[7], Kylie Keplin[1], Nichole Pearson[1], Felicia Lamb[1], Shellee Bercier[1], Brendan J. Keating[6]

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Abstract

Background: The prevalence of variant alleles among single nucleotide polymorphisms (SNPs) is not well known for many minority populations. These population allele frequencies (PAFs) are necessary to guide genetic epidemiology studies and to understand the population-specific contribution of these variants to disease risk. Large differences in PAF among certain functional groups of genes could also indicate possible selection pressure or founder effects of interest. The 50K SNP custom genotyping microarray (CARe) was developed, focusing on about 2,000 candidate genes and pathways with demonstrated pathophysiologic influence on cardiovascular disease (CVD).

Methods: The CARe microarray was used to genotype 216 unaffected controls in a study of pre-eclampsia among a Northern Plains American Indian tribe. The allelic prevalences of 34,240 SNPs suitable for analysis, were determined and compared with corresponding HapMap prevalences for the Caucasian population. Further analysis was conducted to compare the frequency of statistically different prevalences among functionally related SNPs, as determined by the DAVID Bioinformatics Resource.

Results: Of the SNPs with PAFs in both datasets, 9.8%, 21.2% and 47.1% showed allele frequencies among the American Indian population greater than, less than and either greater or less than (respectively) the HapMap Caucasian population. The 2,547 genes were divided into 53 functional groups using the highest emergency criteria. While none of these groups reached the Bonferroni corrected p-value of 0.0094, there were 7 of these 53 groups with significantly more or less differing PAFs, each with a probability of less than 0.05 and an overall probability of 0.049.

Conclusion: In comparison to the HapMap Caucasian population, there are substantial differences in the prevalence among an American Indian community of SNPs related to CVD. Certain functional groups of genes and related SNPs show possible evidence of selection pressure or founder effects.

CRP GENE

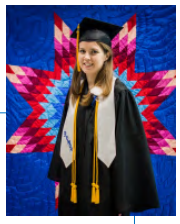
Our immune system makes something called "C-reactive protein" or "CRP" that circulates in our blood. Like every other protein in our bodies, we need to inherit a gene ("blueprint") from our parents to make this protein properly. If there is a serious change in this gene, our CRP may not work at all. If there is a milder change (and all of us have many of these) called a single nucleotide polymorphism (SNP) the effect may be smaller; but still important. Our lab at TMCC was the first to find SNPs (3 so far) in the CRP gene that seem to increase risk for PE. Since then, two other groups of scientists have also found changes in this gene that affect PE.

Even more exciting, in 2015 researchers at the University of Texas found that CRP is made in the baby's placenta as well as in mom's liver (which we knew before). They also showed that more CRP is made in the placenta of babies whose mothers have PE, than in normal pregnancies. This made the idea that CRP is increasing the risk of PE even more likely; and with help from Dr. Cindy Anderson, we obtained some placentas from non-Indian women to re-test these results. Using a new, more challenging technique than what we have done before at TMCC, called "gene expression" analysis, our lab is finding similar results and this helps us be more confident of these findings. We are now in discussions with two tribes in the Oklahoma region that also

Saliva Kits that are used to collect samples from participants

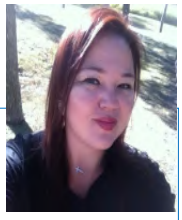
"The greatest single achievement of nature to date was surely the invention of the molecule DNA."
– Lewis Thomas

ASHLEY PARISIEN



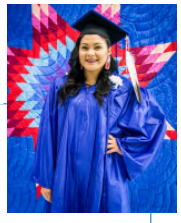
Hello, My name is Ashley Parisien. I was born and raised by the Turtle Mountains. I am a senior in the Secondary Science program at Turtle Mountain Community College. My first experience working in a genetics laboratory was provided by the University of North Dakota through their REU (research experience for undergraduates) program. Shortly after that I was hired in to the Genetics and Pre-eclampsia lab at TMCC. After I complete my Bachelor's degree in Secondary Science at TMCC I plan on pursuing my PhD in one of the science fields.

CRYSTAL A. AZURE



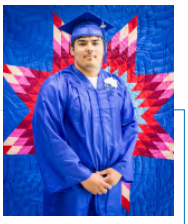
Boozhoo! My name is Crystal A. Azure, enrolled member of the Turtle Mountain Band of Chippewa. I am a returning (first generation) college student pursuing a degree in nursing and will be transferring to UND to obtain my BSN. I have been working on the Genetics/Pre-eclampsia research study for 2 years. I have learned a lot about genetics during this time and I am confident this will help me along my journey to becoming a successful nurse!

MEMPHIS BELGARDE



Hello, my name is Memphis Belgarde. I am an enrolled member of the Turtle Mountain Band of Chippewa. I will be starting my Sophomore year this fall at TMCC. Once finished here, I plan to continue my education at NDSU Fargo studying Medicine. I have had the opportunity to work in the lab on the Genetics & Pre-eclampsia study at TMCC since the summer of 2015 and have learned a lot about genetics. Many thanks to Dr. Best for the wonderful experience.

JESSE RODRIGUEZ



Hello! My name is Jesse Rodriguez. I am an enrolled member of the Turtle Mountain Band of Chippewa. I will be starting my Sophomore year this fall at TMCC with a focus on Pre-Nursing. I will then transfer to NDSU Fargo to further my education of becoming a Registered Nurse. While attending TMCC I was able to work on the Genetics & Pre-eclampsia Study with Dr. Best. I have learned a lot working in the lab and about genetics. It has been a great experience. Thank you a lot Dr. Best for all you have taught me.

DR. LYLE BEST

Hi, my name is Dr. Lyle Best. I have worked with people in the surrounding area since 1977, both as a family doctor and as a teacher at the community college. In 2013 my wife (Sue) and I moved to join my son's family on their ranch 14 miles south of Watford City. I still help teach residents in Minot; but gave up my regular medical practice and part time teaching at Turtle Mountain Community College. I continue to do my research with the Genetics and Preeclampsia Study by visiting TMCC each month and maintaining close contact with the students that work on our project. I am also involved in 3 other research projects in American Indian communities, the Strong Heart Study (heart disease), Factors Influencing Pediatric Asthma (Cheyenne River Sioux) and another project attempting to reduce arsenic exposure from private wells.