

## **“The Natural History Study in Oakland, CA and Building the DNA Repository for Rett syndrome”**

Contributed by Dr. Jeffrey Neul, Baylor College of Medicine and the Duncan Neurological Research Institute at Texas Children's

The blood collection went extremely well in Oakland with 40 families participating and 108 people providing blood samples. Unfortunately, there were a number of people who had previously agreed to participate but were unable to due to time constraints of the blood draw team. I want to extend a sincere thank you to everyone who participated and the entire Oakland team for making it happen, and my heartfelt apologies to those who wanted to participate but were unable. We are working out details to possibly have similar blood draws occur at the monthly Katie's Rett clinic at Children's Hospital Oakland. Hopefully we will have more details on that to follow.

Currently, we are working out the possibility to do similar blood draws in Chicago, but we are awaiting approval from Rush's Internal Review Board. Nonetheless, anyone who will be attending that site visit and is interested in participating in the blood sample collection should contact my research coordinator, Amber Pearce, at 832-822-1790, to register interest. We will proceed with obtaining consent at this time. Just a note-although the consent forms mention skin biopsies, this is not something that will occur at the Chicago site visit. Also, the information mentions that we would like to try to collect samples from parents and siblings. At this time, we are only focusing on siblings who are the same gender and about the same age. Additionally, the only person who we absolutely would like a collection from is the person with Rett syndrome, so if one parent cannot make it or if the child is adopted the family is still eligible to participate. Also, even those people who have already given blood can give blood again-we are collecting additional types of samples (for RNA and plasma) that we have never collected before.

If we are able to do the blood draws in Chicago, it will be very, very important for interested families to contact us beforehand. Although we would like to provide the opportunity to decide to participate at the site visit, the Chicago site is very busy and we may need to restrict any blood draws to those people who have already agreed to participate.

Many people ask me the purpose of the blood collection. The overall purpose to provide biological samples from everyone enrolled in the Natural History Study. This will allow us to retain these materials and compare to the wealth of clinical information we have obtained in the study. One of the first things we will be doing is looking for genetic mutations in genes other than *MECP2* for those people with Rett syndrome who do not have any identified genetic mutations. There are over 60 such people enrolled in the Natural History Study.

Another top thing that we will be doing is determining the X-chromosome inactivation for everyone enrolled in the study. We know that this contributes to clinical variation in Rett syndrome.

In the future, I hope that we can check all the mothers for the mutation in *MECP2* found in their children. This would let us know how many people are carriers of the mutated *MECP2*.

Finally, a major goal is to use these samples to find other biological sources of clinical variation in Rett syndrome. We know that even in people with the same mutation in *MECP2* there may be clinical differences-for example, some people can walk whereas others cannot. We hope to use the blood samples and the clinical information from the Natural History Study to try to identify genetic or other biological factors that may account for this variation. We hope that by finding these things, we may be able to use that information to develop treatments that would improve the function of everyone.

On a related note, we will be doing similar blood collections in Houston for routine visits to Drs. Neul and Glaze. My team will be contacting families in the month preceding a routine clinic visit to discuss the research and obtain consent from interested parties. It is important and necessary for us to discuss this before the scheduled visit because we need to coordinate a separate visit at that time with the blood drawing team in the research center.