Hello Families!

As you know, we are committed to sharing what we have learned from your participation in the Simons VIP research study. We are excited to announce that the first round of community results have been posted in the members-only section of the website. **You will have to log-in to view the results.**


Prior to reviewing the results and graphs, we strongly encourage you to watch the following webinars. They provide an introduction to the VIP Community Results and give instructions on how to read the community results graphs.

⇒ Introduction to VIP Community Results (2:39 minutes)  
[https://www.youtube.com/watch?v=iX3FeoB5XUE](https://www.youtube.com/watch?v=iX3FeoB5XUE)  
This video gives an overview to the types of results that are being shared.

⇒ Understanding VIP Community Results Graphs (3:13 minutes)  
[https://www.youtube.com/watch?v=7rSnFM0uZDw](https://www.youtube.com/watch?v=7rSnFM0uZDw)  
This video will help you to understand how to interpret the community results and graphs.

At this time, group results are posted only for 16p11.2 deletions and duplications. As more 1q21.1 families and more families with changes in single genes participate, we will be updating and adding to these results. Individual results are in process; we hope to have these ready to share by early April 2015! Stay tuned!

Questions about what you’re reading? [Email us](mailto:).  

Sincerely,  
The Simons VIP Study Team  

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This newsletter features the following topics:  
⇒ **Pg2**: Family Meeting Updates: t-shirts and agenda  
⇒ **Pg3**: Research Article Summary (16p11.2 and mGlur5)  
⇒ **Pg4**: 16p11.2—scoliosis, 1q21.1—gene list!  
⇒ **Pg5**: Meet our new coordinator, Kara.

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**Facebook Groups**

‘Single gene’ families, we are SO EXCITED to begin our relationship with you to help expand our understanding of your children’s gene changes. We’re hoping that you have found our groups on Facebook as another way to connect with one another. If you haven’t, check them out and join!  

[ADNP, GRIN2B, CUL3, SYNGAP1, SMARCC1, SCN2A, REST, DYRK1A, DST, CTNNB1, CHD2, BCL11A, ASLX3, KDM6B, ARID1B, CHD8, ANKR1D11, FOXP1, MBDS, MED13L, KMT2E, PTEN, SMARCC2](#)
NEW!!!! 16p11.2 T-Shirts

Available in either blue or black, these shirts have the same logo on both the back and the front left pocket-area of the T-shirt.

Sizes: Youth Small to Adult 5X (can also be ordered in tall sizes!)
Prices: Youth Small to Adult XL = $15; Adult 2X to 5X = $17
⇒ Prices do not include shipping and handling
⇒ S&H is based on location and number of shirts ordered
Contact Belinda to order! supermomchat3@gmail.com

More Meeting Information:

We’re excited about the talks for 1q21.1 families this year! We hope 1q families are planning to attend!

Room Rates:

$99.00 for king or two double beds; $149.00 for junior suites at the Westin in Tysons Corner, DC.

We expect to launch the registration website on March 13, 2015 which will include a special reservation link to the hotel.

The Agenda:

All 3 days: Research rooms are open; Ask the Expert time slots are available. You’ll be able to sign up for a 1:1 session to talk with experts.

Friday: The doors open at 9AM, but we don’t have any talks scheduled until the afternoon.
Friday’s focus is 1q21.1 from 4-6 PM.

We recommend coming early on Friday if you have plans to participate in research activities, meet with other families, or have fun outside of the hotel.

We’ll have childcare available from 9AM to 6:30PM, and a welcome dinner starting at 6:00PM.

Saturday: The doors open at 7:00 AM. Morning sessions are applicable to all attendees, regardless of your genetic diagnosis.

From 1-3:30PM, there will be talks specific to 16p11.2 families.

Breakfast, Lunch, and Dinner are provided.

No research activities will occur during the sessions on Saturday!

Sunday: We’ll be offering more research opportunities and additional time for families to connect with each other.

Thanks to your feedback, we’ve built long breaks and multiple group meals into the schedule; we recommend taking time to talk with each other!

Stay tuned for additional updates and watch for registration information coming soon!
Contribution of mGluR5 to pathophysiology in a mouse model of human chromosome 16p11.2 microdeletion

The VIP Summary: Treating Autism in 16p11.2?

Read the abstract at: http://bit.ly/1C332pA

Before we can get into some of the exciting details from this article, we need to start off with some background information. As you may already know, there are hundreds of genetic causes of autism, Fragile X syndrome and 16p11.2 deletion syndrome being two of the most common. The 16p11.2 deletion is thought to be the most common genetic cause of autism, accounting for up to 1% of all cases of autism. Fragile X syndrome is the second most common genetic cause of autism that involves an entirely different chromosome (the “X” chromosome). You might start hearing more about Fragile X syndrome in relation to 16p11.2 deletion syndrome, which is why we wanted to give you some background information about how common they are, and how these two different genetic causes of autism actually affect similar biological processes in the brain that result in autism.

Even though the scientific details of this research study can be overwhelming to read, we have some take-home points that our Simons VIP families may find interesting. Until very recently, there weren’t specific medications available to treat autism. Within the past several years, many researchers, including Mark Bear (an author of this article) and his research team, have worked toward understanding the biology of Fragile X syndrome with the goal of creating a medication to treat symptoms of this syndrome. They began with mouse models and eventually worked toward studying the use of this new medication in people who have Fragile X syndrome. While the preliminary results were not perfect, they were promising, so the FDA approved a second phase of drug trials for Fragile X syndrome in late 2013.

Does this mean we can treat the symptoms of autism? In some kids with 16p11.2 deletion or with Fragile X, it might be possible. The reason for this is because 16p11.2 deletion and Fragile X both lead to problems with the same protein in the body that is important for managing messages related to memory and learning; this protein is called mGluR5. Because of this shared messaging problem, there’s a possibility for a shared treatment that targets this protein, a type of drug called an mGluR5 antagonist.

Does this mean we can expect the same results for our 16p11.2 families? Not necessarily, but it does mean that we have a place to start. One major difference that will have to be considered is that while 16p11.2 deletion and Fragile X do both involve problems for mGluR5, they are different problems. In people with Fragile X syndrome, the mGluR5 problem causes too much messaging, while in 16p11.2 deletion, too few messages are made.

Randi Hagerman (Director of the MIND Institute at UC Davis) says, “I think that the mGluR5 antagonists are going to be helpful for young children with fragile X, but I think they could also be helpful for many young children with autism, particularly this 16p11.2 microdeletion subgroup.”

We might not have more information about this possibility for a long time, but this is definitely an exciting time. Cheers to the future!

Simons by the Numbers
As of February 2015... there are 125 16p11.2 families participating and 28 1q21.1 families participating in Phase 2!!!!
What do we know about genes involved in 1q21.1?

In the “typical” 1q21.1 deletion or duplication, there are about 20 genes that are missing (deleted) or extra (duplicated). Some have not been researched at all, and have been left out of the summary.

The genes we understand (even a little bit) are described below:

**NBPF8, NBPF10, NPPF11, NBPF12, NBPF13P, NBPF25P**

These genes that begin with “NBPF” have been found in children with features like macrocephaly, autism, schizophrenia, intellectual disability, congenital heart disease, neuroblastoma, and problems with the kidney and urinary tract.

This gene family contains many **pseudogenes** (see definition in box to the left).

**PRKAB2** Important for regulating energy in cells (involved in making fatty acids and cholesterol for cells)

**FMO5** Two missing copies of this gene are associated with a condition called “Trimethylaminuria,” which causes an unusual odor.

**GJA8** Important for the growth of specific cells in the eye called “lens fiber cells.” Missing copies of this gene (deletions) can result in an increased chance for cataracts.

**CHD1L** Important in chromatin remodeling (this is like “behind-the-scenes” work with preparing DNA to be used, read, or copied).

**BCL9** The function of this gene is unknown when it is deleted or duplicated in a person. Errors in this gene have been found in patients with B-cell acute lymphoblastic leukemia. The errors with this gene are thought to happen in a person’s cancer cells (which are usually genetically different than the cells in the rest of a person’s body. We do not think that people who have deletions or duplications of this gene are at an increased risk for leukemia.

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**What is a pseudogene?**

Pseudogenes are thought to be inactive gene. (“Pseudo” means “fake” in Latin.)

They are similar to normal genes, but are not functional.

The information or “genetic sequence” of a pseudogene is often similar to another gene that has a job in the body.

Psuedogenes arise because of copying errors that have happened in the past. They are actually copies of other functioning genes, that were incorporated into a person’s DNA a very long time ago, but no longer have a job.

Psuedogenes are considered “non-coding” DNA.

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**Does your child have scoliosis? 16p11.2 and TBX6 gene**

There is an increased chance for scoliosis in people with 16p11.2 deletion.

The **TBX6** gene is part of the typical 16p11.2 deletion. People with the deletion have only one copy of the **TBX6** gene because the second copy is missing (or “deleted”).

The **TBX6** gene is important for early development of the spine and skeletal muscle.

Many people with the deletion do not have scoliosis.

So then, why do some people with the deletion have scoliosis and not others?

The reason for this is likely due to a specific genetic change on the other **TBX6** gene on chromosome 16 (the one that’s NOT deleted). This genetic change is natural variation, meaning in most circumstances, it has absolutely no noticeable effect on a person’s health. However, this certain genetic change on one copy of chromosome 16 **in combination with** the deletion on the other copy seems to greatly increase the chance for scoliosis.
Meet Your Newest Coordinator!

We are SO excited to welcome our newest Study Coordinator, Kara! We love having her in the office! Kara received her B.S in Biology from Mansfield University in 2010 and received a Master of Public Health degree in Epidemiology from The George Washington University in 2012. Kara has 5+ years’ experience working as a research coordinator where she focused on a wide range of studies from chronic disease to rare genetic conditions. Kara currently works at Geisinger Medical Center in Pennsylvania as a Research Coordinator in the Genomics Medicine Institute. In her free time, she enjoys running, hiking with her dog, watching baseball games, learning to play the banjo, and spending time with friends and family.

Kara is excited to join the Simons VIP team!

You can get in touch with any of us by calling 855-329-5638 or by emailing us at coordinator@simonsvipconnect.org