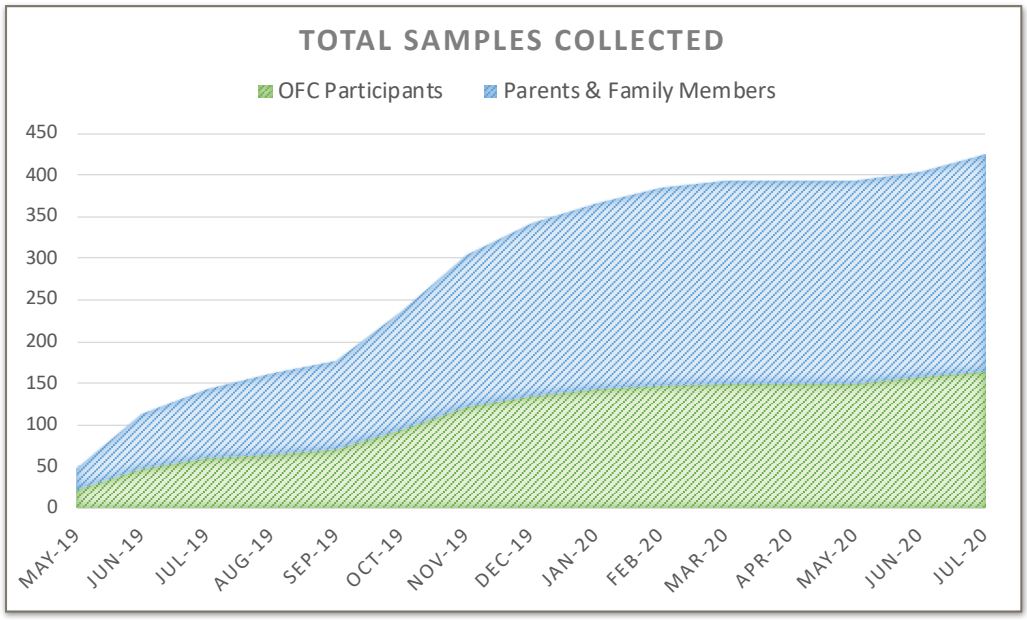
Emory Cleft Project

Summer Newsletter

LESLIE LAB ~ AUGUST 2020 ~ ISSUE 3 ~ VOLUME 1



Recruitment Update:

After briefly suspending sample collections for our study, we are now recruiting and enrolling new participants, and have resumed shipping and receiving sample collection kits. Since our last newsletter, we have passed several benchmarks, including receiving over 300 completed surveys and over 400 returned samples from our cleft families.

349

FAMILIES

Currently enrolled in our study since enrollment began March 2019

314

SURVEYS

Number of online surveys that have been completed so far by participants

426

SAMPLES

Received from individuals with OFCs, their parents, and other family

Study Reminders

If you haven't completed your surveys- we still want to hear from you! Please contact us to get your access link.

If you have enrolled in our study but have not yet received or returned your samples, or if you need help with collection including a new sample collection kit, please contact us!

Don't forget to send pictures to our secure email for our records!

If you have recently changed your home or mailing address, email, or phone number, please provide us with your updated contact information!

Publication Update:

The lab of Dr. Elizabeth Leslie recently published a study that identified a specific set of genetic variants in individuals with orofacial clefts (OFCs). The unique set of variants summarized in this study are variants that were found in the affected individuals but not in their parents; these variants are commonly called *de novo* mutations. *A link to the full manuscript is available on our website.*

What are *de novo* mutations?

De novo mutations **(DNMs)** are variations (changes) in genes that can occur randomly in the sperm of the father, the egg of the mother, or in the early stages of the baby's development during pregnancy. There are different kinds of DNMs; for this study we focused on DNMs that were located within areas of genes that contain "codes" for making proteins (**coding DNMs**). These "codes" give instructions for how certain proteins needed for the baby's development are formed and how they work. By changing the codes, DNMs can directly affect the proteins, which can impact development in a number of different ways. Some DNMs make changes to the genetic code that prevents the proteins made by that gene from functioning in the same way that it would without the mutation- these kinds of changes are referred to as **loss-of-function variants**.

What was the study about?

While DNMs are known to increase risk of other birth defects, their role in OFCs has not been fully explored. The goal of this study was to identify DNMs in individuals with OFCs. The data for this study came from a group of participants that were genetically screened as part of the **Gabriella Miller Kids First Pediatric Research Consortium**, established in 2015 with the aim of addressing gaps in the understanding of the genetic contributions to structural birth defects (such as OFCs) as well as pediatric cancers.

What did we find?

Overall, we found that individuals with OFCs had significantly more **loss-of-function DNMs** than we would expect to see by chance, specifically in genes which produce proteins in craniofacial tissues, as well as genes that are associated with known inherited OFC syndromes. This analysis also revealed roles for specific sets of genes in OFC development. The analysis in this study is the largest genetic exploration of coding DNMs to date. Our findings clearly demonstrate that coding DNMs in sets of genes that are both **biologically relevant** *(i.e. in areas related to craniofacial development)* and **clinically relevant** *(i.e. in areas previously identified for known OFC syndromes)* may contribute to the risk of Orofacial Clefts. **Our next steps are to replicate these findings with samples collected from our Emory Cleft Project families**.

An important part of the Emory Cleft Project's mission is to keep participants and other OFC families up-to-date and informed about our study progress. In addition to newsletters, we will continue to post study updates, summaries and links of recent publications, and other relevant information on our website (emorycleftproject.org) and social media accounts. We greatly appreciate your participation and continued support of our research!

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