

New Genetic Discovery

Dear Friends

This newsletter is prompted by the recent discovery that mutations in the C9ORF72 gene are the most common cause known to date of both familial and sporadic ALS. We are proud to have been part of one of two teams of scientists that published these results side by side. Our ability to contribute to this international effort was made possible by your active and generous participation in our research studies. We want to write and thank each of you for joining us in this partnership and for all that you are doing to help advance ALS research.

We started studying familial ALS not only because of the potential benefits for families with ALS, but also because we believe that advances in our knowledge of the genetics and biology of familial ALS (fALS) have great potential to improve our understanding of all ALS. Studying fALS and sporadic ALS are mutually helpful - what we learn from each helps move us closer to developing effective therapies for all patients with ALS. Our last newsletter highlighted two discoveries (mutations in the TARDBP and ubiquilin-2 genes) that made the important connections between familial and sporadic ALS. The C9ORF72 story is another great example and even more important, because it is so common and it may cause both familial and sporadic ALS.

For more information about this new genetic discovery, please visit www.als-research.org. Since

many of you have asked about how this new genetic discovery creates new opportunities for you and your family to participate in research, we have devoted the rest of the newsletter to answering this question.

Until recently, we knew the genetic cause of ALS (i.e. SOD1, TARDBP, FUS, VCP, etc.) in only 25-30% of fALS families. Our collaborative efforts to identify new genetic causes of ALS were driven by our desire to learn the genetic cause of fALS in as many families as possible. Now, with mutations in the C9ORF72 gene identified, it should be possible to identify the genetic cause of fALS in 50-60% of families – double that compared to what we knew just a 6 months ago. This means that many more people will be able to participate in Pre-fALS, our study of individuals at genetic risk for developing ALS.

We also believe that C9ORF72 represents an attractive target for gene therapy. We have started to explore this and will work diligently towards a clinical trial of a treatment that may help people with both familial and sporadic ALS; and hopefully a treatment to prevent fALS. There is, however, much that we still need to learn about this gene and clinical trials may still be several years hence. For those 40-50% of families whose genetic cause is still unknown, we will continue to partner with geneticists in an effort to discover new genes. Our ability to make progress is critically dependent on your ongoing engagement and participation.

Thank you.

The ARC Team

Research Opportunities

- If you have ALS, irrespective of whether or not you have a family history of ALS, please contact us to donate a blood sample for genetic testing
- If you are healthy but have a family history of ALS and we are able to identify the genetic cause of ALS in your family, then you may be eligible to participate in the Pre-fALS study

With questions about this new genetic discovery, what it means for you and how it might impact your ability to participate in research, please contact us at: fals@med.miami.edu