FTD DISORDERS REGISTRY®

The VOICE of FTD

SUMMER 2021

Sponsored Genetic Testing Programs for FTD

What are they? How do they differ? Which one is right for you?

A recent increase in the number of new clinical trials that target specific types of frontotemporal degeneration (FTD) caused by gene variants, or mutations, has prompted potential participants to learn their genetic status. To identify patients for these trials, drug companies have begun **sponsoring genetic testing programs**.

These programs offer genetic testing at no charge to those who meet certain criteria. This enables them to get tested — and possibly understand the genetic cause of their FTD, if there is one — no matter their economic status. Sponsors provide financial support for the testing and often receive de-identified variant and clinical information as well as contact information.

"Sponsored genetic testing programs (SGTP) fill a void between what insurance companies will cover and what needs to be known to determine if someone qualifies" for a study, stated Karmen Trzupek, MS, CGC, Director, Rare Disease Genetics and Clinical Trial Services with InformedDNA. "There are also reasons for those who do not wish to participate in studies to consider genetic testing."

The programs exist because insurance companies in the United States determine coverage for genetic testing based on whether the results would change how the person's medical treatment would be managed, Trzupek said. "That change in medical management must be based on evidence and what is currently FDA approved."

All clinical trials by definition are experimental and investigational, and therefore they are not FDA approved. There currently are no approved treatments for FTD. In many cases, this leaves the financial burden of genetic testing on those diagnosed with FTD and their families.

"That's going to drastically reduce the pool of patients and we're not going to have enough to fill clinical trials," Trzupek said. "And it's going to lead to huge discrepancies between the haves and the have-nots in the population who can participate."

Lack of diverse representation in research studies can create bias for the results.

People may choose to seek genetic testing through their doctor. However, Trzupek said that doctors often

Please note that this glossary is available to help you understand the scientific terms used in this article. Glossary terms are shown in bold the first time they appear.

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cannot get testing covered through insurance because it is not the current standard of care for FTD. Some doctors have success getting insurance to cover FTD genetic testing when they order it for patients who are unusually young or have strong family histories, but not for most patients. As a result, when doctors order genetic testing for FTD today, many of them order it through one of the same sponsored testing programs described at the end of this article.

In some diseases, genetic testing can be used as a primary method of diagnosis.

"From an insurance perspective, if 90 percent of patients would get a positive genetic test result, then the insurance companies might change their minds and say this should be the first line of testing when a doctor suspects FTD because when it is positive, that would eliminate other tests or a period of uncertainty," she said. "But we aren't there yet."

Knowing genetic status allows persons diagnosed with FTD to make informed decisions pertaining to their medical care and participation in clinical trials.

"We are rapidly entering this phase where most clinical trials are going to be **precision medicine**-based therapeutics. They are very specifically targeted to certain types of disease," Trzupek said. "Precision medicine isn't all genetic, it's just therapeutics designed to target very specific subtypes of disease based on what's causing them."

"We don't think about frontotemporal dementia as one disease. We think about it as GRN-associated frontotemporal dementia, MAPT-associated frontotemporal dementia," she noted.

Reasons to have genetic testing

For persons diagnosed with FTD, learning your disease's genetic status has benefits to you, your family, and science. This is true whether your test results are positive or negative and whether you choose to participate in research.

Some people choose to undergo genetic testing because they want to be a part of something bigger, they want to contribute. Many who have a dominantly inherited disease say that part of the reason they participate in clinical trials is for the younger people in their family — for their kids, their grandkids, their nieces, and nephews.

Reasons people say they want to have genetic testing done include:

- They want to know if they would qualify for a clinical trial or therapy.
- They want to understand any genetic risks for their family.
- They want to broadly contribute to research and to leave this place better.
- Their physician suggested genetic testing.

Knowing your genetic status now may be beneficial in the future for clinical trials or treatments. For example, someone who tests positive for the progranulin variant (*GRN*) may decide not to participate in a study now

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because the nearest site is far away, thus requiring a lot of travel which would be a burden to them and their family. However, a year or two later there could be a new phase for the trial with a nearby location. The person's physician, also knowing their genetic status, could then contact them with the information to reassess whether they are interested in participating.

The availability of these programs has improved access to genetic testing for the FTD population. It also creates a communication pathway for persons who test positive for an FTD gene variant to be informed about future advances in FTD treatments.

Reasons to have genetic counseling

Counseling both before and after testing is an important part of the whole process, Trzupek noted. This is important for making an informed decision about whether to have the testing done as well as for understanding the results if you do.

"There should always be mechanisms in place to ensure there is support for individuals undergoing genetic testing," she said. "Patients need to have somebody who sits down and talks with them about their genetic test results. We want to make sure they get access to good information and can ask questions."

Results may be as simple as positive or negative. However, they also could be inconclusive, with genetic variants of unknown significance (VUS). These need more study to determine if they can cause FTD.

Also, the result may come back negative, but if there are family members with FTD there still could be a genetic component that just hasn't been discovered yet. Researchers continue to find new genes. This means that sometimes genetic testing has to be done again looking at any new genes before a cause for FTD can be determined.

Here are questions to ask before having genetic testing done for FTD:

- What am I being tested for?
- Is this test for a specific FTD gene?
- If this test is for a panel, which genes are included?
- What is the potential that I will need to be tested again later?
- Is this the same test I would get if I went to my doctor?
- What happens with my data?
- Could this impact my insurance?
- Could this impact the insurance of my family?
- If it is found out to be hereditary, could that impact my child's ability to get insurance? Or could it impact her deductible?

Resources for Genetics in FTD

The following handouts were created in collaboration with the Penn FTD Center to provide information to help people understand the genetics of FTD:

1. Understanding the Genetics of FTD
2. Who Should Consider Genetic Testing for FTD, and Why?
3. Understanding Genetic Testing
4. Understanding Genetic Counseling

In addition, we have provided a selection of resources on the Registry's new Genetics in FTD page.

Sponsored genetic testing programs for FTD

Unfortunately, there isn't much information available in the public domain about available sponsored programs and research studies offering genetic testing for FTD.

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To fill this void, an analysis of available programs was prepared by Erynn Gordon, MS, CGC, of Ripple Genetic Consulting for The Association for Frontotemporal Degeneration (AFTD). Her report includes information about the three currently available FTD programs, their benefits and their limitations.

These programs vary by what gene tests they do, whether they only test persons diagnosed with FTD or also test unaffected family members, and if testing is available outside the United States. All of these programs test for the progranulin gene (*GRN*), for which there are several studies for different types of treatments. (Check out the Registry's Find A Study page.)

All of the programs use certified labs and have certified genetic counselors with experience in neurodegenerative diseases. Each program offers testing and post-test counseling at no cost, but the cost of pre-test counseling varies from $0 to $125. The good news is that all of these programs limit access to personal health information (PHI) and use the genetic counseling service provider to share available clinical trials.

Dr. Wheaton, Director of the FTD Disorders Registry and also a genetic counselor, said, "We are partnering closely with AFTD to help inform and educate the FTD community so that they can make decisions that are right for their families" Depending on the purpose of the testing or family history, one program may be a better fit than another."

The FTD sponsored programs are listed below in alphabetical order. You can also view the information in this chart.

ALECTOR

General Information

- Eligibility:
  - Persons affected: Yes; however patients with personal or family history of amyotrophic lateral sclerosis (ALS) or a known mutation in another FTD gene are excluded.
  - Unaffected persons with family history: Yes
- Cost: $0
- Testing available outside the U.S.: Yes, using Invitae in Australia, exploring other countries
- Primary Program Limitations: Exclusion of genes other than *GRN*

Laboratory Information

- Lab: Blueprint Genetics Laboratory
- CLIA Certified: Yes, except New York state
- Genes Included:
  - *GRN*
- Test Limitations: Excludes all genes other than *GRN*
- Sample type: Buccal (cheek) swab; other options may be available

Genetic Counseling (GC)

- GC Provider: InformedDNA
- Counselors certified by ABGC: Yes
- Counselors with neurodegenerative disease experience licensed in all states requiring licensure: Yes
- Counselors experienced in neurodegenerative disease: Patients are only scheduled with genetic counselors on InformedDNA's neurology team
- Pre-testing counseling provided: Yes
- Post-testing counseling provided: Yes
- Offers in-house physician ordering: Yes, after pre-test genetic counseling

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Privacy/Legal Considerations

- Validation of Patient Competence: Clinical judgment; genetic counselor will ask for power of attorney (POA) or have the patient sign a healthcare surrogacy form identifying a family member to speak on their behalf.
- Data sharing: Results go to patient and physician. No personal health information (PHI) is shared. Sponsor does collect patient information through their site. ("I agree for authorized contracted service providers and clinical trial sites to contact me in relation to clinical trials for FTD and to contact me in the future to determine my/the patient's interest in related activities.")
- Consent: Sponsored testing under a research protocol; written consent to participate.

Links

- Alector website - patient screener
- InformedDNA website for program

PASSAGE BIO

General Information

- Eligibility:
  - Persons affected: Yes
  - Unaffected persons with family history: No
- Cost: $0
- Testing available outside the U.S.: No
- Primary Program Limitations: Affected individuals only

Laboratory Information

- Lab: Prevention Genetics
- CLIA Certified: Yes
- Genes Included:
  - *GRN*
  - *C9orf72*
  - *MAPT*
- Test Limitations: *C9orf72* expansion test result typically does not include exact repeat number
- Sample type: Buccal (cheek) swab; other options may be available

Genetic Counseling (GC)

- GC Provider: InformedDNA
- Counselors certified by ABGC: Yes
- Counselors with neurodegenerative disease experience licensed in all states requiring licensure: Yes
- Counselors experienced in neurodegenerative disease: Patients are only scheduled with genetic counselors on InformedDNA's neurology team
- Pre-testing counseling provided: Yes
- Post-testing counseling provided: Yes
- Offers in-house physician ordering: Yes, after pre-test genetic counseling

Privacy/Legal Considerations

- Validation of Patient Competence: Clinical judgment; genetic counselor will ask for power of attorney (POA) or have the patient sign a healthcare surrogacy form identifying a family member to speak on their behalf.
- Data sharing: Results go to patient and physician. De-identified information goes to sponsors, no protected health information (PHI) is shared.
- Consent: Verbal consent for testing documented in visit summary; written consent in states if required. Written consent for counseling.

Links

- Passage Bio website - press release
- InformedDNA website for program

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Prevail THERAPEUTICS
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PREVAIL THERAPEUTICS

General Information

- Eligibility:
  - Persons affected: Yes; program includes testing for patients diagnosed with amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), frontotemporal degeneration (FTD), Alzheimer's disease with onset before 65 years of age, hereditary prion disease, or unaffected individuals with a family history of any of these conditions diagnosed in a relative under the age of 65.
  - Unaffected persons with family history: Yes
- Cost: $0 (optional pre-test counseling is $125)
- Testing available outside the U.S.: Yes, Australia, Brazil, Canada
- Primary Program Limitations: Exclusion of *C9orf72* gene; cost to patient for pre-test counseling

Laboratory Information

- Lab: Invitae
- CLIA Certified: Yes
- Genes Included:
  - *GRN*
  - *MAPT*
  - Others: *ALS2, ANG, ANXA11, APP, CHCHD10, CHMP2B, DCTN1, ERBB4, FUS, HEXA, HNRNPA2B1, ITM2B, KIF5A, OPTN, PFN1, PRNP, PSEN1, PSEN2, SETX, SNCA, SOD1, SORL1, SPG11, SQSTM1, TARDBP, TBK1, TFG, TREM2, UBQLN2, VAPB, VCP, ATP13A2, DDHD1, ERLIN1, FIG4, LRRK2, MATR3, NEFH, SIGMAR1, TIA1*
- Test Limitations: Excludes *C9orf72*
- Sample type: Saliva; other options may be available

Genetic Counseling (GC)

- GC Provider: Genome Medical
- Counselors certified by ABGC: Yes
- Counselors with neurodegenerative disease experience licensed in all states requiring licensure: Yes
- Counselors experienced in neurodegenerative disease: Patients are only scheduled with genetic counselors on Genome Medical's neurology team
- Pre-testing counseling provided: No, available for $125
- Post-testing counseling provided: Yes
- Offers in-house physician ordering: Yes, after pre-test genetic counseling

Privacy/Legal Considerations

- Validation of Patient Competence: Clinical judgment; genetic counselor will defer testing and ask for a power of attorney (POA) if needed.
- Data sharing: Results go to patient and physician. De-identified information goes to sponsors, no protected health information (PHI) is shared. Sponsors may receive contact information for healthcare providers (HCP) who use the program.
- Consent: Verbal consent for testing documented in visit summary. Written consent for counseling.

Links

- Prevail Therapeutics sponsorship statement
- Invitae website for program

Join the Registry.
Tell Your Story.
Advance the Science.

"Together, we can make a difference!"

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