

Cry your eyes out: detecting huntingtin in tears

Is someone cutting onions? Expanded huntingtin can now be detected in tears to help scientists track disease progression.



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A recently published collaboration between academic researchers and pharmaceutical companies was successful at detecting huntingtin in tears. The scientists were looking for a new, easy way to track Huntington's disease (HD). If you don't mind shedding a tear or two, they found it!

Biomarkers - biological metrics in tune with disease progression

Tracking disease progression is not only medically important to ensure patients are living a healthy life, but it's also important for developing medicines for diseases like HD. Biological metrics that are in tune with disease progression are called biomarkers. There are different kinds of biomarkers, from images of organs, to tests of metabolism, to measurements made in body fluids.



Biomarkers that track with disease progression help determine how good of a job medicines are doing. If biomarkers for HD improve, it means a drug is working!

Biomarkers are tools that researchers can use to assess how well a potential medicine is working. If a drug slows or stops the progression of a disease according to one or more biomarkers, it could mean that drug is working!

HD researchers have been working to identify biomarkers that not only track with disease progression, but also change before someone ever starts to show symptoms. Having very early HD biomarkers would allow researchers to know if a medicine is helping someone before they ever start to show disease onset. Since lots of studies are starting to indicate that the earlier we treat HD, the better off someone will be, good biomarkers will be critical for future trials.

How do we currently track HD progression?

We've known for a long time that HD causes brain cells to die. So imaging, like MRIs, has been used to track brain cell loss as HD progresses. However, it's not always easy and convenient (or cheap!) to jump in an MRI machine. There are big advantages to finding easier, more accessible ways to track HD progression.

The HD research field has been moving toward identifying biomarkers in biofluids, like blood and the cerebrospinal fluid (CSF) that bathes the brain and spine. The two most notable biofluid biomarkers for HD have been neurofilament light (NfL) and the huntingtin protein (HTT) itself.

NfL has been detected in both blood and CSF. NfL is released from brain cells when they die. So as HD progresses and more brain cells are lost, amounts of NfL rise. Researchers have shown that NfL is increased in people with HD up to 24 years before they even start to show clinical symptoms! This currently makes NfL our most sensitive biomarker to track HD progression.

“They found that amounts of expanded HTT were higher in tears from people that carry the gene for HD, whether they currently had symptoms or not. ”

Getting more specific

However, NfL isn't specific for HD. It's released from brain cells that are dying for any reason. This could make it tricky to precisely follow HD progression if there are other reasons someone might have lost brain cells, like an illness or a hard hit to the head. To specifically track HD, researchers have turned to HTT itself.

Detecting expanded HTT in blood and CSF has been difficult. Overall, expanded HTT isn't produced by the body in large amounts, so there isn't much there to begin with. This means ultra-sensitive techniques must be used. HTT is also inside the cell, making it hard to get to in blood. It can be accessed more easily in CSF, but that requires a lumbar puncture. Because of this, researchers are now turning to other biofluids, like tears!

It's just something in (both my) eyes

No one prefers to get a jab in their vein or back, if other options are available. To see if biomarkers of HD progression can be obtained more easily, researchers from the Netherlands and Germany teamed up and looked at tear fluid.

To get the tears, a small strip of special paper is placed on the lower eyelid, just touching the eye. The tears are wicked onto the paper and the strip is removed after 5 minutes.



New biomarkers and novel ways to detect them offer researchers more tools for their toolbox.

Tears contain a surprising number of proteins – close to 1,500! Biomarkers from tears are also being explored to track other diseases, like Alzheimer's, Parkinson's, and multiple sclerosis. Because of this, the researchers thought tears might be a good source for HD biomarkers.

They found that amounts of expanded HTT were higher in tears from people that carry the gene for HD, whether they currently had symptoms or not. While their data were quite accurate in determining if someone carried the gene for HD, this test doesn't appear to be sensitive enough to determine years from symptom onset or distinguish those who are experiencing symptoms from those who aren't.

A new tool for the box

Finding new and novel ways to identify biomarkers expands our toolbox and offers easier ways for people with HD to track disease progression. Using tears to look at expanded HTT means researchers now have a new tool to examine HD in a fluid that can be collected in a non-invasive way.

Researchers will continue to advance biomarkers that are easy to collect and track with HD progression very early. Having sensitive biomarkers that can be used to measure HD before someone ever shows symptoms will set us up for success when we start testing preventative treatments. When that day arrives, we'll be ready with tears of joy.

Leora Fox works at the Huntington's Disease Society of America which has relationships

with pharmaceutical companies, including Vico Therapeutics. [For more information about our disclosure policy see our FAQ...](#)

GLOSSARY

CSF A clear fluid produced by the brain, which surrounds and supports the brain and spinal cord.

huntingtin protein The protein produced by the HD gene.

multiple sclerosis a disease of the brain and spinal cord, in which episodes of inflammation cause damage. Unlike Huntington's disease, MS isn't genetically inherited.

metabolism The process of cells taking in nutrients and turning them into energy and building blocks to build and repair cells.

biomarker a test of any kind - including blood tests, thinking tests and brain scans - that can measure or predict the progression of a disease like HD. Biomarkers may make clinical trials of new drugs quicker and more reliable.

magnetic resonance A technique using powerful magnetic fields to produce detailed images of the brain in living humans and animals

HTT one abbreviation for the gene that causes Huntington's disease. The same gene is also called HD and IT-15

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