[MUSIC PLAYING]

DR. MEEUSEN: Ceramides are a combination of a fatty acid and a sphingosine molecule. And they're able to rapidly and interconvert between a sphingosine, a sphingomyelin, and a ceramide. Depending on where they are expressed in the tissue, as well as which particular fatty acid is involved, they can have a variety of cellular functions. Some of these functions include membrane integrity, cell signaling-- including the cell-cycle arrest and apoptotic pathways.

And we've identified four specific ceramide species, in collaboration with some metabolomics researchers. And these four specific ceramide species, we believe, are very highly linked to cardiovascular disease processes. And we've developed a liquid chromatography-tandem mass spectrometry assay, which can very precisely and accurately measure those four species in circulating plasma.

The studies have uncovered three different patient population. First is, patients that have coronary artery disease that's been established by angiography or other imaging modalities. And amongst these patients, a baseline ceramide level is able to predict whether or not they'll have a fatal myocardial infarction within one to five years. The second study, which was performed at Mayo Clinic, looked at consecutive angiography patients that were seen for a variety of indications, including abnormal stress tests, or even suspicion of an MI. And in this population, again, ceramides were able to predict which individuals would go on to need a coronary artery bypass graft, or some other type of percutaneous intervention, and even those individuals that would have a stroke or a fatal MI within the next five years.

Finally, a study involving normal, healthy individuals was looked at, and we found that a baseline ceramide measurement was able to predict who was going to have a fatal MI, even amongst individuals that were otherwise healthy and had no history of coronary artery disease. In all cases, ceramide were independent predictors of adverse cardiovascular events. And we were able to find that they were independent of age, sex, blood pressure, body mass index, and specifically-- comparing with other biomarkers-- ceramides are independent of the LDL cholesterol level, HDL cholesterol level, and certain inflammatory biomarkers, such as c-reactive protein, fibrinogen, and even Lp-PLA2, whether it's concentration or activity.

There's been some published data that has shown individuals taking a low or moderate dose of statins-- simvastatins, specifically-- can improve their ceramide concentration, so it will lower the appropriate ceramides. The next step in our ceramides research would be to determine whether or not the reductions in ceramide levels that we see with patients taking a statin are actually conferring improved outcomes. The secondary of interest involves PCSK9.

So this is a new, up-and-coming therapeutic modality available to cardiologists, in that there are some inhibitors now of PCSK9 that have been shown to improve outcomes and lower LDL in ways that have not previously been accessible. And there's been a published study involving the four ceramide species measured by our test that has shown that individuals with a loss of function mutation in their PCSK9 actually have lower ceramide concentrations than control individuals.

There are a variety of reasons to order a biomarker. In certain instances, you're trying to establish an individual's risk. In some instances, you want to determine whether residual risk remains. And in some instances, we're trying to determine whether or not a person who is showing up with clinical suspicion of an acute coronary syndrome, or even a myocardial infarction-- or heart attack-- we want to determine whether or not this is truly something where we need to take an inventive action.

This test has, so far, been shown to be very predictive of adverse cardiovascular events amongst individuals in all of those categories. Other biomarkers, such as LDL cholesterol, or HDL cholesterol, or even Lp-PLA2 and hs-CRP-- the more advanced biomarkers-- are able to predict risk amongst individuals that have either an established risk already present, in that they're known to have coronary artery disease by imaging, or even in individuals that are otherwise healthy.

However, a ceramides test is being able to, independently, above and beyond those measures, also identify individuals that are at risk of having an adverse cardiovascular event within a very short frame. We're talking one to five years from the time of measurement. Additionally, it seems, on the early, preliminary data, that these are-- the ceramide species are-- modifiable factors. So statins might be able to reduce or improve a ceramide score, as well as the PCSK9 inhibitors.