ALZHEIMER'S MARKERS IN THE BLOOD

Researchers are investigating a host of molecules found in the blood that could reveal pathological processes in the brain. Here are some examples.

Amyloid plaques

BIOMARKER: Aβ42 AND Aβ40

PATHOLOGY INDICATED: AMYLOID PLAQUES

Isoforms of amyloid-β, particularly Aβ42 and Aβ40, are thought to signal the buildup of amyloid plaques in the brain, which, according to the amyloid cascade hypothesis, gradually aggregate between neurons, triggering a sequence of pathological processes. Lower-than-normal levels of Aβ42 and the ratio of Aβ42:Aβ40 in the cerebrospinal fluid (CSF) are two of the best-validated biomarkers for Alzheimer's, and growing evidence suggests measuring them in the blood may be similarly telling.

Inflammation

BIOMARKER: YKL-40, A.K.A. CHITINASE-3-LIKE PROTEIN 1

PATHOLOGY INDICATED: INFLAMMATION

Amyloid plaques and neurofibrillary tangles can spark chronic inflammation in the brain, which may hasten Alzheimer's progression. One protein that's been evaluated as a potential biomarker for this process in Alzheimer's is YKL-40 (also known as chitinase-3-like protein 1), which has been linked to inflammatory diseases. YKL-40 is elevated in the blood of patients with early Alzheimer's symptoms, and a 2010 study revealed that YKL-40 is upregulated in glial cells in areas of the brain with amyloid plaques.

Neurofibrillary tangles

BIOMARKER: TAU AND P-TAU

PATHOLOGY INDICATED: NEUROFIBRILLARY TANGLES

High CSF levels of tau and of a phosphorylated form of the protein (known as p-tau) may reflect tau's aggregation into neurofibrillary tangles in the brain. High levels of tau and p-tau in the CSF have, like aβ42 and aβ42:aβ40, been well-validated as biomarkers for Alzheimer's and are now being looked at in blood. Researchers at the National Institute on Aging have also looked at levels of tau, p-tau, and other biomarkers in circulating extracellular vesicles, with results rivalling the performance of CSF biomarkers and imaging in predicting Alzheimer's onset.

Axonal injury

BIOMARKER: NEUROFILAMENT LIGHT

PATHOLOGY INDICATED: AXONAL INJURY

As Alzheimer's progresses, amyloid plaques, tau tangles, and/or inflammation cause injury to neuronal axons. Elevated blood and CSF levels of neurofilament light, a protein building block of axons, may indicate this neural injury in Alzheimer's as well as other neurodegenerative conditions. Because it's not specific to Alzheimer's, neurofilament light can't be used by itself to screen for the disease, but it's sparked interest as a potential marker for monitoring the disease course of individual patients.