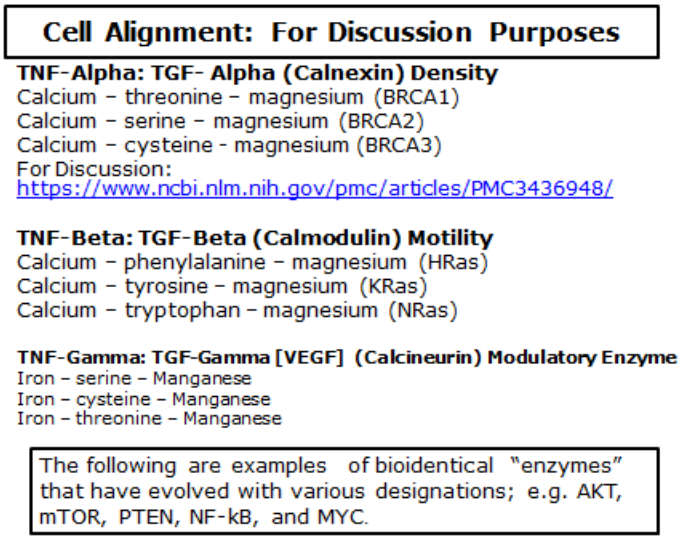
Pericytes - Role and Elemental Composition.

The document affixed to this article can verify the role of pericytes relative to the connectivity to the endothelial cells of the blood brain barrier.

Bioinformatic search can verify pericyte as being correlated to all three forms of TNF, TGF as well as calnexin, calmodulin and calcineurin; see below.

In summary, these cells provide connectivity to the endothelial cells that are positive - negative and translation (enzymatic) for DNA regulation.



https://medicalxpress.com/news/2019-06-cells-secrete-substance-brain-neurons.html

JUNE 24, 2019

Certain cells secrete a substance in the brain that protects neurons

by University of Southern California

USC researchers have discovered a secret sauce in the brain's vascular system that preserves the neurons needed to keep dementia and other diseases at bay.

The finding, in a mouse model of the human brain, focuses on specific cells called pericytes and reveals that they play a previously unknown role in brain health. Pericytes secrete a substance that keeps neurons alive, even in the presence of leaky blood vessels that foul brain matter and result in cognitive decline.

The study, which appears today in *Nature Neuroscience*, helps explain the cascade of problems that lead to neurodegeneration after stroke or traumatic brain injury, as well as in diseases like Alzheimer's and Parkinson's—and suggests a potential strategy for therapy.

"What this paper shows is if you lose these vascular cells, you start losing neurons. The link with neurodegeneration was really not that clear before," said senior author Berislav Zlokovic, director of the Zilkha Neurogenetic Institute at the Keck School of Medicine of USC.

The discovery comes at a time when scientists are beginning to understand Alzheimer's disease as the result of multiple processes that begin long before memory loss sets in. Many researchers are shifting their focus from the amyloid plaques that accumulate in the brain later in life toward other targets earlier in the timeline.

Zlokovic, for example, studies the layers of cells that make up blood vessels in the brain. His previous research shows that the more permeable, or leaky, a person's brain capillaries, the more cognitive disability they have.

For this new experiment in mice, Zlokovic zeroed in on pericytes in the brain's blood vessels. Pericytes help regulate blood flow and keep blood vessel walls sealed tight. When researchers artificially removed pericytes, they saw rapid degeneration of the blood-brain barrier, a slowdown of blood flow and the loss of brain cells.

To further understand the role of pericytes, the scientists infused mice with a protein, or growth factor, secreted by pericytes in the brain and not found elsewhere in the body. They found that, even with pericyte cells artificially removed, the growth factor protected neurons and the brain cells didn't die. The results persisted even with constricted blood flow.

Because these pericytes are implicated in many diseases—including Huntington's, Parkinson's, stroke, brain trauma and amyotrophic lateral sclerosis—the research offers intriguing possibilities for further investigation.

"This opens up an entirely new view of the possible pathogenesis of Alzheimer's disease," Zlokovic said.

Comprising the BBB and Other Barriers in the Body

Guards of the blood brain barrier identified

Pericytes crucial to protecting central nervous system

By Rachel Ehrenberg

Of all the body's organs, the brain is the most like Area 51: Entry to the region is severely restricted, thanks to a barricade of cells and molecules known collectively as the blood-brain barrier. Increased surveillance by scientists has now pinpointed the barrier's senior operatives, cells that are tasked with monitoring the razor wire–like barricade that keeps all but a select few from entering the brain.

In two papers published online October 13 in *Nature*, scientists report that specialized cells called perictyes are crucial in the blood-brain barrier's development and its maintenance in adulthood. A better understanding of how these pericytes function could help elucidate why some people fare especially poorly after traumatic brain injury or get particular neurological diseases such as cerebral palsy, scientists say. And new research could also lead to tricks for selectively opening or closing the blood-brain barrier, letting in medications that might combat diseases such as Alzheimer's.

One of the new studies demonstrates that pericytes are necessary for cementing the barrier's cells into a nearly impenetrable wall surrounding blood vessels in the central nervous system. The work also establishes a timeline: In mice, the blood-brain barrier develops well before birth, researchers from Stanford and the University of California, San Francisco report. Pericytes also appear to keep the barrier's cells on lockdown, dialing down the activity of genes that, if left to their own devices, would spur the transport of molecules across the barrier and into the brain. MCFIP-Literature indicates that the pericytes are not the cells that comprise the entire BBB but specialized ones that are linked to veins, vessels and arteries that pass through the BBB.

The second new study establishes that pericytes play a key role in regulating the blood-brain barrier in adult mice and also identifies a drug that appears to slow the transport of molecules across a leaky blood-brain barrier. In mutant mice lacking functional pericytes, the leukemia drug imatinib quickly halted the willy-nilly passage of molecules into the brain, researchers from Sweden and Germany report. MCFIP- A cursory review indicated the drug has an impact of NO synthesis.

"We are now doing experiments with imatinib-like substances," says Christer Betsholtz of the Karolinska Institute in Stockholm, who led the second study. "We would like to understand how imatinib is closing the barrier." MCFIP - See the comment from above.

Pericytes are found all over the body: Wherever there are blood vessels, there are pericytes around them. For a long time researchers thought that pericytes' primary task was to help control flow in blood vessels. But around the blood vessels of the retina and the blood-brain barrier, pericytes are especially plentiful; in the last decade these cells have come under increased scrutiny as regulators of these important barriers.

The importance of the blood-brain barrier cannot be understated, says Norman Saunders of the University of Melbourne in Australia. Not only does the barrier block access by baddies such as bacteria and parasites, it also prevents the unchaperoned entry of electrically charged molecules called ions. Since brain cells communicate via electrical impulses, the barrier literally keeps the brain from going haywire, Saunders says.

"If it weren't for the blood-brain barrier, our sensory experience would be reduced to a series of flashes and bangs," says Saunders, recalling a quip of his late colleague and blood-brain barrier research giant Hugh Davson.

While pericytes were definitely on the short list of key regulators of the blood-brain barrier, many researchers were focusing on astrocytes, the star-shaped brain cells that help the brain's thinking cells, neurons, do their thing. But research suggests that astrocytes don't develop until after birth, which led some people to erroneously conclude that the blood-brain barrier therefore also doesn't develop until infancy. MCFIP- Some studies support the possibility that it does not develop fully until 11> years of age.

The new research firmly establishes that the blood-brain barrier is developed before birth, and that pericytes have a lot to do with that development. The cells also keep the barrier operating during adulthood. Mice genetically engineered to have fewer working pericytes have leakier blood-brain barriers, both teams report. This increased permeability seems to be partially due to structural problems — the normally supertight junctions between the barrier's cells become cocked and crooked. MCFIP-The integrity of the BBB seems be supported by pericytes at the juncture of all vasculature. We have identified the substances and signaling molecules that facilitate the permeability as well as the "cocked and crooked" outcomes that appear to be the result of "over adhesion." .

But more important than the dysfunctional junctions is the misbehavior of the barrier's import and export machinery. Without pericytes, the barrier's cells take up many more molecules from the blood than they should, and dump those molecules into the brain. This includes molecules associated with the immune system — substances that cause swelling and inflammation — a healthy response in most body tissues but not in the brain, says Richard Daneman of the University of California, San Francisco, who led one of the studies.

"A major function seems to be keeping the immune system out," he says. "You don't see immune cells in the brain — but in certain disease scenarios, multiple sclerosis, strokes — you get damage from the immune system in the brain."

A malady that strikes people with diabetes may also be related to pericyte problems. After years with the disease, pericytes associated with the blood vessels around the retina start to disappear,

says Andrius Kazlauskas of the Schepens Eye Research Institute at Harvard Medical School. Once the cells are gone, immune system molecules can invade, inflammation occurs and a person can't see, says Kazlauskas. The condition is known as diabetic retinopathy.

"This work says that keeping the pericytes happy, keeping them alive, is likely to keep the vasculature happy," he says. "That's huge; conceptually, that's a breakthrough. It is really intolerable for vision when the retina swells."

Also intriguing is evidence that the leukemia drug imatinib slowed leakage, Kazlauskas says. Perhaps related drugs will eventually have a place in treating diabetic retinopathy.

In the future, there may even be genetic tests that tell people how healthy their pericyte population is, says neuroscientist Joan Abbott of the blood-brain barrier group at King's College London. "We've been puzzled as to why some people after brain trauma do better than others," Abbott says. If some people are born with fewer or faulty pericytes due to genetics, their blood-brain barriers may be leaky from the start.

http://www.sciencenews.org/view/generic/id/64295/title/Guards_of_the_blood-brain_barrier_identified