Medical Xpress

Researchers discover new way to block inflammation

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Researchers at NYU Langone Medical Center have discovered a mechanism that triggers chronic inflammation in Alzheimer's, atherosclerosis and type-2 diabetes. The results, published today in *Nature Immunology*, suggest a common biochemical thread to multiple diseases and point the way to a new class of therapies that could treat chronic inflammation in these non-infectious diseases without crippling the immune system. Alzheimer's, atherosclerosis and type-2 diabetes—diseases associated with aging and inflammation—affect more than 100 million Americans.

When the body encounters a pathogen, it unleashes a rush of chemicals known as cytokines that draws immune cells to the site of infection and causes inflammation. Particulate matter in the body, such as the cholesterol crystals associated with vascular disease and the amyloid plaques that form in the brain in Alzheimer's disease, can also cause inflammation but the exact mechanism of action remains unclear. Researchers previously thought that these crystals and plaques accumulate outside of cells, and that macrophages—immune cells that scavenge debris in the body—induce inflammation as they attempt to clear them.

"We've discovered that the mechanism causing chronic inflammation in these diseases is actually very different," says Kathryn J. Moore, PhD, senior author of the study and associate professor of medicine and cell biology, Leon H. Charney Division of Cardiology at NYU Langone Medical Center.

The researchers found that particulate matter does not linger on the outside of cells. Instead, a receptor called CD36 present on macrophages draws the soluble forms of these particles inside the cell where they are transformed into substances that trigger an inflammatory response. Says Dr. Moore, "What we found is that CD36 binds soluble cholesterol and protein matter associated with these diseases, pulls them inside the cell, and then transforms them. The resulting insoluble crystals and amyloid damage the macrophage and trigger a powerful cytokine, called interleukin-1B, linked to a chronic inflammatory response."

These findings hold exciting clinical implications. When the researchers blocked the CD36 receptor in mice with atherosclerosis (in which cholesterol thickens the arteries), the cytokine response declined, fewer cholesterol crystals formed in plaques, and inflammation decreased. Consequently, atherosclerosis also abated.

Other less-targeted strategies to control inflammation may hamper the immune response, but the CD36 strategy spares certain cytokines to fight off pathogens, while blocking CD36's ability to trigger interleukin-1B.

"Our findings identify CD36 as a central regulator of the immune response in these conditions and suggest that blocking CD36 might be a common therapeutic option for all three diseases," says Dr. Moore.

More information: Paper: dx.doi.org/10.1038/ni.2639

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