Identifying underlying causes of immune deficiencies that increase shingles risk

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Early life infections with varicella zoster virus cause chickenpox, but the virus can remain dormant in the nervous system for decades and reactivate to cause herpes zoster, commonly known as shingles. Shingles is characterized by a painful skin rash and blisters, and it predominantly affects the elderly. Shingles also occurs at a higher rate in people diagnosed with coronary artery disease (CAD), which affects immune system function in part through changes in infection-responsive immune cells called macrophages. The specific immune mechanisms underlying age- and CAD-related viral reactivation are not well understood.

This week in the *JCI*, a study led by Cornelia Weyand at Stanford University reports that macrophages derived from individuals diagnosed with CAD suppress the activation and proliferation of T cells. Excessive accumulation of the metabolic intermediate pyruvate in these macrophages increased expression of a signaling molecule called PD-L1 that drives T cell suppression. The overabundance of pyruvate in macrophages suggests that metabolic dysregulation may contribute to immune dysfunction in individuals affected by CAD.

The activity of this immunosuppressive pathway in CAD patients provides insights into a mechanism for immune deficiencies that permit reactivation of long-latent viruses. These findings are a step toward developing new strategies that correct metabolic dysregulation in immune cells to prevent shingles and other infections in at-risk populations.

More information: Ryu Watanabe et al, Pyruvate controls the checkpoint inhibitor PD-L1 and suppresses T cell immunity, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI92167