WHITEPAPER

Meet the Marker: TIM3

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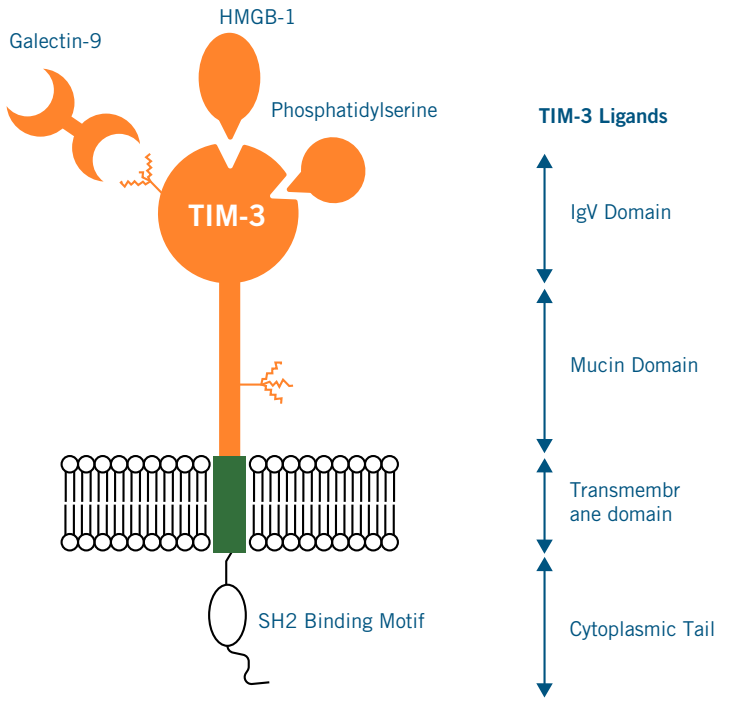
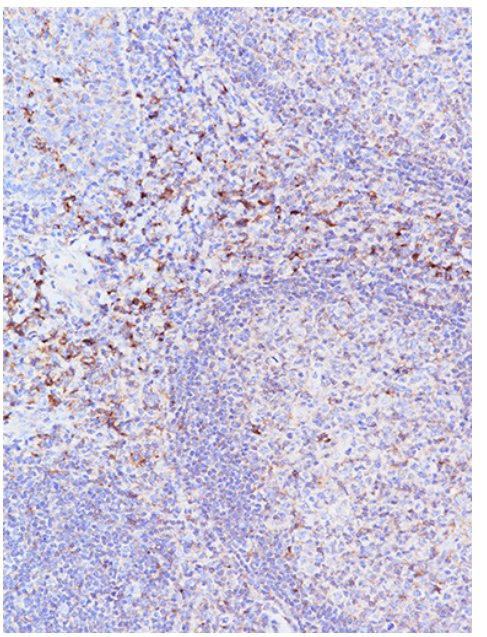
The immune system serves to protect the body not only from external threats such as bacteria and viruses but also from internal threats such as cancer. Research has suggested that it plays a role in recognizing and attacking cancerous cells when they arise, a function known as "immunosurveillance."[2] The significance of immunosurveillance has been bolstered by the finding that immunodeficiency or immunosuppression seems to cause patients to be more susceptible to tumor development.[2] It is theorized that the existence of immunosurveillance has led to a sort of arms race between the immune system and cancer itself wherein the immune system works to root out and eliminate cancer cells while the cancer works to evade and suppress the actions of the immune system.

One such mechanism that cancerous growths exploit to suppress the immune system is the promotion of T cell dysfunction or exhaustion.[2] T cell exhaustion describes a state of dysfunction where T cells no longer proliferate and stop responding to antigen stimulation.[2] In this state, the immune system T cells will fail to fulfill their defensive functions such as secreting cytokines or targeting abnormal cells for destruction.[2] This state can be induced through chronic, continuous exposure to the antigen, such as in the case of chronic viral infections or cancers.[3]

T cell immunoglobulin and mucin domain-containing protein 3 (TIM3) is an immunoregulatory protein that has been found to be an indicator of T cell exhaustion.[3] In healthy tissues, TIM3 plays an important role in maintaining normal immune system function by regulating immune response and inflammation.[3] TIM3 deficiency has been found in patients suffering from autoimmune diseases.[3] Overexpression of TIM3 has been found to be a marker of T cell dysfunction and exhaustion in chronic viral infections and cancer.[1,3] In cases of viral infections, such as hepatitis C, hepatitis B, and HIV, TIM3 levels are positively correlated with viral load and disease progression.[3] In cancer, overexpression of TIM3 appears to exacerbate tumor progression, being correlated with unfavorable disease prognosis. In cases of colon, gastric, cervical, non-small cell lung cancer, and clear cell renal carcinoma, high levels of TIM3 expression have been associated with lower survival.[3] Additionally, TIM3 has been found to be highly expressed by leukemic stem cells but not by normal hematopoietic stem cells.[3]

Since high levels of TIM3 expression have been associated with immune system dysfunction and therefore increased cancer malignancy and unfavorable disease outcomes, TIM3 has become an attractive target for anti-tumor therapy research.[2] In patients with more advanced cancers, studies have found that co-blockade of TIM3 and its associated protein, programmed cell death 1 (PD1), can improve anti-tumor T cell response.[3]





Tonsil stained with TIM3 [BLR033F] antibody

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