

Acidic niche keeps lymphatic system in check during immune response

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In the fight against cancer, the immune system is the first line of defense. The lymphatic system specifically is essential to protecting the body against foreign invaders. Activation of immune cells in the lymph nodes leads to the production and release of antibodies, and activation of lymphocytes, including T cells, to battle infection. But little is known about how activation of immune cells in the lymph nodes can occur without enabling effector functions that could also damage the lymphatic system.

In a new article published in *Nature Communications*, Moffitt Cancer Center researchers describe a novel acidic niche within [lymph nodes](#) that plays an integral role in regulating T cell activation.

"Acidosis is a potent inhibitor of effector T cell functions," said Robert Gillies, Ph.D., chair of the Department of Cancer Physiology at Moffitt. "Oxygen levels are reported to be low in lymph nodes and that hypoxic tissue is acidic. We wanted to determine if lymph nodes were also acidic."

For this study, Moffitt researchers used fluorescence and magnetic resonance imaging to identify a naturally occurring acidic niche within lymph nodes. Upon further analysis, they discovered that the T cells were the source of that acidity. They say the results pinpoint localized acidosis as a critical component of the adaptive immune response.

The findings demonstrate the potential role for the lymph node microenvironment in shaping T cell biology. T cells activated by [antigen-presenting cells](#), such as dendritic cells, produce an acidic environment that is balanced by the enhanced capacity to generate lactic acid.

"The low extracellular pH of lymph nodes does not impair the T cell's activation, but it does suppress the cytokine production, which is likely what protects lymph nodes from being attacked by the [immune system](#)," said Gillies.

The researchers say this robust physiological mechanism can be exploited by cancers, resulting in evasion of immune surveillance by malignant tissue and tumors. They believe this could be managed by manipulating the acidity in combination with immunotherapies such as T-cell checkpoint blockade therapy. However, more research is needed to confirm.

More information: Hao Wu et al, T-cells produce acidic niches in lymph nodes to suppress their own effector functions, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-17756-7](https://doi.org/10.1038/s41467-020-17756-7)

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