Lay Summary:

Our project aimed to understand how the growth of tumor cells in lymph nodes affects the immune response. We discovered that T cells, which are important for fighting tumors, are kept away from these cancerous lymph nodes. We studied both human breast cancer patients and mice with breast tumors to see if this pattern was consistent. We found that in both cases, there were very few T cells within lymph node tumors, even though healthy lymph nodes were full of them. This lack of T cells in tumor-invaded lymph nodes indicates a weak immune response that cannot contain tumor growth. We also studied why the blood vessels in these cancerous lymph nodes are not working properly. We suspected that the tumor cells might be causing physical damage to the blood vessels to reduce blood flow, similar to how tumors affect blood vessels in the original tumors. We imaged blood vessels in live mice to determine were functioning in these lymph nodes with tumors. As the tumors in the nodes grew, we saw that the blood flow within them decreased. We then experimented with introducing T cells into mice with tumor-invaded lymph nodes and found that fewer T cells were entering these areas, suggesting that the dysfunction of these blood vessels prevented T cell entry.

To investigate further, we used a device that mimics the physical forces caused by tumor growth. This helped us understand how these forces from the tumor affects T cell entry. We discovered that this physical force limits the ability of T cells to enter tumors. To tackle this problem, we used a drug called losartan, which is used to treat high blood pressure. This drug can reduce the physical forces caused by tumors and improve the blood vessels' function. When we treated mice with losartan, we saw an increase in the number of T cells entering the tumor-invaded lymph nodes. Future work will test whether losartan could potentially be used alongside immune therapies to enhance T cell infiltration and improve their effectiveness in fighting tumors.