353 ADOPTIVELY TRANSFERRED TH17 CELLS ENGAGE HOST B CELLS FOR DURABLE TUMOR DESTRUCTION

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Background Adoptive T cell transfer (ACT) therapy elicits robust immunity in some patients with aggressive malignancies. However, many individuals do not respond or relapse. Therefore, our team aimed to create a therapy that can sustain long term anti-tumor immunity. We reported that Th17 cells, a subset of $CD4^+$ T cells, can eradicate melanoma when infused into mice, but the mechanism behind this enhanced immunity is unclear.

Methods To model $CD4^+$ T cell ACT, we used a transgenic mouse model where $CD4^+$ T cells express a TCR that recognizes tyrosinase-related protein 1 found on melanoma. These cells are polarized to Th17 cells and infused into lymphodepleted mice bearing established melanoma tumors.

Results We first wanted to understand if Th17 cells were engaging host immune cells to mediate tumor killing. To determine if transferred Th17 cells rely on host immune cells, we employed a combination of *in vivo* antibody depletions and genetically deficient mice. Surprisingly, anti-tumor Th17 cells did not require host $CD8^+$ or $CD4^+$ T cells but did require host B cells for sustained anti-tumor immunity. Moreover, by using an unbiased analysis of RNA transcripts in the tumor-draining lymph nodes of mice, we found that Th17 cell therapy induces transcripts associated with B cell development, B cell maturation, antibody-secretion, and antigen presentation. Host B cells enhanced Th17 cell persistence and promoted their differentiation into IFN-γ producers. Transferred Th17 cells cause the production of class switched tumor specific antibodies in an IL-21 dependent manner, but only when these Th17 cells are tumor antigen specific. Interestingly, the transfer of these antibodies alone can partially protect mice against tumor challenge. Finally, we found that IL-21 and ICOS are critical for this sustained anti-tumor immunity.

Conclusions These data suggest that transferred Th17 cells and host B cells harmonize to sustain immunity against melanoma. Our findings highlight Th17 cell ACT as a novel way to engage B cell responses to cancer. Ongoing experiments are investigating the mechanism behind these cells' cooperation.

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