UC DAVIS HEALTH | SCHOOL OF MEDICINE

Department of
Medical Microbiology & Immunology

Special Seminar

Department of Medical Microbiology and Immunology
Cancer Immunology Faculty Recruitment

Wednesday, July 10, 2019 at 10:30 a.m.

"Pediatric patients with acute lymphoblastic leukemia generate functional neoantigen-specific CD8+ T cell responses despite low mutation burden"

Publication reference

Pediatric patients with acute lymphoblastic leukemia generate abundant and functional neoantigen-specific CD8+ T cell responses. Zamora AE1, Crawford JC1, Allen EK1, Guo XJ1,2, Bakke J3,4, Carter RA5, Abdelsamed HA1, Moustaki A1, Li Y5, Chang TC5, Awad W1, Dallas MH6, Mullighan CG7, Downing JR7, Geiger TL7, Chen T3, Green DR1, Youngblood BA1, Zhang J5, Thomas PG8,2. Sci Transl Med. 2019 Jun 26;11(498). pii: eaat8549. doi: 10.1126/scitranslmed.aat8549.

Abstract

Cancer arises from the accumulation of genetic alterations, which can lead to the production of mutant proteins not expressed by normal cells. These mutant proteins can be processed and presented on the cell surface by major histocompatibility complex molecules as neoepitopes, allowing CD8+ T cells to mount responses against them. For solid tumors, only an average 2% of neoepitopes predicted by algorithms have detectable endogenous antitumor T cell responses. This suggests that low mutation burden tumors, which include many pediatric tumors, are poorly immunogenic. Here, we report that pediatric patients with acute lymphoblastic leukemia (ALL) have tumor-associated neoepitope-specific CD8+ T cells, responding to 86% of tested neoantigens and recognizing 68% of the tested neoepitopes. These responses include a public neoantigen from the ETV6-RUNX1 fusion that is targeted in seven of nine tested patients. We characterized phenotypic and transcriptional profiles of CD8+ tumor-infiltrating lymphocytes (TILs) at the single-cell level and found a heterogeneous population that included highly functional effectors. Moreover, we observed immunodominance hierarchies among the CD8+TILs restricted to one or two putative neoepitopes. Our results indicate that robust antitumor immune responses are induced in pediatric ALL despite their low mutation burdens and emphasize the importance of immunodominance in shaping cellular immune responses. Furthermore, these data suggest that pediatric cancers may be amenable to immunotherapies aimed at enhancing immune recognition of tumor-specific neoantigens.

July
10

Anthony Zamora, Ph.D.
Postdoctoral Fellow
St. Jude Children's Research Hospital

July 10, 2019
10:30 – 11:15 a.m.
GBSF 1005

Medical Microbiology & Immunology
School of Medicine

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