HHS Public Access

Author manuscript

N Engl J Med. Author manuscript; available in PMC 2018 October 05.

Published in final edited form as:

N Engl J Med. 2017 February 16; 376(7): e11. doi:10.1056/NEJMc1616637.

T-Cell Transfer Therapy Targeting Mutant KRAS

Asaf Maoz, M.D.,
USC Norris Comprehensive Cancer Center Los Angeles, CA

Gad Rennert, M.D., Ph.D., and
Technion Carmel Medical Center Haifa, Israel

Stephen B. Gruber, M.D., Ph.D.
USC Norris Comprehensive Cancer Center Los Angeles, CA, sgruber@usc.edu

TO THE EDITOR:

Tran and colleagues note that thousands of patients per year in the United States could be eligible for T-cell-based immune-therapy targeting KRAS G12D. We agree. In our National Institutes of Health-funded, population-based study, we have characterized 4346 colorectal adenocarcinomas since 1998.[1] To date, the prevalence of *KRAS* mutations is 1441 of 4346 (33.2%), with 37.9% of the *KRAS*-positive tumors harboring G12D mutations. HLA typing available for 3734 patients shows that 687 (18.4%) have at least one copy of HLA-C*08:02. We found that 85 of 3734 patients (2.3%) with colorectal cancer share the same HLA type and *KRAS* mutation as described by Tran et al. We have also sequenced the T-cell receptor (TCR) beta chain of tumor-infiltrating lymphocytes to characterize the adaptive immune response in 295 tumors so far, in addition to expert pathological assessment.[2] We detected 6338 shared TCR-β sequences among 2 or more patients, including 5 TCR-β sequences uniquely shared among patients with tumors positive for *KRAS* G12D and HLA-C*08:02 and 7 TCR-β sequences also shared by patients with *KRAS* G12D and HLA-C*08:02 and other combinations of *KRAS* mutations and HLA (Fig. 1).

References

1. Poynter JN, Gruber SB, Higgins PD, et al. Statins and the risk of colorectal cancer. N Engl J Med 2005;352:2184–92. [PubMed: 15917383]
2. Rozek LS, Schmit SL, Greenson JK, et al. Tumor-infiltrating lymphocytes, Crohn's-like lymphoid reaction, and survival from colorectal cancer. J Natl Cancer Inst 2016;108:108.

No potential conflict of interest relevant to this letter was reported.

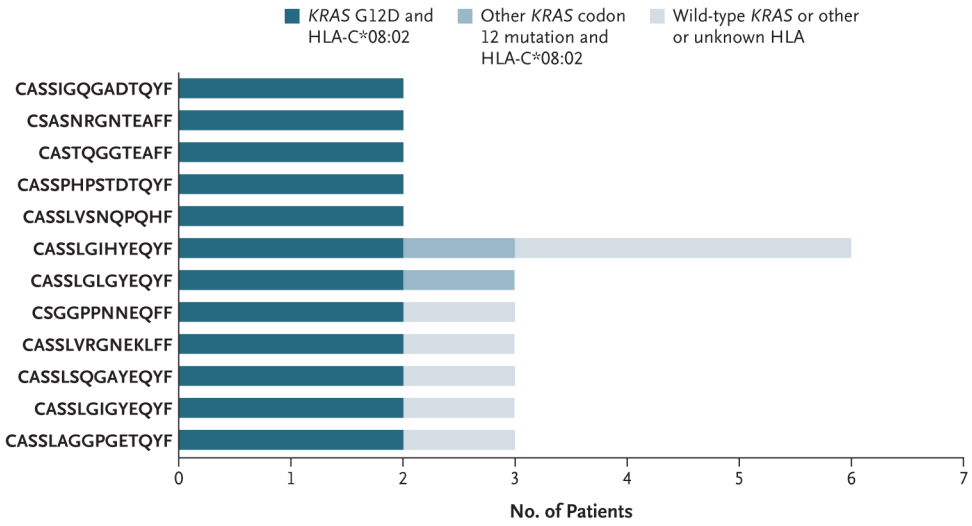

Figure 1.

Patients with Shared T-Cell Receptor β Sequences Whose Tumors Harbor *KRAS* Mutations Presented by HLA-C*08:02.