



Published in final edited form as:

*N Engl J Med.* 2017 February 16; 376(7): e11.

## T-Cell Transfer Therapy Targeting Mutant KRAS

Andrew J. Rech, Ph.D., Robert H. Vonderheide, M.D., D.Phil.

University of Pennsylvania, Philadelphia, PA

### TO THE EDITOR:

Tran et al. (Dec. 8 issue)<sup>1</sup> describe a remarkable case of a patient with metastatic colorectal cancer treated with autologous T cells specific for mutant KRAS G12D and restricted to the major histocompatibility complex class I allele HLA-C\*08:02. The authors hypothesize that in the United States alone, thousands of patients per year may be eligible for T-cell-based immunotherapy targeting KRAS G12D. To estimate how common this opportunity may be, we identified 151 patients with *KRAS*G12D mutations out of 6125 patients in the Cancer Genome Atlas. Of these, only 4 had the HLA-C\*08:02 allele as determined by a validated computational method.<sup>2,3</sup>

We then investigated immune activity in tumor samples using established gene signatures.<sup>4,5</sup> Comparing *KRAS*G12D-positive tumors with disease-matched *KRAS*wild-type tumors, we found no evidence of unique immune activity. Nor did we find evidence of unique immune activity in patients with the HLA-C\*08:02 allele, regardless of *KRAS* mutation status.

Immunotherapy targeting KRAS G12D in patients with the HLA-C\*08:02 allele appears to be an important but rare opportunity. Evaluation of other *KRAS* mutations and alleles is warranted.

### References

1. Tran E, Robbins PF, Lu Y-C, et al. T-cell transfer therapy targeting mutant KRAS in cancer. *N Engl J Med* 2016;375:2255–62. [PubMed: 27959684]
2. Szolek A, Schubert B, Mohr C, Sturm M, Feldhahn M, Kohlbacher O. OptiType: precision HLA typing from next-generation sequencing data. *Bioinformatics* 2014;30:3310–6. [PubMed: 25143287]
3. Shukla SA, Rooney MS, Rajasagi M, et al. Comprehensive analysis of cancer-associated somatic mutations in class I HLA genes. *Nat Biotechnol* 2015;33:1152–8. [PubMed: 26372948]
4. Rooney MS, Shukla SA, Wu CJ, Getz G, Hachohen N. Molecular and genetic properties of tumors associated with local immune cytolytic activity. *Cell* 2015;160:48–61. [PubMed: 25594174]
5. Balli D, Rech AJ, Stanger BZ, Vonderheide RH. Immune cytolytic activity stratifies molecular subsets of human pancreatic cancer. *Clin Cancer Res* 2016 12 22 (Epub ahead of print).

rhv@upenn.edu.

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