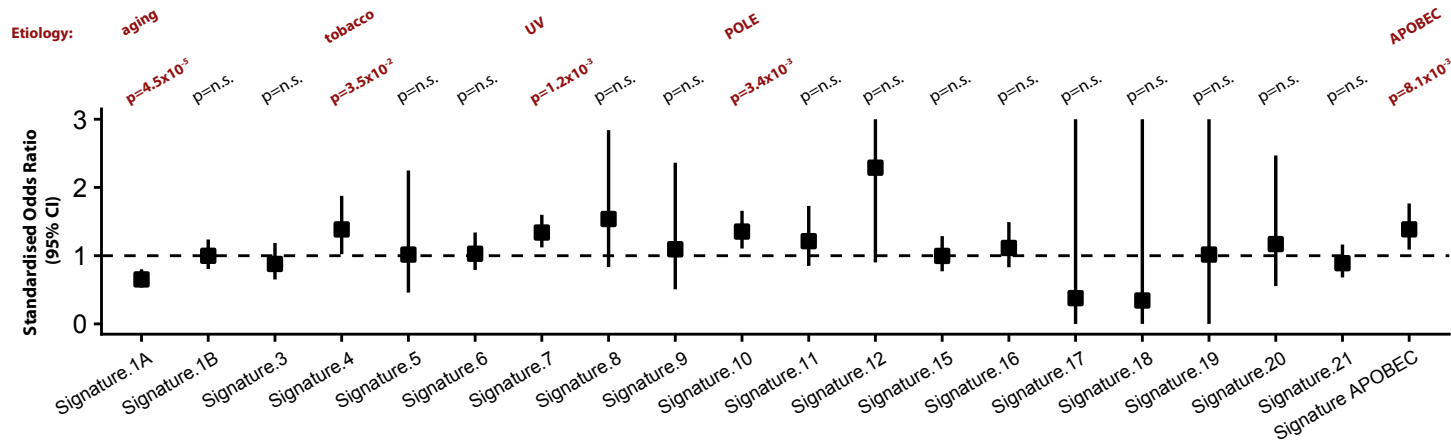


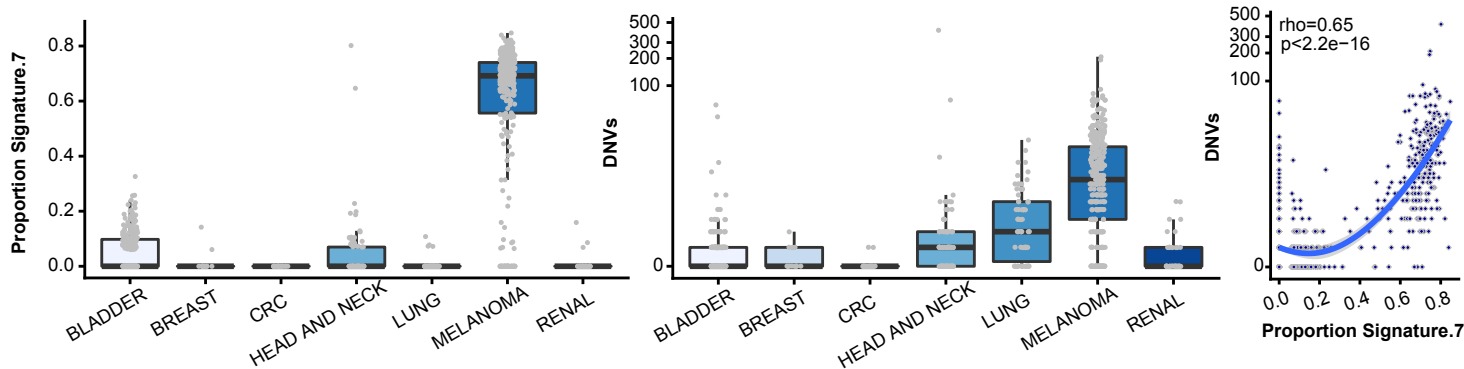
A

Mutational signatures associated with response to immune checkpoint inhibitor therapy:
(all tumors with ≥ 50 mutations, total $n=774$ patients, p-value from meta-analysis)

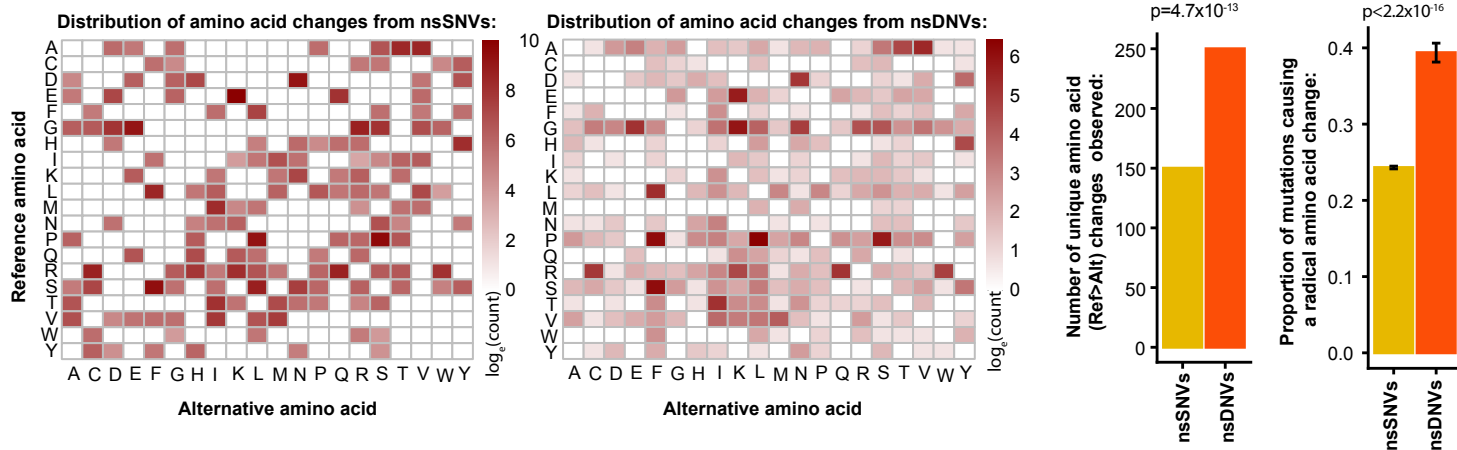
P-values remain significant
after adjusting for TMB

**B**

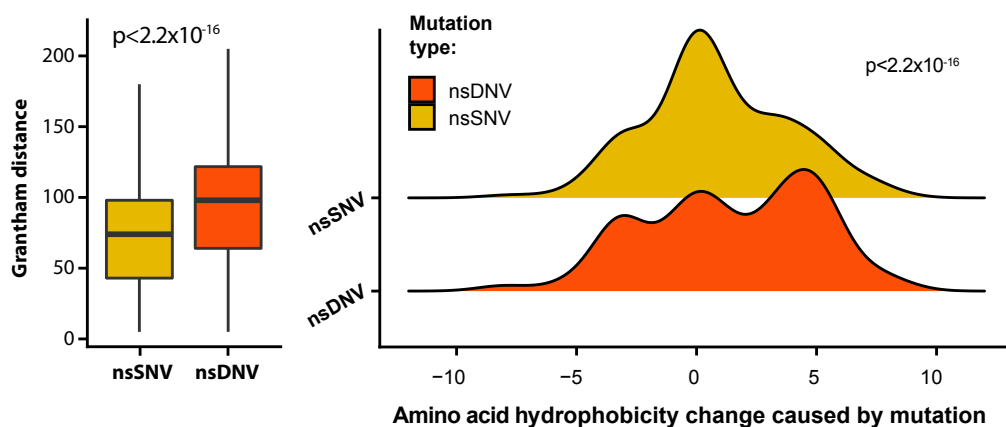
Signature 7 (UV) mutations in melanoma are associated with dinucleotide variants (DNVs):

**C**

DNVs permit a broader set of amino acid alterations compared to SNVs, with more radical changes:

**D**

DNVs associate with a higher change in grantham distance and greater increase in amino acid hydrophobicity per mutation:

**E**