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Titel des Beitrags:
Immunological characterization of missense mutations occurring within cytotoxic T cell-defined p53 epitopes in HLA-A*0201+ squamous cell carcinomas of the head and neck.

Abstract:
Previous analyses of p53 in 40 HLA-A*0201(HLA-A2)(+) squamous cell carcinomas of the head and neck (SCCHN) indicated that 6/13 p53 missense mutations that were detected, S149C, T150R, V157F, Y220C, Y220H and E271K, occurred within HLA-A2-restricted cytotoxic T lymphocyte (CTL)-defined p53 epitopes. Of the 6, the p53 S149C, Y220C and Y220H peptides were immunogenic. Anti-p53 mutant S149C and Y220H effector cells cross-reacted against the parental wild type sequence (wt) p53 peptides, whereas anti-p53 Y220C effector cells were specific for the mutant peptide, p53 Y220C cDNA-transfected HLA-A2(+) SaOS cells, and an HLA-A2(+) SCCHN cell line naturally expressing the mutation. These results indicate that the p53 Y220C mutation can be processed and presented for CD8(+) T cell recognition. Furthermore, using an autologous PBMC/tumor system, anti-p53 Y220C peptide-effector cells recognizing the autologous tumor could also be generated. Our analysis of p53 in 10 additional HLA-A2(+) SCCHN tumors detected the p53 Y220C in 2/10 tumors raising the overall frequency of the p53 Y220C mutation to 6/50 (12%) HLA-A2(+) SCCHN tumors. In contrast, independent of their HLA class I genotypes, the p53 Y220C mutation frequency for all human tumors
analyzed to date is approximately 1.5%. This unexpectedly high frequency of the p53 Y220C mutation in HLA-A2(+) SCCHN suggests that vaccines targeting this mutation would not only be expected to induce robust anti-tumor immune responses in HLA-A2(+) subjects, but also be more widely applicable than previously envisioned for any given p53 missense mutation.