ABSTRACT

HLA-B*57 is associated with slower disease progression to AIDS, and CD8+ T cell responses to B*57-restricted epitopes are thought to contribute to this protective effect. In this study, we evaluate the B*57-restricted p24 KAFSPEVIPMF (KF11) immune response which is immunodominant during chronic infection. Previously, we observed that the KF11 clade variants KGFNPEVIPMF [A2G,S4N] and KAFNPEIIMPF [S4N,V7I], sharing a position 4 mutation, are differentially recognized by KF11-specific T cells. By combining structural and cellular studies, we now demonstrate that the KF11 and [A2G,S4N] epitopes induce distinct functional responses in [A2G,S4N] and KF11-specific T cells, respectively, despite minimal structural differences between the individual B*57-peptide complexes. Recently, we also elucidated the highly distinct structure of KF11 in complex with B*5703, and have now characterized the CD8+ T cell repertoire recognizing this epitope. We now report striking features of TCR conservation both in terms of TCR Valpha and Vbeta chain usage, and throughout the hypervariable region. Collectively, our findings highlight unusual features of the B*5701/B*5703-KF11-specific immune responses which could influence disease progression and that might be important to consider when designing future vaccine regimens.