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Abstract (oral session)

The cytomegalovirus protein pUL32 is highly conserved among clinical strains although a major target of the humoral and cellular immune response

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Objectives. The Cytomegalovirus (CMV) large tegument protein pUL32 (pp150) generates a strong humoral and cellular immune response to the multiple epitopes that are dispersed over the 150 kDa protein. In analogy to other CMV antigens, host immune pressure may be expected to generate genetic diversity in the UL32-gene. Particularly CMV strains in patients with chronic lymphocytic leukaemia (CLL) may be under a strong evolutionary force. The immunoglobulin (Ig) expressed on selected leukemic cells interacts with pUL32 and these cells constitute >90% of the leukocyte fraction in CLL patients. Nevertheless, knowledge on genomic diversity of the UL32 gene coding for pUL32 among clinical strains is very limited, so far. Methods. We screened 200 consecutive CLL patients for the presence of CMV-DNA and sequenced the UL32 gene to determine the genomic diversity among clinical CMV strains. Results were analyzed with respect to CMV-seropositivity and sequence of the Ig expressed on leukemic cells. As references, UL32 sequences of CMV strains were used that were detected in patients with primary CMV infection (n=5), in additional CLL patients treated with an anti-CD52 antibody (n=4), or previously studied and available via PubMed (n=14). Results. CMV-DNA was detected in 3% and CMV-specific IgG antibodies in 71.5% of the 200 CLL patients. Interestingly, CMV-DNA was detectable in 2 CMV-seronegative patients. IgVH gene usage was associated neither with detection of CMV-DNA nor with CMV-seropositivity. Phylogenetic analysis of the different UL32 sequences (n=28), including the 5 sequences from CLL patients, revealed a low sequence variability (<1%). Moreover, the variability of UL32 observed between clinical strains was not restricted to specific stretches of the gene but was uniformly distributed over the entire analyzed sequence. Conclusion. In contrast to other CMV antigens, such as glycoprotein B, pUL32 was found to be highly conserved among clinical CMV strains. The function of pUL32 appears to be essential to CMV considering the low evolutionary rate of UL32 despite a presumably strong host immune pressure. Incorporation of pUL32 into novel vaccine strategies has the potential to generate a strong immune response in all vaccinated individuals.