Evidence for the origin of CCR5 Delta32 mutation: detection of hot spot of DSBs in blood cells in the region of the gene where the deletion occurs

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CCR5 gene specifies CCR5 chemokine receptor that is used by HIV-1 and some other viruses to enter CD4+ T cells especially during initial infection. It was found that in Europe and western Asia average frequencies of the deletion of precisely the same 32 nucleotides (delta 32) in the gene changing the open reading frame are about 10% (see Novembre et al., PLoS Biol., 2005 and the references therein). The mechanism that is responsible for the origin of the deletion is not known yet. We hypothesized that physiological hot spots of DSBs in this particular site of the gene could serve as a natural genome edition tool. To test the supposition we used quantitative PCR across a putative region possessing hot spots of DSBs (Tchurikov et al., JMCB, 2015). Two short adjacent DNA fragments of the CCR5 gene, one of which spans the delta 32 region were amplified. A pair of DNA samples was used for amplification with two sets of DNA primers. One template was DNA isolated from blood, and another – PCR amplified DNA from the same cells covering the whole region selected for analysis. The DNA does not possess the delta mutation. In these experiments we detected that both regions are amplified at the same rate only if PCR-synthesized DNA was used. When the DNA from blood cells was used as a template, we reproducibly observed about 20-30% lower rate of amplification of the fragment spanning the region of delta 32 region. The data suggest the presence of hot spots of DSBs in the region of CCR5 gene where delta 32 resides. The data are consistent with the idea that the hot spots of DSBs and subsequent non homologous recombination could be responsible for the origin of delta 32 deletion. The study was supported by the grant from Russian Science Foundation No. 21-14-00035.