論 文 審 査 の 結 果 の 要 旨

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（論文審査の結果の要旨）

Epstein-Barr virus (EBV) is a ubiquitous virus in humans and latently infects B cells. In some individuals, however, EBV develops chronic active infection (CAEBV) and causes life-threatening complications due probably to cytokinenemia induced by EBV-infected T or natural killer (NK) cells. Profiles of EBV latent gene expression in EBV-infected T and NK cells show variations, and only EBV nuclear antigen-1 and EBV-encoded small non-polyadenylated RNAs (EBERs) are commonly expressed in non-neoplastic infected T and NK cells in CAEBV. Therefore, we investigated the function of EBERs in human T cell lines.

The plasmid coding EBERs was introduced into human T lymphocyte virus-I-negative human T-cell lines in a site-directed manner by using Flp recombinase–mediated integration kit Flp-In™ System, and stable transformants were established. The alteration of cytokine expression in EBERs-expressing transformants was examined by real-time RT-PCR analyses. The activation of the downstream signaling cascade from dsRNA were examined by Western blot analyses. Accordingly, the current study has revealed the function of EBERs in human T cell lines as follows:

1. The transformants of MOLT-14 cells (γδ T cells) expressed EBERs, but the transformant of Jurkat and MOLT-4 cells (both αβ T cells) did not.
2. EBERs-expressing MOLT-14 cells produced the larger amount of interleukin (IL)-10 than that from the mother cell line.
3. The mRNA expression of tumor necrosis factor α, interferon γ, and IL-1β in MOLT-14 cells did not affected by EBERs.
4. The phosphorylation of dsRNA-dependent protein kinase (PKR) and that of IκBα□ which act in the downstream of PKR, increased in EBERs-expressing clones.

In conclusion, EBERs expressed in stable transformants seemed to function in T lineage cells, but, did not induce the cytokine with macrophage-activating activities. The production of IL-10 through EBERs expression, however, might initiate other human immune diseases with unknown etiology.

以上の論文審査の結果、主査、副査は一致して本論文を学位論文として価値があるものと認めた。