2-5.

The prevalence of Merkel cell polyomavirus in primary eyelid Merkel cell carcinomas and association with clinical and histopathological characteristics

（大学院博士課程 2 年眼科学分野）
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【Background】 Merkel cell carcinoma（MCC）is a rare malignant tumor, and 2.5% of all MCCs occur in the eyelid. Merkel cell polyomavirus（MCPyV）infection is known to be a critical risk factor for the development of MCC. Various reports on cutaneous MCC have shown that the differences in clinicohistopathological characteristics depend on the presence of MCPyV, but the situation in eyelid MCC is unknown. This study aimed to assess the prevalence of MCPyV in patients with eyelid MCC and examine the clinical and histopathological characteristics of MCPyV-associated eyelid MCC.

【Method】 Nine patients treated for eyelid MCC between 2006 and 2021 were included in this retrospective study. Clinical data were retrieved from medical records. Histopathological characteristics of eyelid MCCs were examined by immunohistochemical staining using 12 antibodies. MCPyV infection was evaluated using various PCR primer sets and two immunohistochemical markers, and MCPyV viral load was quantified.

【Result】 All patients were Japanese with mean age of 76.4 years. Six patients were classified as stage I, and three patients as stage II. One patient died of distant metastatic disease eight months after surgery for MCC. Immunohistochemistry showed typical MCC findings of CK20 and neuroendocrine marker positivity. PCR and immunohistochemistry detected MCPyV antigen in all patients, and quantitative PCR confirmed high viral loads in all samples.

【Conclusion】 We confirmed the high prevalence of MCPyV in eyelid MCC. These findings are valuable information to understand the pathophysiology of eyelid MCC.

2-6.

LAG-3-mediated trogocytosis of MHC class II indirectly regulates CD4$^+$ T cell activation

（免疫学）
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LAG3 is one of the co-inhibitory receptors to regulate T cell activation and well-known to bind to MHC class II（MHC-II）. Since LAG-3 is involved in several diseases such as autoimmune diseases and cancer, LAG3 is focused as a therapeutic target of them. However, it remains unclear how LAG3 actually suppresses T cell activation. We here attempted to clarify this issue using a molecular imaging analysis. LAG3 on CD4$^+$ T cells translocated into TCR signalosomes, known as “microclusters”, and accumulated at the center of the immunological synapse forming a cSMAC dependently on LAG3-MHC-II binding. As similar behavior to LAG-3, MHC-II complexes bearing not only cognate peptides but also non-cognate ones accumulated at the cSMAC by interaction between MHC-II and LAG3 on CD4$^+$ T cells. These peptide-MHC-II complexes at the cSMAC were subsequently trogocytosed into LAG3-expressing CD4$^+$ T cells in a clathrin-dependent manner, leading to the reduction of MHC-II molecules on antigen-presenting cells. Furthermore, we demonstrated that LAG-3-expressing CD4$^+$ T cells indirectly suppressed CD4$^+$ T cell responses both in vitro and in vivo. These data indicate a novel mechanism of indirect suppression of CD4$^+$ T cell activation, in which T cells expressing LAG3 captures MHC-II from APCs in the trogocytotic and also peptide-independent manner.