

order to thrive. Interestingly, we revealed a dramatic increase of immature granulocytes only in bone marrow of EBV-infected mice. In addition, GM-CSF, a cytokine that is essential for differentiation of the myeloid lineage, was significantly increased in EBV-infected mice. These results were also reproduced in patients with EBV-related disorders.

This research revealed that abnormal hematopoiesis was occurred in mice following EBV infection. Considering the above results, the hematopoietic alteration might be involved in a cause of lymphoproliferative disorders in human by reduction of tumor immunity.

## 2-3.

### Expression of intracellular cytokines in twins with intractable epilepsy associated with lissencephaly

(社会人大学院博士課程2年小児科・思春期科学分野)

○高松 朋子

(小児科・思春期科学分野)

山中 岳、春日 晃子、竹下 美佳

森地振一郎、石田 悠、小穴 信吾

柏木 保代、河島 尚志

(医学総合研究所 免疫制御研究部門)

溝口 出、善本 隆之

**Purpose :** Involvement of immunological processes in the pathogenesis of epilepsy has been suggested on the basis of accumulating evidence. This study aimed to determine whether twins presenting with intractable epilepsy exhibited immune system dysfunctions. Despite sharing a common diagnosis of lissencephaly and the same genetic mutation, the twins had different developmental prognoses: twin A had a severe developmental delay, while twin B had a moderate developmental delay.

**Methods :** Through flow cytometry, we examined the intracellular cytokine profiles of peripheral blood mononuclear cells collected from the twins and their plasma cytokine levels in reference to two age-matched controls.

**Results :** The twins had a higher percentage of interleukin-1 beta (IL-1 $\beta$ )-positive CD14<sup>+</sup> monocytes

than the controls. Twin A had higher percentages of IL-1 receptor antagonist (IL-1RA)-positive and tumor necrosis factor-alpha (TNF- $\alpha$ )-positive CD14<sup>+</sup> monocytes than twin B and the controls. The plasma cytokine levels of IL-1 $\beta$ , IL-1RA, and TNF- $\alpha$  were lower in twin A than in twin B and the controls.

**Conclusions :** While a slight difference in the proportions of cytokine-producing cells between the twins was observed, it is unclear how this difference is involved in their respective pathophysiology. Further studies with more patients should assess whether minor differences in the number of cytokine-producing cells can influence the pathogenesis of intractable epilepsy.

## 3-I-1.

### DNA-damaging drugs in combination with a macrolide antibiotic enhance cytotoxicity for non-small cell lung cancer cells

(大学院博士課程3年呼吸器内科学分野)

○鳥山 和俊

(呼吸器内科)

阿部 信二

(生化学)

高野 直治、風間 宏美、森谷 昇太

宮澤 啓介

For the treatment of lung cancer, new drugs such as tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors are being developed one after another, but patients who show interstitial pneumonia or do not carry gene mutations of targets for each TKIs are not applicable for them. Therefore, conventional DNA-damaging drugs are still useful for such patients. In recent years, it has been revealed that cancer cells utilize autophagy for their own growth and that autophagy acts cytoprotectively when cancer cells are exposed to anticancer drugs. Because hydroxychloroquine (HCQ) is the only clinically available autophagy inhibitor but causes severe retinopathy and cardiomyopathy, the development of other autophagy inhibitors is desired. Our group has been reported that macrolide antibiotics have an autophagy inhibitory effect and that their combined use with TKIs or proteasome inhibitors