A Clinical study on activity of NAMPT and SIRT1 gene expression in neutropenia with cancer chemotherapy

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Background: Neutropenia with cancer chemotherapy frequently causes the delay of treatment, dose reduction and febrile neutropenia. However, the risk factor of the neutropenia is still unclear. It was reported that nicotinamide phosphoribosyltransferase (NAMPT) activity and sirtuin 1 (SIRT1) gene expression noticing NAD-SIRT1 pathway were essential for differentiation of neutrophil mediated by granulocyte-colony stimulating factor.

Method: We measured the activity of NAD-SIRT1 pathway and vitamin B3 (VB3) which is a substrate of NAMPT in cancer patients and examined correlations with transition of neutrophil and grade 4 neutropenia due to chemotherapy. The activity of NAMPT in patient plasma was measured by ELISA, and SIRT1 gene expression in mononuclear fraction was measured by real-time PCR.

Results: A total of 21 chemo-naive small and non-small cell lung cancer patients were enrolled. We obtained blood samples at before, 2, 4 days of starting treatment, nadir and before starting 2nd course treatment. The activity of NAMPT at before the treatment was significantly lower in the group of grade 4 neutropenia (N = 9) than the group which did not occurred neutropenia (N = 12) (0.69 vs 1.63 ng/mL, p = 0.003). The SIRT1 gene expression and plasma concentration of VB3 were not significantly difference between these two groups. By the comparison with the healthy volunteer, NAMPT activity was significantly higher in cancer patients, however, there was no statistical difference in the grade 4 neutropenia group.

Conclusion: In this study, we showed the possibility that NAMPT activity before the treatment was the predictive factor of the neutropenia with cancer chemotherapy. It will be necessary to confirm a role of NAD-SIRT1 pathway in cancer patients receiving chemotherapy, and evaluate the association between NAMPT activity and patient backgrounds.