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学位論文の題名	A folylpoly-γ-glutamate synthase single nucleotide polymorphism associated with response to pemetrexed treatment combined with platinum for non-small cell lung cancer （非小細胞肺癌治療におけるプラチナ製剤併用ペメトレキセド治療の反応性に関連のある folylpoly-γ-glutamate synthase の遺伝子多型） Lung Cancer. 102: 15-20, 2016
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Abstract

Objectives: In this study, we investigated whether single nucleotide polymorphisms (SNPs) in folylpoly-γ-glutamate synthase (FPGS), which catalyzes the polyglutamation of pemetrexed (PEM), is related to FPGS expression and the response to PEM in non-small cell lung cancer (NSCLC).

Materials and Methods: We first examined FPGS protein expressions according to FPGS SNPs genotype groups in 15 lung adenocarcinoma cell lines. Next, 101 non-squamous NSCLC patients treated with PEM and platinum drugs were classified into FPGS SNP genotype groups to investigate the relation between FPGS SNP genotypes and treatment outcome.

Results: When the 15 adenocarcinoma cell lines were classified into FPGS SNP 2572C>T genotype groups, we found that the FPGS protein expression was significantly higher in the CC genotype group than in the TT+CT genotype group ($p = 0.0022$). In contrast, there was no significant difference in FPGS expression when another FPGS SNP was analyzed. We also examined the FPGS SNP 2572C>T genotype in 101 non-squamous NSCLC patients treated with PEM and platinum drugs. Among these 101 patients, response rate was significantly higher in the CC genotype group than in the TT+CT genotype group ($p = 0.0034$). When we examined the patients treated with PEM, platinum drugs and Bev, almost all (29/33) were classified into the TT+CT genotype group. The response rate, progression-free survival, and over-all survival were all significantly better in the patients of the TT+CT genotype group who also received Bev than in those who did not receive Bev ($p = 0.034, 0.021, 0.018$, respectively).

Conclusion: FPGS SNP 2572C>T is a predictive marker of the efficacy of PEM and platinum drugs for NSCLC.