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学位論文の題名	ZNF671 DNA methylation as a molecular predictor for the early recurrence of serous ovarian cancer (ZNF671 の DNA メチル化は漿液性卵巣がん早期再発の予測因子である) Cancer Science 2019;
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<Background> Serous ovarian cancer is the most frequent type of epithelial ovarian cancer. Despite the use of surgery and platinum-based chemotherapy, many patients suffer from recurrence within 6 months, termed platinum resistance. Currently, the lack of relevant molecular biomarkers for the prediction of the early recurrence of serous ovarian cancers is linked to the poor prognosis.
<Method> To identify an effective biomarker for early recurrence, we analyzed the genome-wide DNA methylation status characteristic of early recurrence after treatment.
<Result> The patients in The Cancer Genome Atlas (TCGA) dataset who showed a complete response after the first therapy were categorized into 2 groups: early recurrence serous ovarian cancer (ERS, recurrence ≤12 months, n = 51) and late recurrence serous ovarian cancer (LRS, recurrence >12 months, n = 158). Among the 12 differently methylated probes identified between the 2 groups, we found that ZNF671 was the most significantly methylated gene in the early recurrence group. A validation cohort of 78 serous ovarian cancers showed that patients with ZNF671 DNA methylation had a worse prognosis (P < .05). The multivariate analysis revealed that the methylation status of ZNF671 was an independent factor for predicting the recurrence of serous ovarian cancer patients both in the TCGA dataset and our cohort (P = .049 and P = .021, respectively). Functional analysis revealed that the depletion of ZNF671 expression conferred a more migratory and invasive phenotype to the ovarian cancer cells.
<Conclusion> Our data indicate that ZNF671 functions as a tumor suppressor in ovarian cancer and that the DNA methylation status of ZNF671 might be an effective biomarker for the recurrence of serous ovarian cancer after platinum-based adjuvant chemotherapy.