[Format-H07]

論文審査の結果の要旨及び担当者

（申請者氏名）Tzvetozar Roussev Mehandjiev

論文審査担当者	（職）	氏　名
主　査	大阪大学教授	木村正
副　査	大阪大学教授	古井英一
副　査	大阪大学教授	大薗恵一

論文審査の結果の要旨

流産歴のある243人の患者で、メチレンテトラヒドロ葉酸還元酵素（MTHFR）のC677T多型について遺伝子型決定を行った。脱落膜と絨毛間腔の血栓と線維化をグレード０－３に分類して解析を行ったところ、TT遺伝子型とTアレルはグレード３の血栓や線維化に対して保護的に作用することを見出した。これらの症例について、MTHFRのC677T多型検査やそれに基づく適切な治療を受けるべきことが示唆されることから
学位に値するものと認める。

論　文　内　容　の　要　旨
Synopsis of Thesis

氏　名 Name	Tzvetozar Roussev Mehandjiev
論文題名 Title	Impact of maternal methylenetetrahydrofolate reductase C677T polymorphism on intervillous and decidual pathology with pregnancy loss （メチレンテトラヒドロ葉酸還元酵素遺伝子C677T多型が流産における絨毛間腔部および脱落膜病変に与える影響）

論文内容の要旨

〔目　的(Purpose)〕

The association between methylenetetrahydrofolate reductase (*MTHFR*) C677T polymorphism and intervillous and decidual pathology in patients with pregnancy loss (PL) was investigated.

〔方法ならびに成績(Methods/Results)〕

Methods: We performed a cross-sectional study on 243 patients presenting with pregnancy loss for the degree of intervillous fibrin (IF) and thrombosis (IT), and decidual fibrin (DF) and thrombosis (DT) and determined their *MTHFR* C677T genotypes. Overall differences in age, body mass index (BMI), gravidity, parity, number of pregnancy losses, and gestational period when the pathologic samples were obtained, also were determined. *Results*: There were no significant differences in age, BMI, gravidity, parity, number of pregnancy losses, and gestational period, relative to *MTHFR* C677T genotype (TT vs. CT vs. CC). There were significantly more T allele carriers and TT genotype patients among patients with severe IT (odds ratio [OR], 1.653; $P = 0.033$ and OR, 2.246; $P = 0.032$, respectively) and those with severe IT and DT (OR, 2.602; $P = 0.012$ and OR, 3.375; $P = 0.035$, respectively). The CC genotype was protective against the four studied pathologic grades.

〔総　括(Conclusion)〕

To our knowledge, this is the first study showing that the *MTHFR* C677T TT genotype and T allele are associated with severe intervillous and decidual pathologies in patients with pregnancy loss. Differences in pathologic grades of *MTHFR* C677T TT genotype could support the hypothesis that further periconceptional treatment for pregnancy loss could be customized depending on single nucleotide polymorphisms.