学位の種類	博士（医学）
報告番号	甲第１６０３号
学位記番号	第１１３８号
氏名	堀　いくみ
授与年月日	平成 30 年 3 月 26 日
学位論文の題名	CTCF deletion syndrome: clinical features and epigenetic delineation (CTCF 遺伝子欠失を認めた 2 女児の臨床的および遺伝学的検討) Journal of Medical Genetics. 2017;54: 836-842
論文審査担当者	主査：　杉浦 真弓 副査：　岡本 尚, 齋藤 伸治

ABSTRACT

Heterozygous mutations in *CTCF* have been reported in patients with distinct clinical features including intellectual disability. However, the precise pathomechanism underlying the phenotype remains to be uncovered, partly because of the diverse function of CTCF. Here we describe extensive clinical and genetic investigation for two patients with a microdeletion encompassing *CTCF*. We performed genetic examination including comprehensive investigation of X chromosome inactivation and DNA methylation profiling at imprinted loci and genome-wide. Two patients showed comparable clinical features to those in a previous report, indicating that haploinsufficiency of *CTCF* was the major determinant of the microdeletion syndrome. Despite the haploinsufficiency of *CTCF*, X chromosome inactivation was normal. DNA methylation at imprinted loci was normal, but hypermethylation at CTCF binding sites was demonstrated, of which *PRKCZ* and *FGFR2* were identified as candidate genes. This study confirms that haploinsufficiency of *CTCF* causes distinct clinical features, and that a microdeletion encompassing *CTCF* could cause a recognizable *CTCF* deletion syndrome. Perturbed DNA methylation at CTCF binding sites, not at imprinted loci, may underly the pathomechanism of the syndrome.