DNA methylation provides the allele specific inactivation of the imprinted gene, p57KIP2

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Genomic imprinting results in parental-specific monoallelic expression and its alteration is known to involve several genetic diseases. The p57KIP2 gene in 11p15.5 encodes a KIP family CDK inhibitor and is reported to be imprinted. The region surrounding p57KIP2 has been implicated for both the Beckwith-Wiedemann Syndrome (BWS) and various cancers. To elucidate the mechanism for inactivation of one allele, cells were treated with DNA demethylation agent or histone deacetylase inhibitors. Only the cells treated with DNA demethylation agent showed the biallelic expression of p57KIP2, indicating that one allele is inactivated by DNA methylation. DNA methylation status in promoter of the p57KIP2 gene was tested by digestion with methylation-sensitive restriction enzymes and a subsequent PCR. DNA from normal fibroblast showed the presence of methylation. DNA from demethylation agent-treated fibroblast showed no methylation as expected. PCR analysis of polymorphic proline-alanine repeat region revealed that only one allele of this region was methylated and the transcription was made from only unmethylated allele. This result suggests that inactivation of one allele by DNA methylation explains the genetic nature for imprinting of the p57KIP2 gene.