Is p57KIP2 mutation a common mechanism for Beckwith-Wiedemann syndrome or somatic overgrowth?

A genetic locus within the chromosome 11p15.5 region has been implicated in the Beckwith-Wiedemann syndrome. C H19 and insulin-like growth factor II (IGF2) play important roles in regulating embryonic growth and are strong candidate genes for the BWS. Both genes are imprinted and located approximately 90 kb apart within the chromosome 11p15.5 region, which frequently undergoes paternal uniparental isodisomy in BWS patients. Loss of imprinting of IGF2/H19 has been found in Wilms tumour and rhabdomyosarcoma, which form part of the BWS. Similar constitutional epigenetic changes have been implicated in the pathogenesis of BWS and detected in some children with non-syndromic overgrowth. p57KIP2 is another imprinted gene which is located within the chromosome 11p15.5 region and is located within 400 kb centromeric to IGF2. Recently, two cases of p57KIP2 mutation were reported in nine cases of Beckwith-Wiedemann syndrome (BWS). Furthermore, a recent report showed that various phenotypic features of the BWS were present in mice homozygous for a p57KIP2 deletion, such as omphalocele, renal medullary dysplasia, and adrenal cortical hyperplasia. p57KIP2 therefore represents another strong candidate 11p15.5 gene for the BWS, so we have investigated whether p57KIP2 mutations are common in BWS and whether mutations can be involved in other overgrowth disorders which are sometimes associated with Wilms tumour. This analysis included 40 cases of BWS (including five familial cases), three cases of hemihyperplasia (one case with Wilms tumour), and 11 cases with extensive somatic overgrowth (one case with Wilms tumour).