BMT from an affected donor in a presymptomatic phase. Identification of PRF1 gene mutations allows diagnostic confirmation, correct genotype determination in the family, confirmed indication for BMT even from alternative donors, proper genetic counselling, and prenatal diagnosis. A detailed genotype-phenotype correlation cannot be performed until a much larger number of patients with and without PRF1 mutations are identified.

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A novel mutation in the endothelin B receptor gene in a patient with Shah-Waardenburg syndrome and Down syndrome

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EDITOR—A case of Down syndrome, total gut Hirschsprung disease (HSCR), and segmental hypopigmentation is described in a neonate presenting with bowel obstruction. In addition to having trisomy 21, this patient was homozygous for a novel mutation in the endothelin B receptor (EDNRB) gene.

A term female infant with karyotype 47,XX,+21 presented on day 3 of life with bowel obstruction. She was of Somali origin and had large areas of segmental hypopigmentation affecting the left side of the face and trunk, the left upper limb, including the hair follicles, and had white scalp hair. At laparotomy she had an annular pancreas, duodenal web, and inspissated meconium in the ileum and colon, for which she underwent a duodenal resection. Histology of the rectal biopsy and appendix was inconclusive at this stage. Intestinal obstruction persisted and on day 20 she underwent a further laparotomy, which showed breakdown of the original anastomosis. Intraoperative frozen sections showed complete aganglionosis throughout the entire large and small bowel, sparing only the stomach and oesophagus; this is incompatible with life. An ileostomy was fashioned, intensive care was withdrawn, and the baby died the following morning. Necropsy confirmed total bowel aganglionosis. Her parents are not known to be consanguineous and there is no history of pigmentary disturbance or bowel disease in either them or her five sibs. Family genetic studies and clinical photographs were declined; a hearing assessment was precluded by her being ventilated and sedated for the duration of her life.

Shah-Waardenburg syndrome describes the association of HSCR with Waardenburg syndrome, and consists of deafness, pigmentary disturbance, and aganglionic megacolon. It is the result of defective development of two neural
The exact position of the mutation in the homozygous state is likely to produce the pleiotropic features observed in these patients.

There are case reports of patients with Down syndrome in association with both HSCR and/or Shah-Waardenburg determining genes. However, this patient had the coexistence of Down syndrome and a novel homozygous mutation of the EDNRB gene. This case emphasises that although HSCR has a well-recognised association with Down syndrome, other causes of HSCR should be considered. Mutation analysis of known susceptibility genes might be helpful in cases of long segment HSCR, especially in those patients with pigmented abnormalities and those with a positive family history of bowel dysfunction.