

P003 Phenotype associated with mutations in the *PMS2* gene
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Recessive mutations in the DNA MMR genes have been occasionally described. We report details on 9 families with recessive mutations in the *PMS2* gene. The phenotype associated with these mutations comprises Café au Lait patches and a characteristic cancer pattern. Haematological malignancies often of T-Cell subtype are seen in the first decade of life. Brain tumours, particularly supratentorial primitive neuroectodermal tumours (S-PNET) are seen later. Colorectal tumours and multiple colorectal polyps are seen in adolescence and in the 20s. S-PNET are extremely rare, 10 cases per year in the UK. The association with *PMS2* is striking; MMR defects have not previously been described in this group of tumours. This is a novel mechanism in childhood brain tumour. Six of our cases are of Pakistani origin. Five of the cases carry the same mutation, R802X in the *PMS2* gene. Haploypye analysis indicates this has arisen as a founder mutation in this population. All five of these families originate from the Mirpur region of North Eastern Pakistan. The sixth case originates from a different area and carries a different mutation. We describe a novel and distinct cancer predisposition syndrome and show that in the Pakistani population in the UK a founder mutation has given rise to recurrent cases.