# 3'UTR poly(T/U) tract deletions and altered expression of EWSR1 are a hallmark of mismatch repair deficient cancers



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The genome-wide accumulation of DNA replication errors known as microsatellite instability (MSI) is the hallmark lesion of DNA mismatch repair (MMR) deficient cancers. Although testing for MSI is widely used to guide clinical management, the contribution of MSI at distinct genic loci to the phenotype remains largely unexplored. Here we report that a mononucleotide (T/U)16 tract located in the 3' untranslated region (3'UTR) of the Ewing sarcoma breakpoint region 1 (EWSR1) gene is a novel MSI target locus that shows perfect sensitivity and specificity in detecting mismatch-repair deficient cancers in two independent populations. We further found a striking re-localization of the EWSR1 protein from nucleus to cytoplasm in MMR-deficient cancers, and that the non-protein coding MSI target locus itself has a modulatory effect on EWSR1 gene expression through alternative 3' end processing of the EWSR1 gene. Our results point to a MSI target gene-specific effect in MMR-deficient cancers.
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