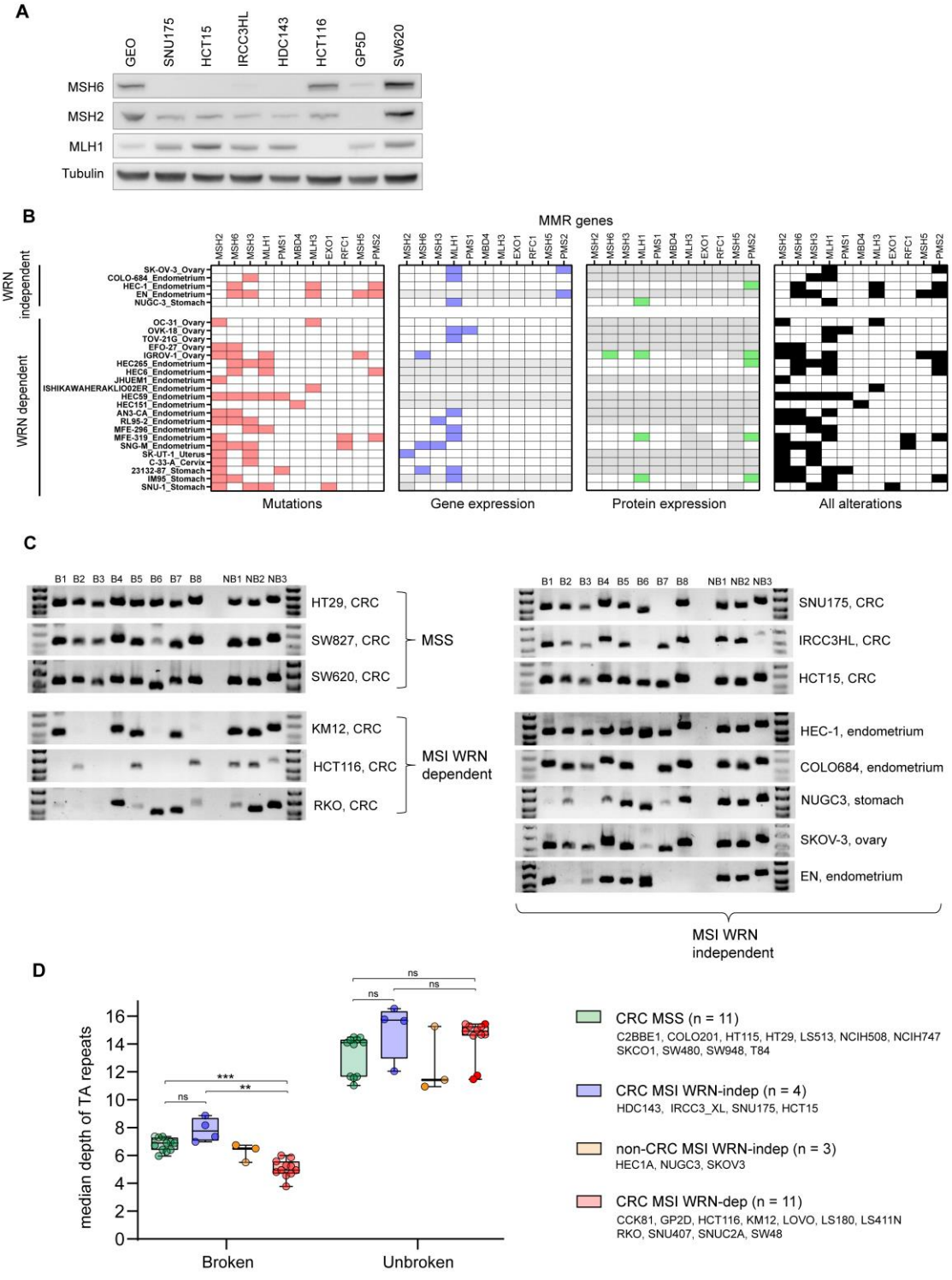

Supplementary Figure 2. Molecular and TA-repeats coverage analysis in MSI-H WRN independent cell lines. ***A****, Validation of MLH1, MSH2 and MSH6 protein expression measured by Western blot in a set of WRN independent MSI dMMR CRC cancer cell lines (images are representative of two independent experiments). SW620 (pMMR/MSS), HCT116 (MLH1 loss) and GP5D (MSH2 and MSH6 loss) were included as positive controls for protein expression.* ***B****, Mutations, gene expression and protein expression alterations of MMR-pathway genes in cancer models from non-CRC dMMR/MSI-predominant lineages. Coloured (red, blue, green and light black) box indicates the presence of the alteration, light grey boxes represent data unavailable.* ***C****, Agarose gels of PCR*

fragments (or lack thereof) at (TA)n repeats in CRC and non-CRC cell lines as indicated. B1–B8 sites were reported as recurrently broken after WRN downregulation in KM12 and HCT116 cells, NB1–NB3 regions did not display any breakage and are included as a negative control for expanded repeats. Data are representative of two independent experiments. ***D****, Box and whisker plots displaying the median sequencing depth of broken and not-broken (TA)-repeat loci in WGS data from MSS and MSI cancer cell lines, as indicated. For coverage analysis, WGS data were unavailable for IRCC3_HL and so we used WGS sequencing data for IRCC3-XL, which is a primary cell line derived from a patient-derived xenograft generated from the same biopsy as IRCC3_HL.*