**Legend for Supplementary Figure**

**Supplementary Figure 1** Differential methylation analysis revealed HR gene promoter methylation in MPNs-LT

**A)** Flow chat illustrating the pipeline of differential methylation analysis in 241 DDR genes.

**B)** Bisulfite treatment and qPCR quantification of RAD50, POLD1, TOP3B and FEN1 promoter methylation in an in-house cohort of 5 MPNs-LT, 75 cMPNs, and 50 healthy donors (two-sample *t*-test, \*\*\**P* < 0.001, \*\*\*\**P* < 0.0001, n.s. not significant).

**Supplementary Figure 2** Single base substitution mutational signature in cMPNs and MPNs-LT

**A)** Comparison of mutational signature 1 (aging), 5 (transcriptional strand T>C substitutions), 6 (mismatch repair deficiency), 12 (unknown aetiology), 20 (mismatch repair deficiency), and 21 (unknown aetiology) between cMPNs and MPNs-LT. (two-sample *t*-test, \**P* < 0.05, n.s. not significant).

**B)** Correlation between mutational signature 5 and signature 3 in the in-house MPNs cohort.