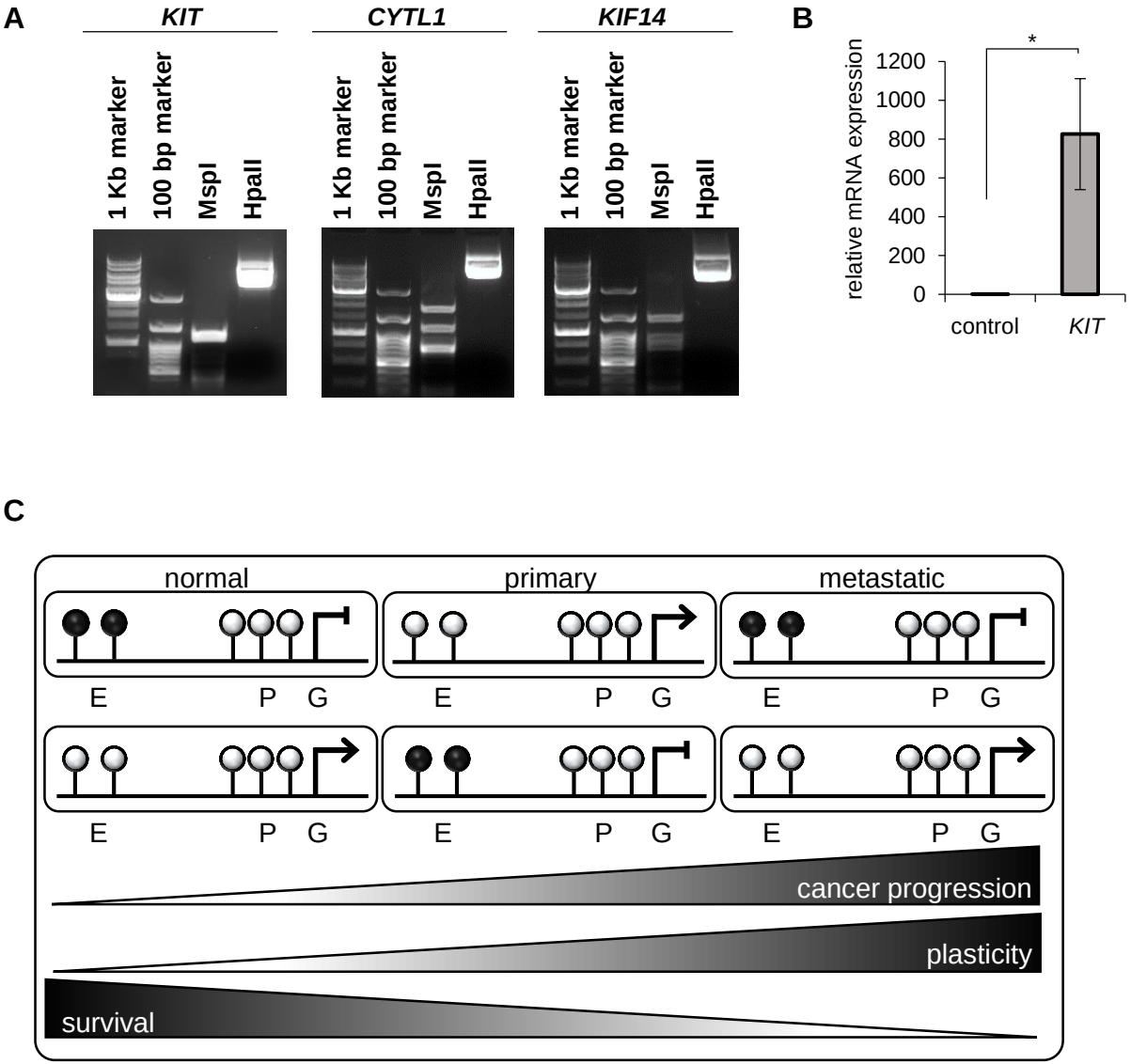

Supplemental Figure S4: Methylation plasticity of melanoma eDMRs is associated with patient mortality

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(A) Validation of in vitro methylation. Luciferase reporter vectors were digested with methylation-sensitive and methylation-insensitive enzymes HpaII and MspI, respectively. The digestion patterns were analyzed on 1% agarose gel electrophoresis. (B) WM3682 melanoma cells were transfected with KIT expression vector or empty vector (control). KIT mRNA expression levels were determined by qRT-PCR and were normalized to levels of GAPDH. Fold changes relative to control are shown. Error bars represent ± SEM, * indicates $P<0.05$ ($N=3$). (C) Model depicting the mechanism by which enhancer ('E') methylation patterns provide an additional layer of epigenetic plasticity in cancer, while promoter ('P') methylation levels remain static. As cancer progresses, cancer plasticity increases, which includes methylation plasticity: enhancers ('E') switch their patterns of methylation, altering their target genes ('G'). Our data suggests that methylome plasticity promotes cancer progression and patient mortality.