The peak of DNAm centered roughly at 0.5 mirrors the effect of partially methylated domains seen in cancer36 (**Fig. 1**), additionally the global hypomethylation and local hypermethylation of DNAm have been seen previously in cancer39–42. We looked at a previously characterized list of cancer differentially methylated regions (cDMRs)35. These cDMRs were defined as having differential DNAm in the colon between healthy and colorectal cancer samples. We see these cDMRs change in the same direction in cancer and with increasing passage. Our hypomethylated passage CpGs are significantly enriched in cDMRs with less DNAm in cancer, and were significantly depleted in cDMRs which have more DNAm in cancer (**FDR <0.05, Fig. 2b**). The opposite was seen for hypermethylated passage CpGs (**FDR <0.05, Fig. 2b**). Heteroskedastic passage CpGs were enriched in cDMRs with less DNAm in cancer (**FDR <0.05, Fig. 2b**), suggesting with passage cDMRs become differentially DNAm similar to colorectal cancer.

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