SUPPLEMENTAL DATA:

GALACTIC COSMIC RADIATION INDUCES PERSISTENT EPIGENOME ALTERATIONS RELEVANT TO HUMAN LUNG CANCER

E.M. Kennedy¹,²#, D.R. Powell³#, Z. Li⁴, J.S.K. Bell¹,³†, B.G. Barwick³, H. Feng², M.R. McCrany³, B. Dwivedi⁵, J. Kowalski⁵,⁶, W.S. Dynan³,⁴,⁶, K.N. Conneely¹,²,⁵ and P.M. Vertino³,⁶*

¹Graduate Program in Genetics and Molecular Biology, Departments of ²Human Genetics, ³Radiation Oncology, and ⁴Biochemistry, Emory University School of Medicine; ⁵Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University; and ⁶the Winship Cancer Institute of Emory University, Atlanta, GA 30322
**Supplemental Figure 1. Time-dependent methylation drift**

a) Comparison of the average methylation (β-value) of each CpG site in the X ray-exposed cohort at the indicated time-after-exposure relative to that on Day 2. Red indicates those CpGs that are significantly hypermethylated with time (n=2,294); green are those sites significantly hypomethylated with time (n=647; p<1e-7).

b) A linear mixed effects model was applied to identify DNA methylation changes significantly associated with time-after-exposure for each exposure type. Shown are scatter plots comparing the significance and direction of change (t-statistics) for CpG sites at which methylation changed significantly with time-after-exposure in the $^{28}$Si exposed series, the $^{56}$Fe exposed series, and the X ray exposed series. A positive t-statistic indicates a gain in methylation (hypermethylated) and a negative t-statistic indicates a loss of methylation (hypomethylation). Light green indicates sites reaching an FDR<0.05 (Benjamini-Hochberg) and blue are those reaching Holm significance (p<1e-7).

c) Venn diagrams comparing the overlap of CpG sites whose methylation change was significantly associated with time in culture [FDR<0.05 (Benjamini-Hochberg)] in the $^{28}$Si exposed series, the $^{56}$Fe exposed series, and the X ray exposed series.

d) Average methylation level (β) over time among CpG sites negatively (left) or positively (right) associated with time stratified by $^{56}$Fe-ion dose. Analysis was restricted to those CpG sites found to be independently associated with both dose and time in the $^{56}$Fe-ion exposed series (n=91).