Supplemental Table 1. Public data on expression of genes annotated to methylated DNA markers (MDM): comparison between esophageal adenocarcinoma (EAC) and normal esophagus (NE). Median transcripts (per million log (base2)) and 95% confidence intervals are shown.

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| --- | --- | --- | --- | --- | --- |
| **MDM** | **Gene Function** | **EAC** | **NE** | ***p*-value** | **Expression** |
| *ARHGEF4* | Signal transduction/ cell cycle | 4.38 [2.53,5.95] | 5.75 [5.34,6.06] | 0 |  |
| *BMP3* | Growth factor | -4.29  [-6.51,-1.69] | -5.57  [-6.51,-4.04] | 0.000333 |  |
| *ELMO1* | Immune response/ Phagocytosis | 3.63 [2.74,4.74] | 2.42 [1.98,2.89] | 0 |  |
| *DMRTA2* | Transcriptional regulation | -0.860  [-5.01,1.68] | -9.97  [-9.97,-9.97] | 0.0000030 |  |
| *FER1L4* | Long noncoding  RNA | N/A | N/A | N/A | N/A |
| *IKZF1* | Transcriptional regulation | 1.26 [0.288,2.26] | 0.434  [-0.167,1.03] | 0 |  |
| *NDRG4* | Signal transduction/ cell cycle | 2.86 [1.60,4.81] | 4.55 [3.90,5.07] | 0 |  |
| *OPLAH* | Glutathione metabolism | 3.77 [3.10,4.34] | 4.07 [3.70,4.36] | 0.03821 |  |
| *ST8SIA1* | Carbohydrate metabolism | 0.112  [-1.12,1,21] | 0.596 [0.126,1.15] | 0.002379 |  |
| *TBX15* | Transcriptional regulation | -1.09  [-2.31,0.04] | -3.82  [-4.61,-3.05] | 0 |  |
| *TSPYL5* | Signal transduction/ cell cycle | 0.547  [-0.783,2.49] | 0.715 [0.323,1.14] | 0.3693 | **=** |
| *ZNF671* | Transcriptional regulation | 0.934 [0.072,1.59] | 0.92 [0.455,1.31] | 0.9151 | **=** |

MDM, methylated DNA marker; EAC, esophageal adenocarcinoma; NE, normal esophagus; N/A, not applicable; , down-regulated; , up regulated; **=**, no change in expression between cancer and normal.

Supplemental Table 2. In The Cancer Genome Atlas, hybridization array measured methylated DNA markers show significant association with esophageal cancer (ESCC and EAC combined) referent to other cancers.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Colon** | **Liver** | **Lung-**  **Adeno** | **Lung-Squamous** |
| **Δ DMRTA2** | -0.238 | -0.492 | -0.256 | -0.098 |
| **P-value** | <0.0001 | <0.0001 | <0.0001 | 0.0001 |
| **Δ ELMO1** | 0.0468 | -0.340 | -0.185 | -0.303 |
| **P-value** | 0.025 | <0.0001 | <0.0001 | <0.0001 |
| **Δ IKZF1** | 0.176 | -0.010 | -0.089 | -0.258 |
| **P-value** | <0.0001 | 0.986 | <0.0001 | <0.0001 |
| **Δ OPLAH** | 0.0379 | 0.0789 | -0.165 | -0.120 |
| **P-value** | 0.103 | <0.0001 | <0.0001 | <0.0001 |
| **Δ TBX15** | -0.024 | -0.106 | -0.116 | -0.069 |
| **P-value** | 0.429 | <0.0001 | <0.0001 | <0.0001 |
| **Δ TSPYL5** | 0.107 | 0.122 | -0.140 | -0.165 |
| **P-value** | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| **Δ ZNF671** | 0.0725 | -0.3422 | -0.322 | -0.142 |
| **P-value** | 0.0014 | <0.0001 | <0.0001 | <0.0001 |

Δ denotes the mean methylation difference between DNA samples extracted from aerodigestive tract cancers referent to esophageal cancer. Negative Δ values indicate greater methylation in esophageal cancers relative to each aerodigestive cancer. Methylation was measured as an average beta value, which is equivalent to methylation ratio from bisulfite sequencing. One way ANOVA with TukeyHSD was used to determine overall and pair-wise methylation differences among different cancer types for each MDM. Adjusted p-value for multiple testing compare differential methylation between each cancer and esophageal cancers.