Figure S1. (A) RT-qPCR analysis of the relative ADAM10 mRNA level in C33a-FL-CA IX cells transfected by esiADAM10 compared with control esiRLUC-transfected cells. Silencing resulted in a highly significant reduction in ADAM10 transcription. Data were analyzed by Student's t-test. (B) RT-qPCR analysis of transient overexpression of a DMP compared with control, mock-transfected cells. Data were analyzed by Student's t-test. (C) RT-qPCR analysis of ADAM10 absence and ADAM17 presence in CHO cells. (D) Effect of GI concentration on inhibition of ADAM17-mediated CA IX ECD shedding in CHO cells (from 0.1 to 100 μM GI). Data were analyzed by one-way ANOVA with Dunnett's test and showed significant effect of 10 μM GI, but non-significant effect of 1 μM GI. Results are expressed as the mean relative levels of mRNA or CA IX ECD ± SD. **P<0.01 and ***P<0.001. RT-qPCR, reverse transcription-quantitative PCR; ADAM, a disintegrin and metalloproteinase; FL, full length; CA IX, carbonic anhydrase IX; esi, enzymatically prepared; ΔMP, dominant-negative mutant of ADAM10; GI, GI254023X; ECD, ectodomain; ns, non-significant.

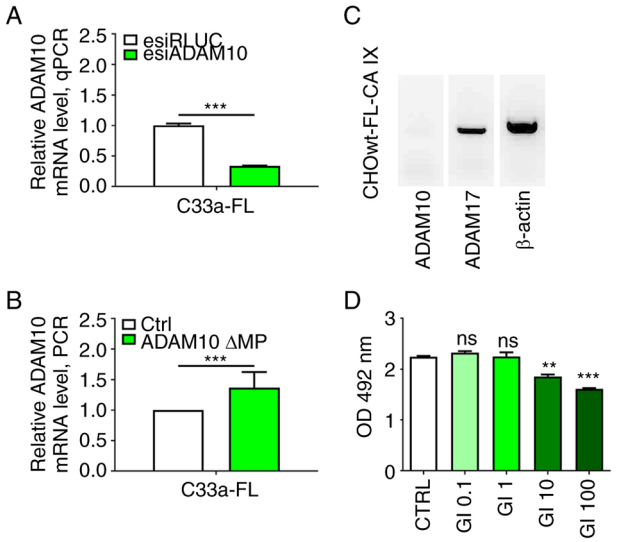

Figure S2. Schematic presentation of ADAM10 and ADAM17 promoter with indicated positions of predicted binding elements for selected transcription factors (adopted from MatInspector). The accurate position of predicted binding sites was calculated according to the transcription start site (indicated with arrow). ADAM, a disintegrin and metalloproteinase.

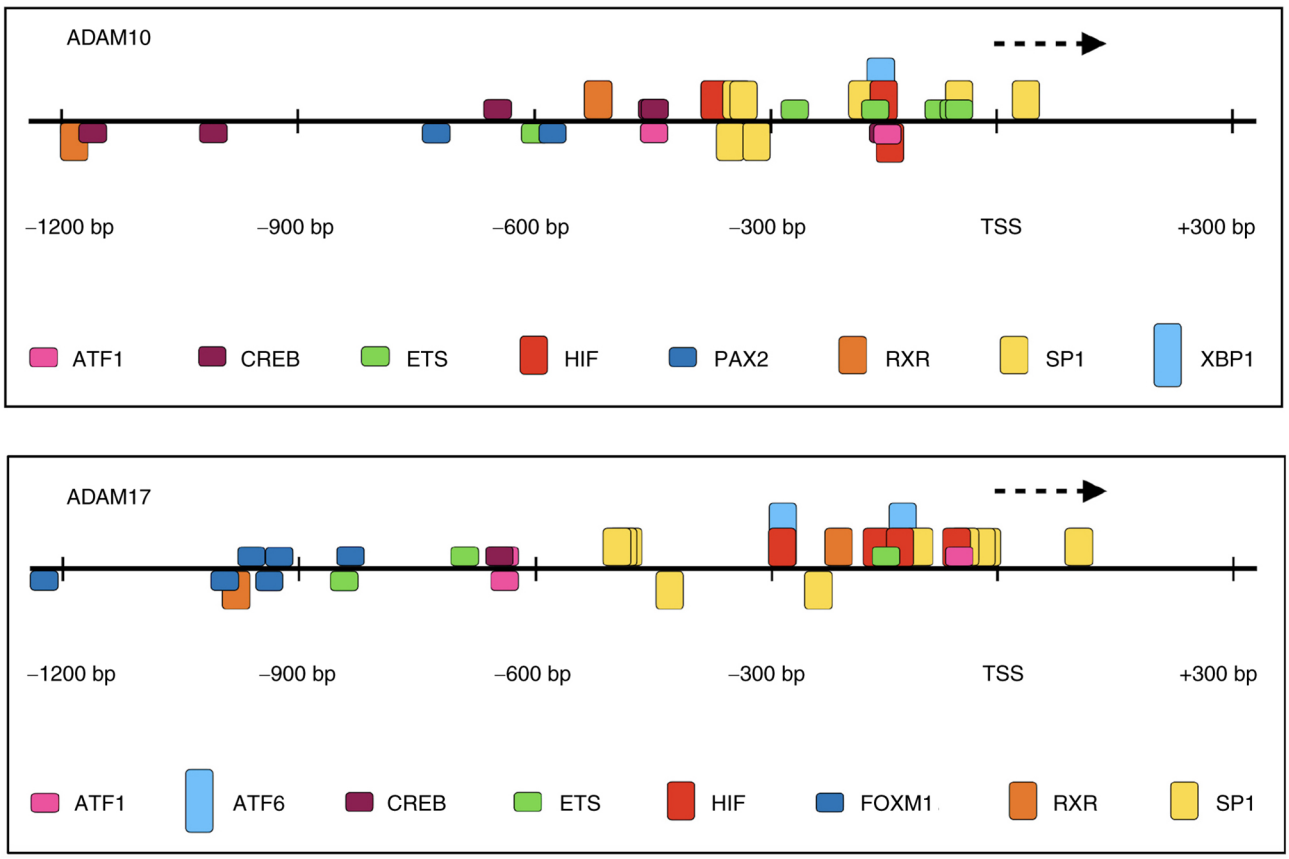

Figure S3. Transcription pattern of CA9, ADAM10 and ADAM17 in tissue specimens of patients with (A) glioblastoma and (B) colorectal carcinoma analyzed *in silico* by IST Online tool using Medisapiens database (https://ist.medisapiens.com). Phenoplots display the clustered heatmap of the genes in a set of samples along with clinical data. Gene expression level is exhibited in color scale ranging from blue (low expression) to red (high expression). The phenoplots presented in this figure clearly show distinct expression patterns of ADAM10 and ADAM17, respectively, only partially overlapping with that of CA IX. Thus, expression of ADAM10 can potentially mediate CA IX cleavage also in tumors that do not express ADAM17. ADAM, a disintegrin and metalloproteinase; CAIX, carbonic anhydrase IX.