

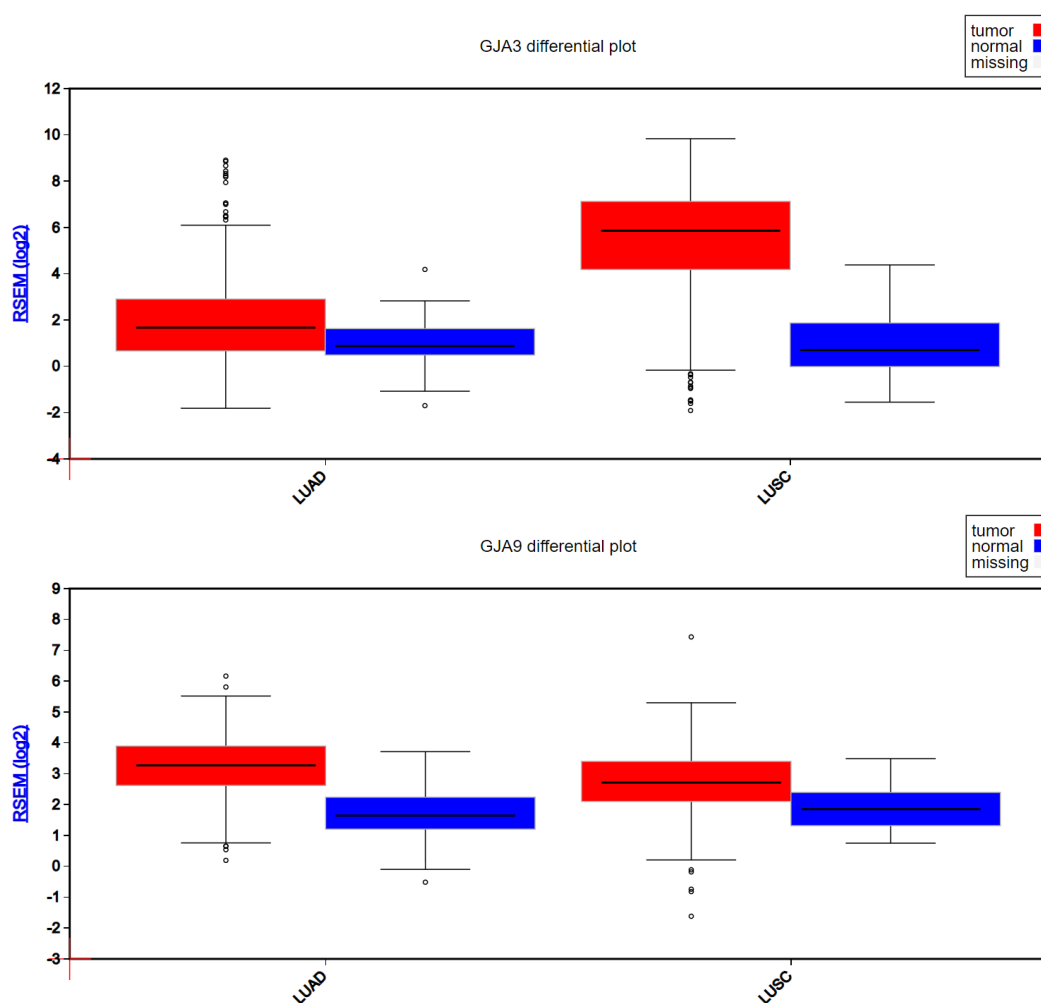
Supplementary Materials: Insight into the Role and Regulation of Gap Junction Genes in Lung Cancer and Identification of Nuclear Cx43 as a Putative Biomarker of Poor Prognosis

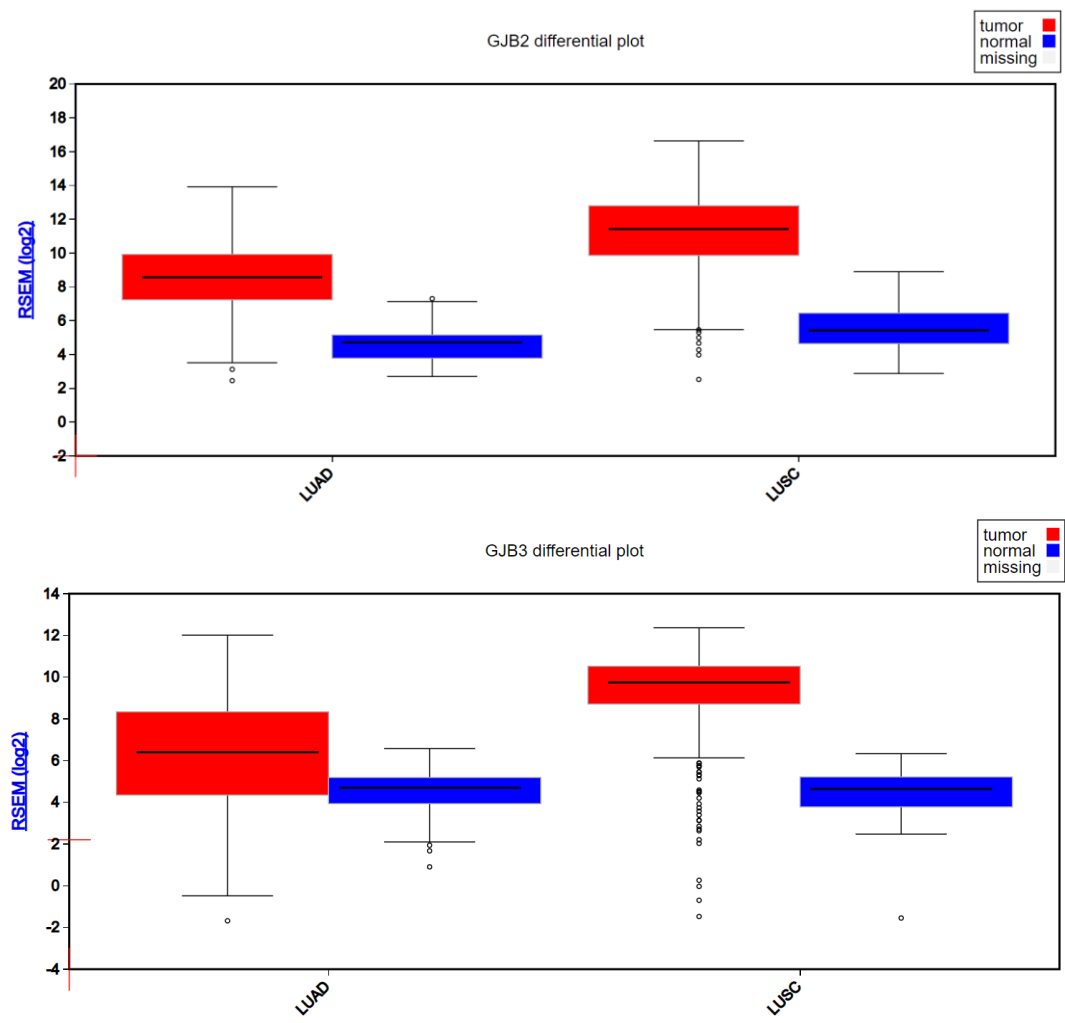
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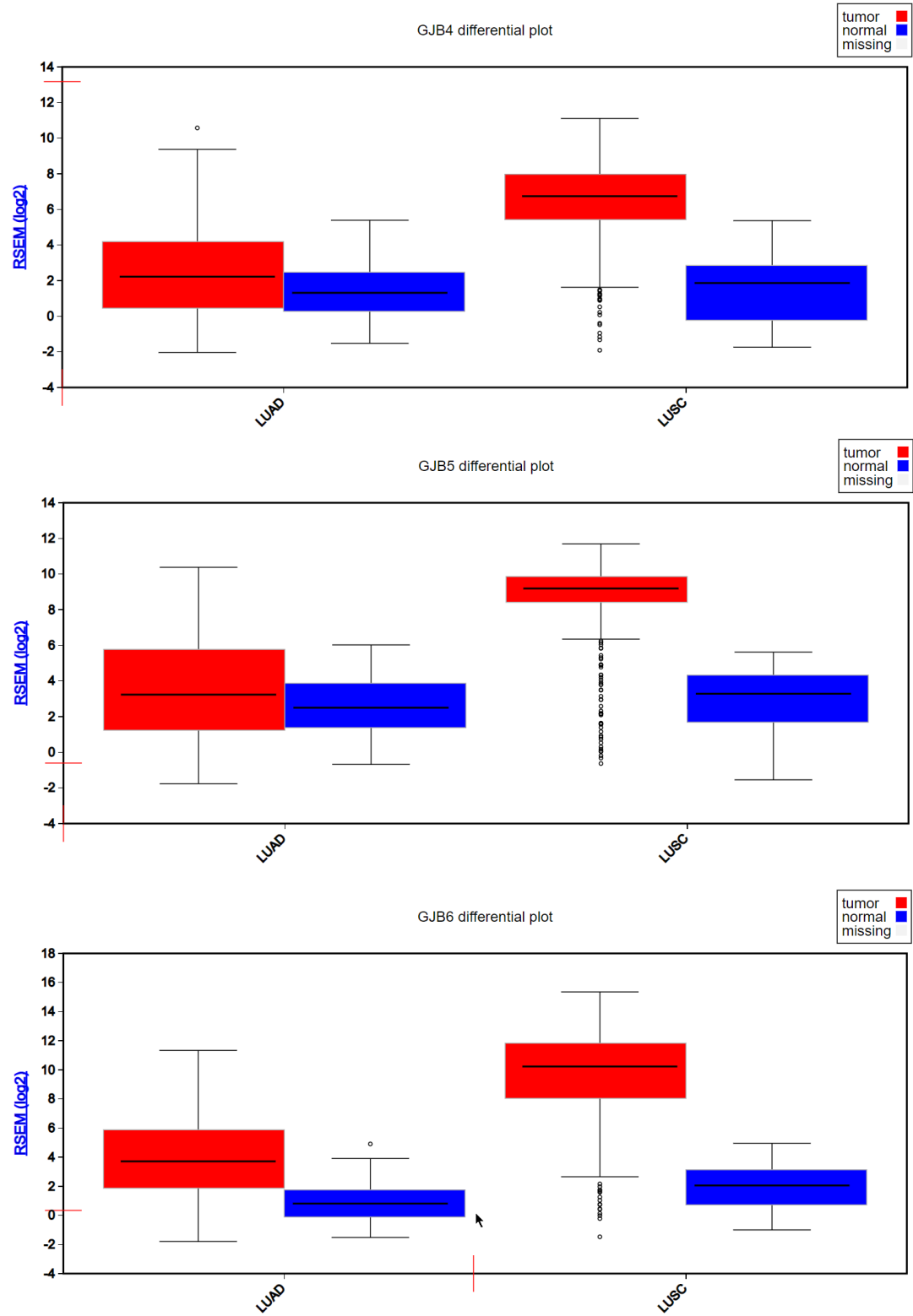
Supplementary Figure S1.

Connexin mRNA expression in healthy lung tissue (blue) and corresponding lung tumour subtypes LUAD and LUSC (red). The figure corresponds to Table 1 (and are grouped into (A) increased, (B) decreased or (C) mixed changes in connexin expression in LUSC and LUAD compared to healthy tissue).

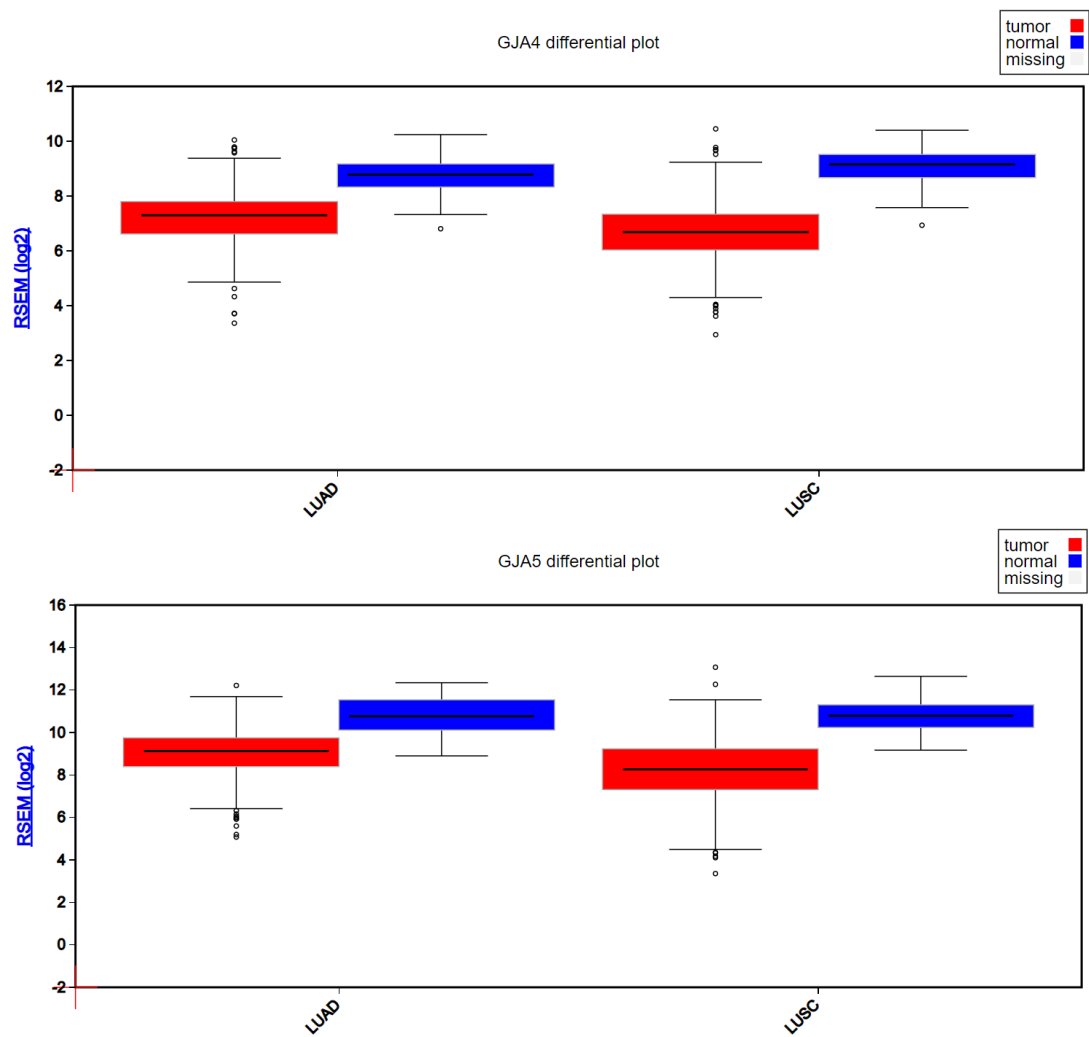
A) Increased expression in LUAD and LUSC tumours:

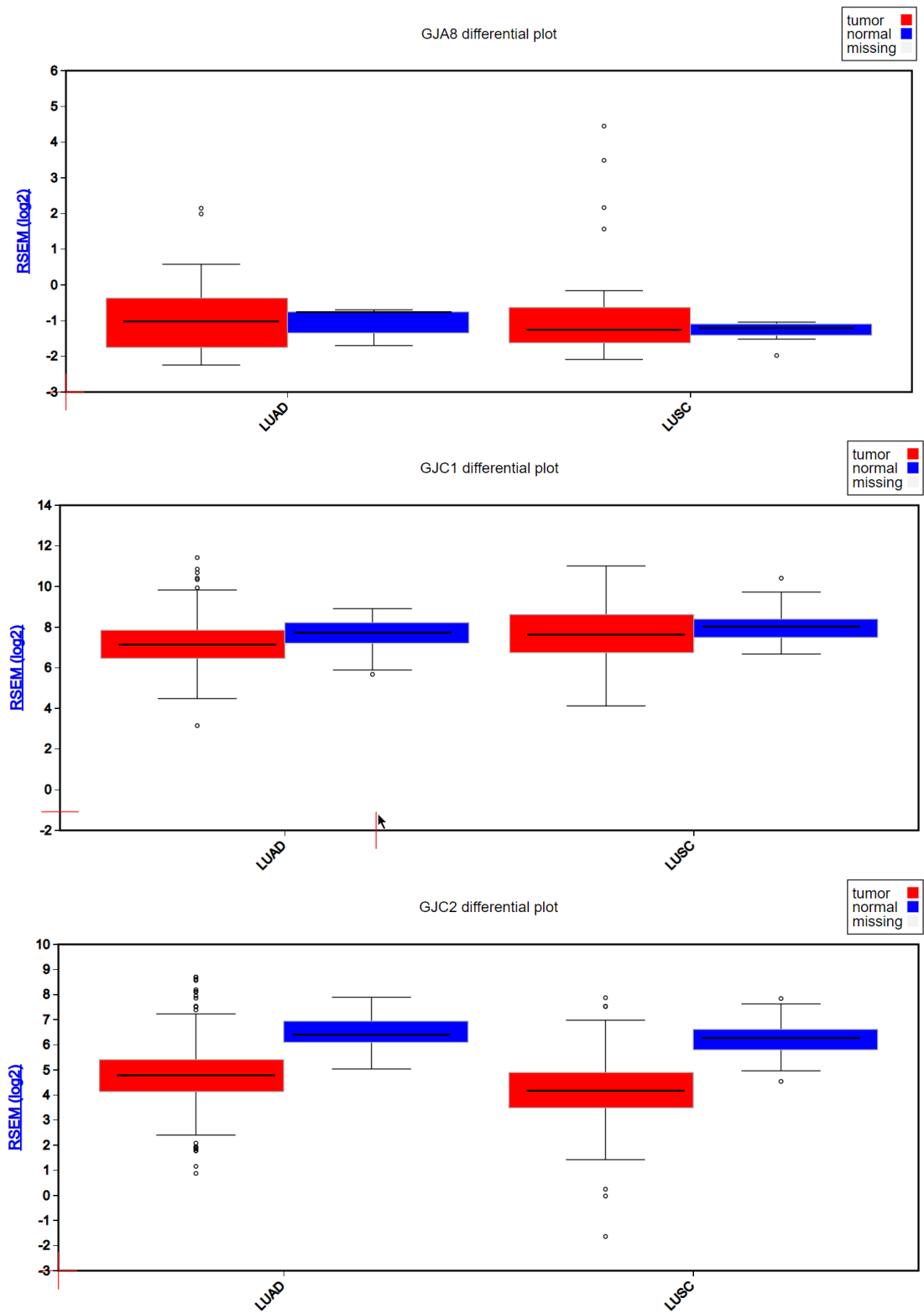


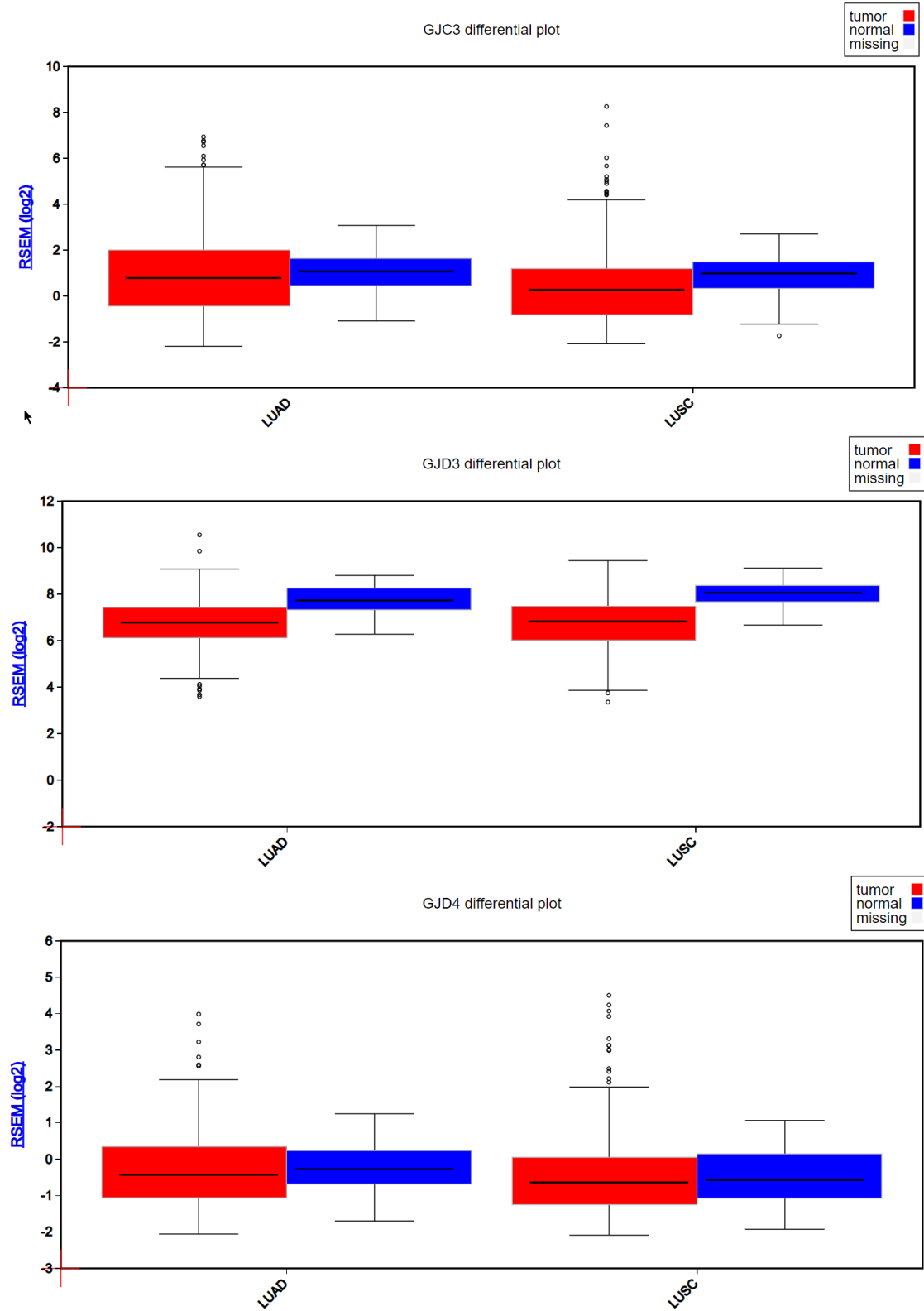




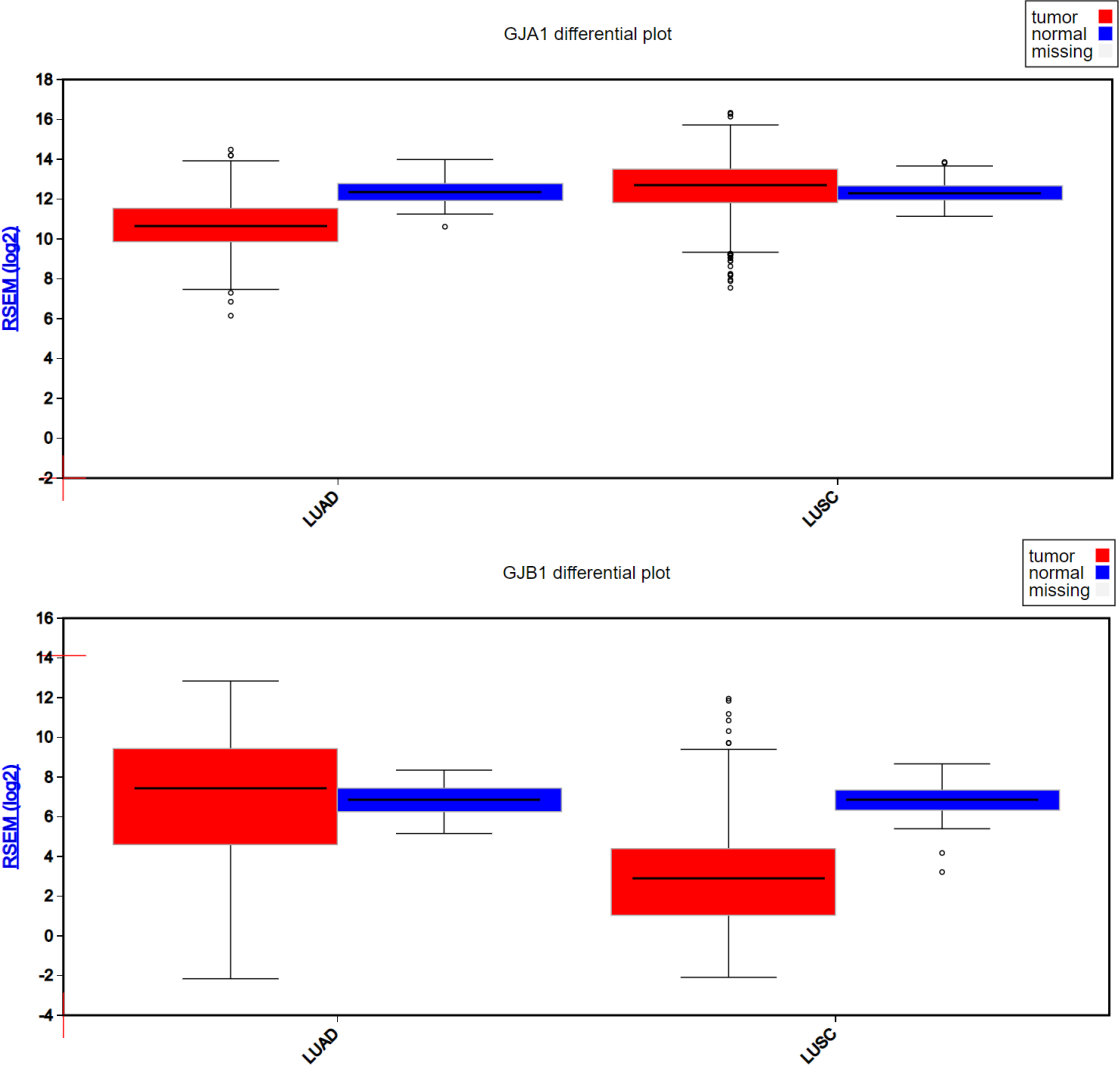
B) Decreased expression in both LUAD and LUSC tumours:

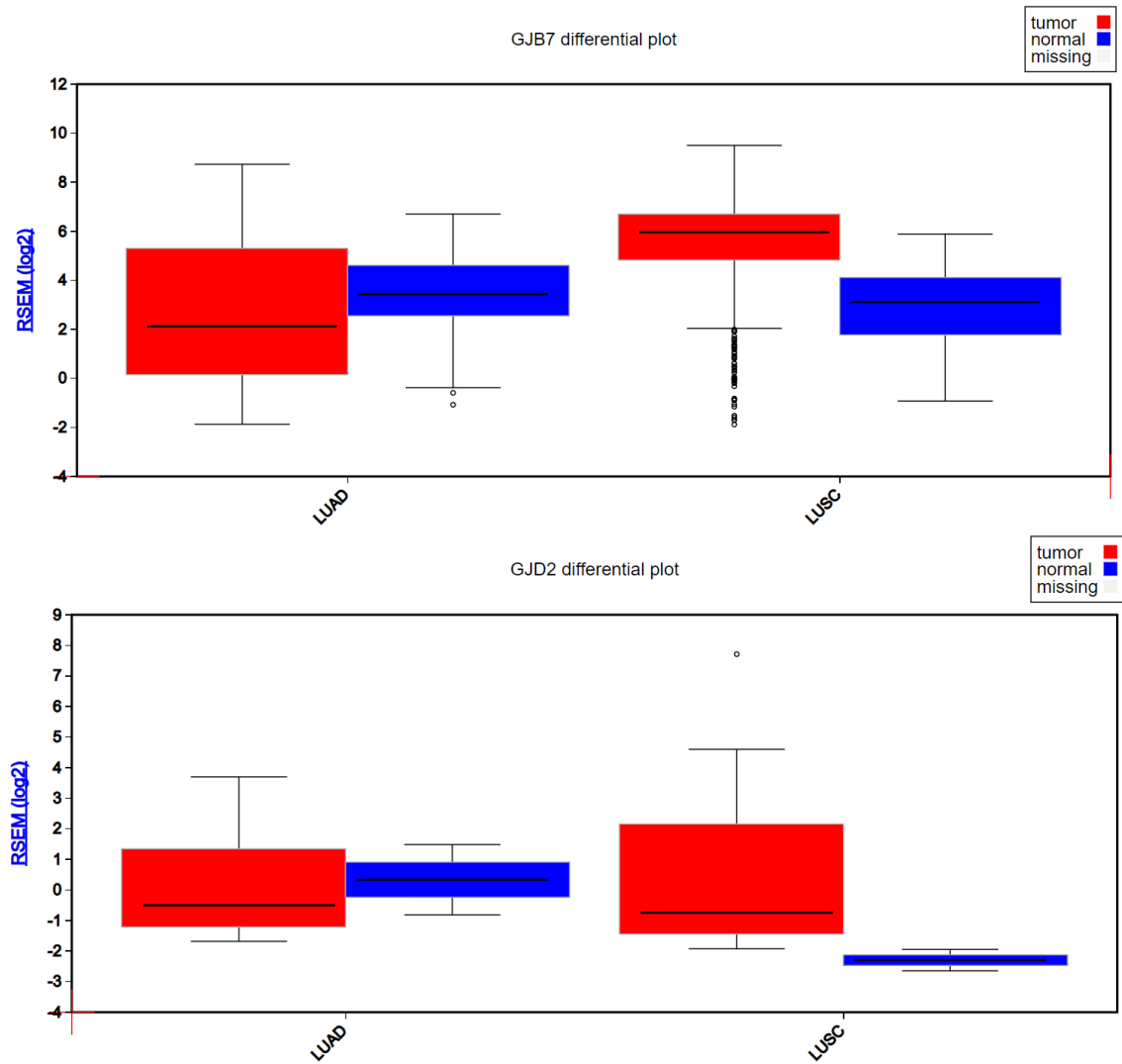






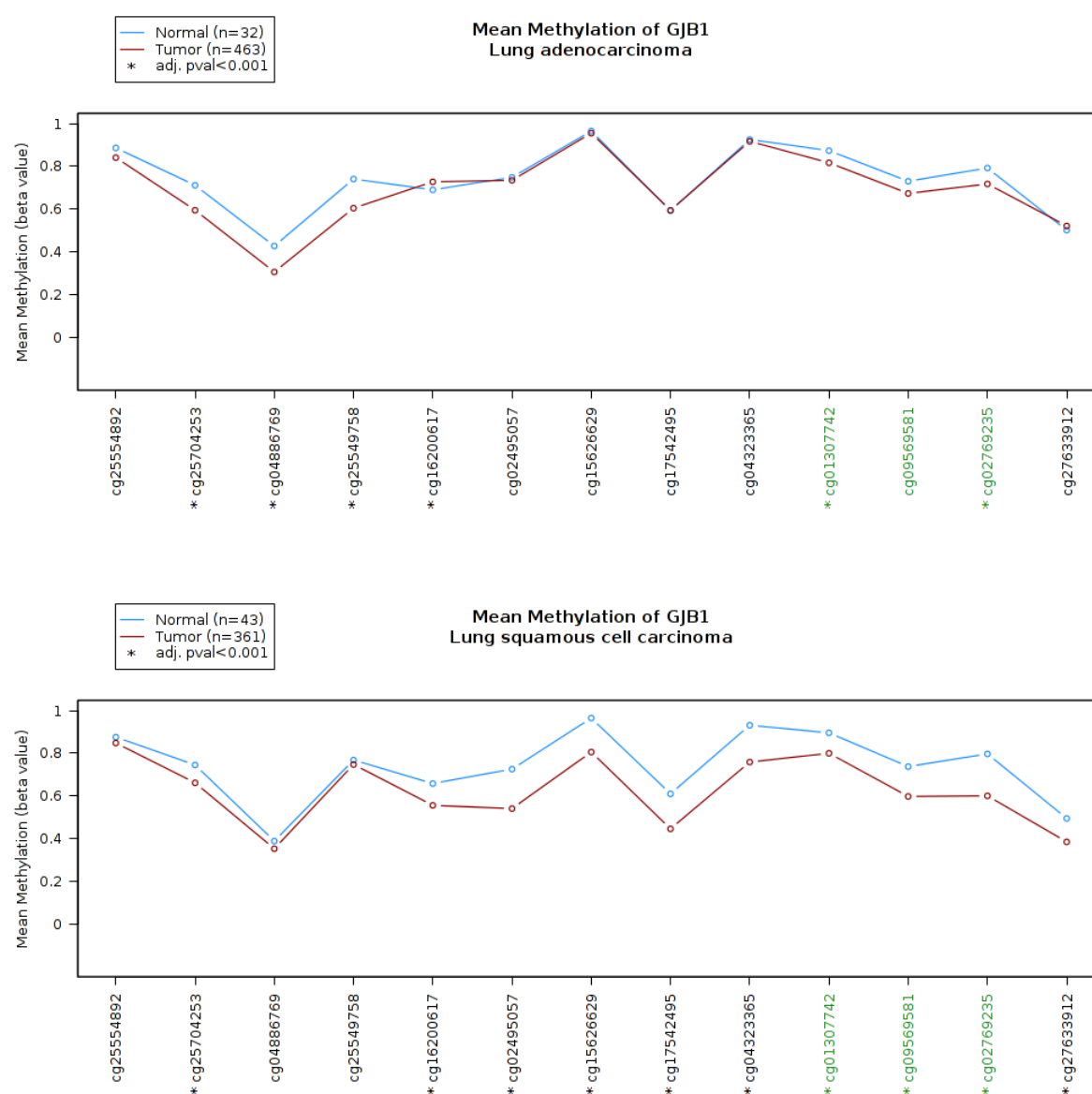
C) Mixed, increased and decreased expression in LUAD versus LUSC tumours:

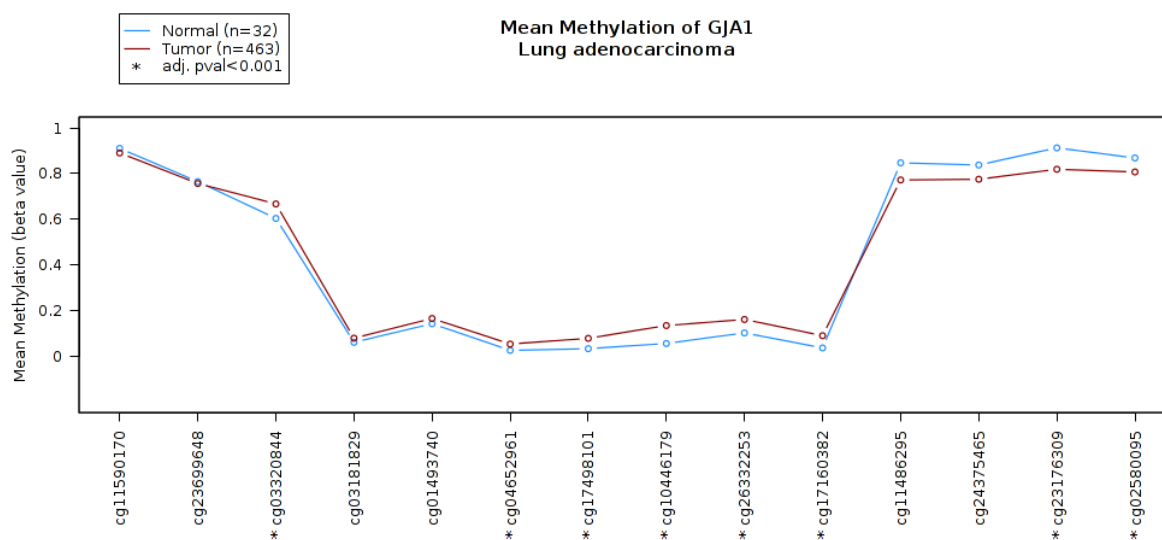
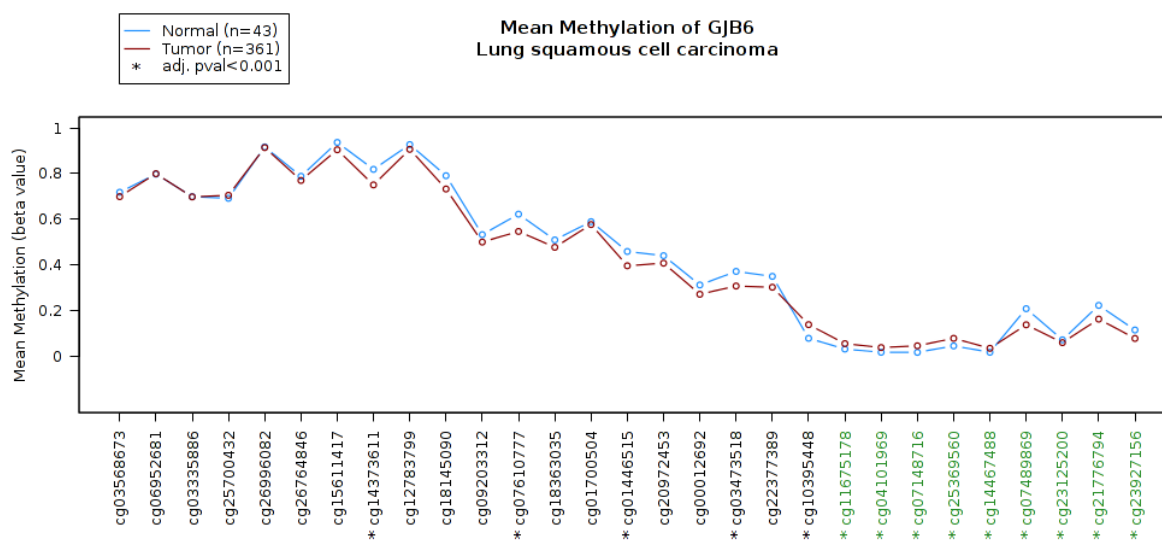
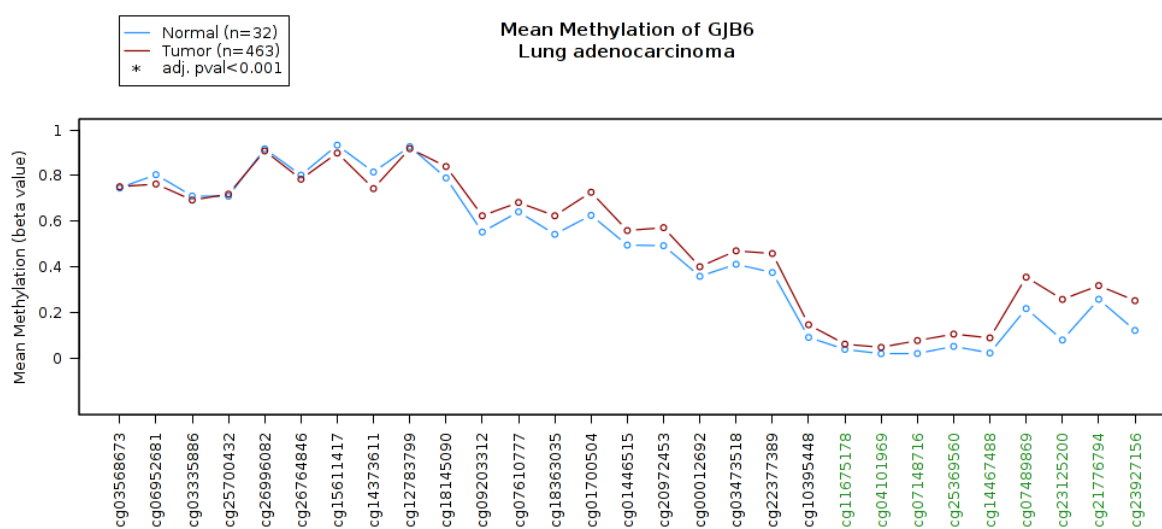


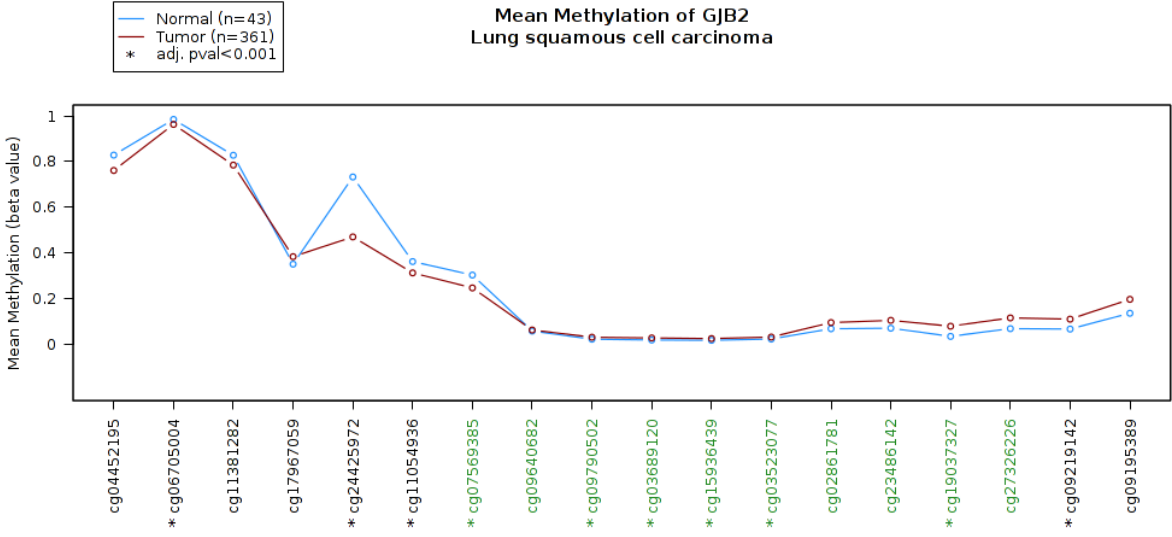
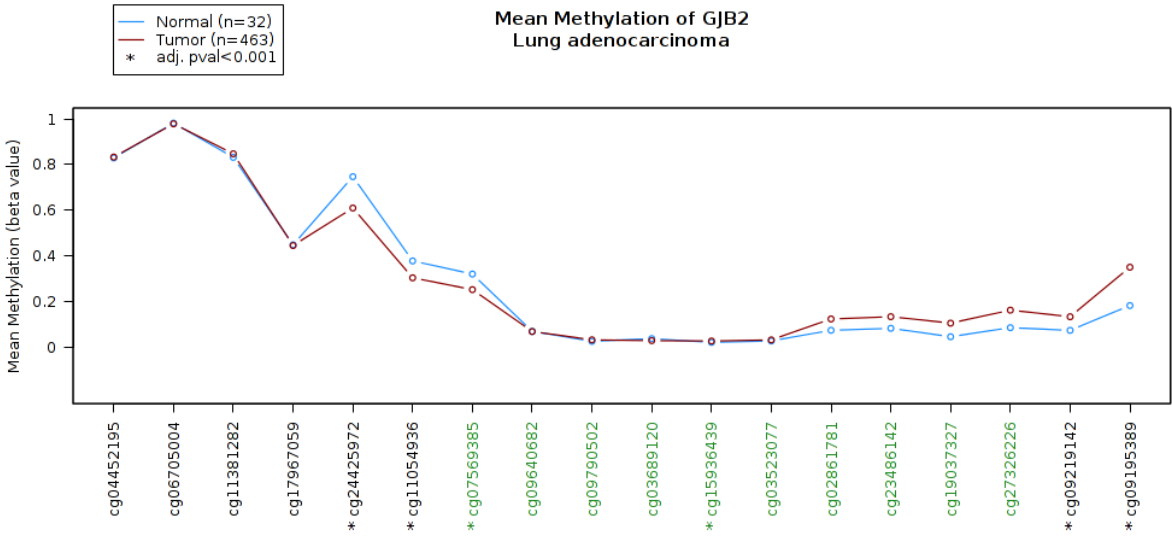
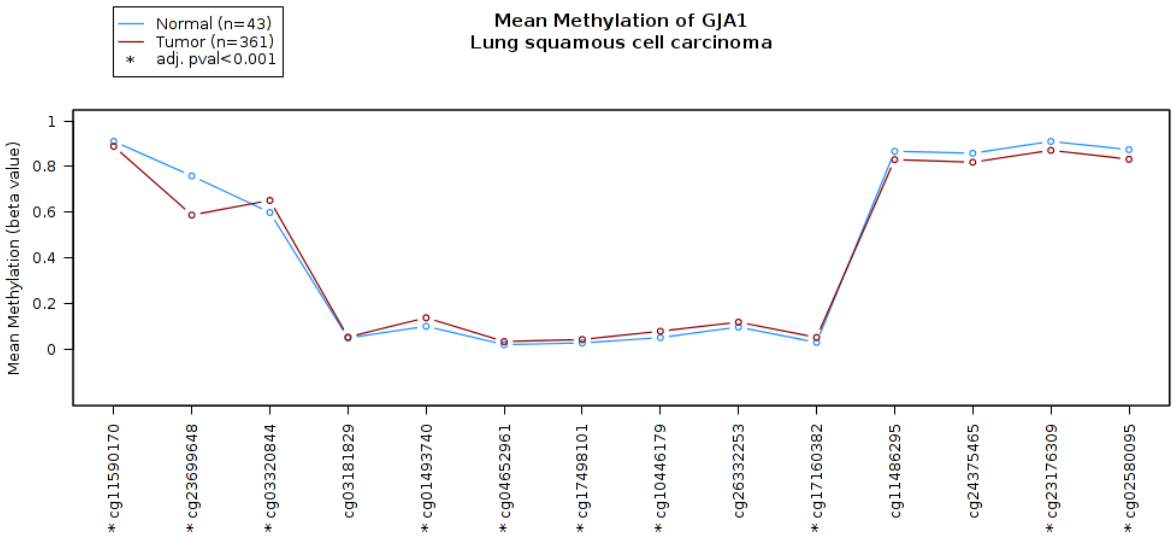


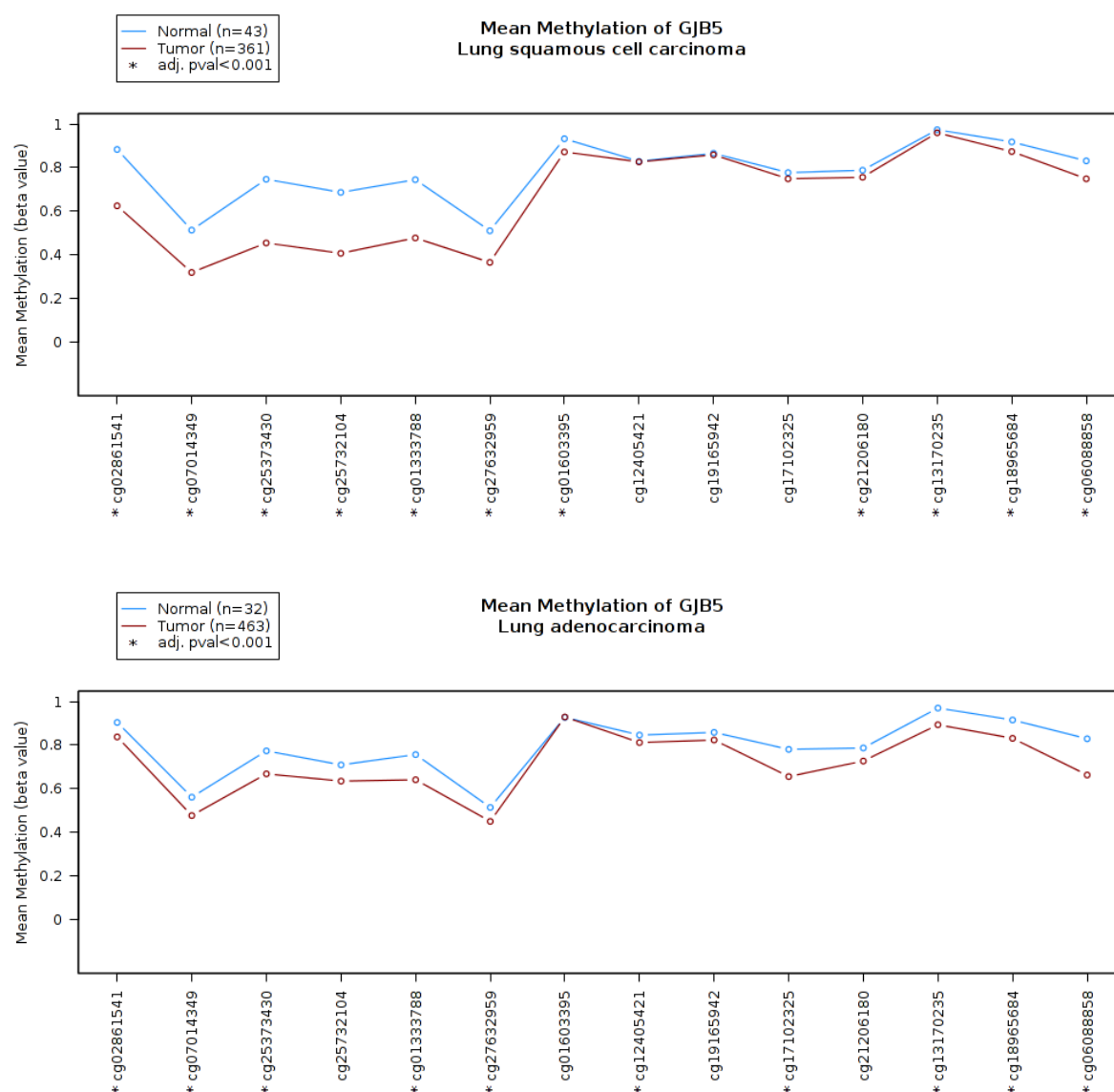
Supplementary Figure S2.

Examples of methylation statuses of key connexin genes in healthy versus tumour tissue. A 450k Methylation Array displaying individual probes along the gene region is shown (equally distributed). Probes in green are part of the CpG cluster of this gene. Significant differences are highlighted with an asterisk on individual probes. These examples illustrate poor correlation for the four connexin genes in focus of this study (GJB1, GJB6, GJB2 and GJA1, all showing moderate or poor correlation) as well as GJB5 which is included as an example of a connexin gene which correlate moderately well between changes in methylation status and mRNA expression. See Figure 3 for a more detailed example of GJB2.



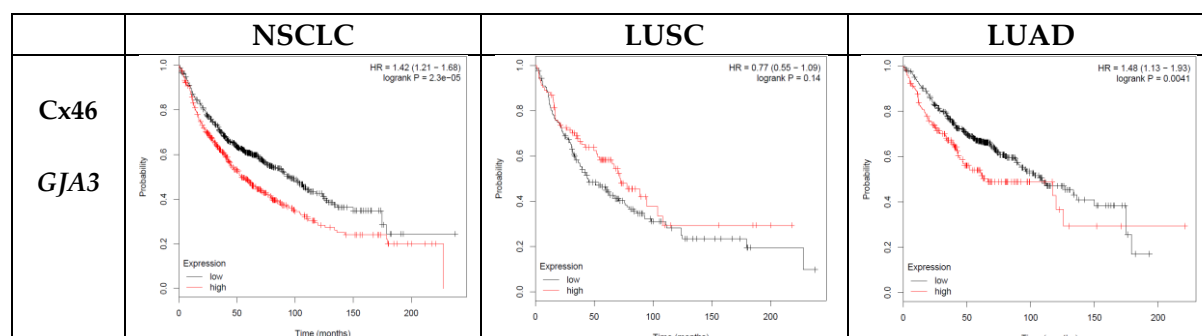


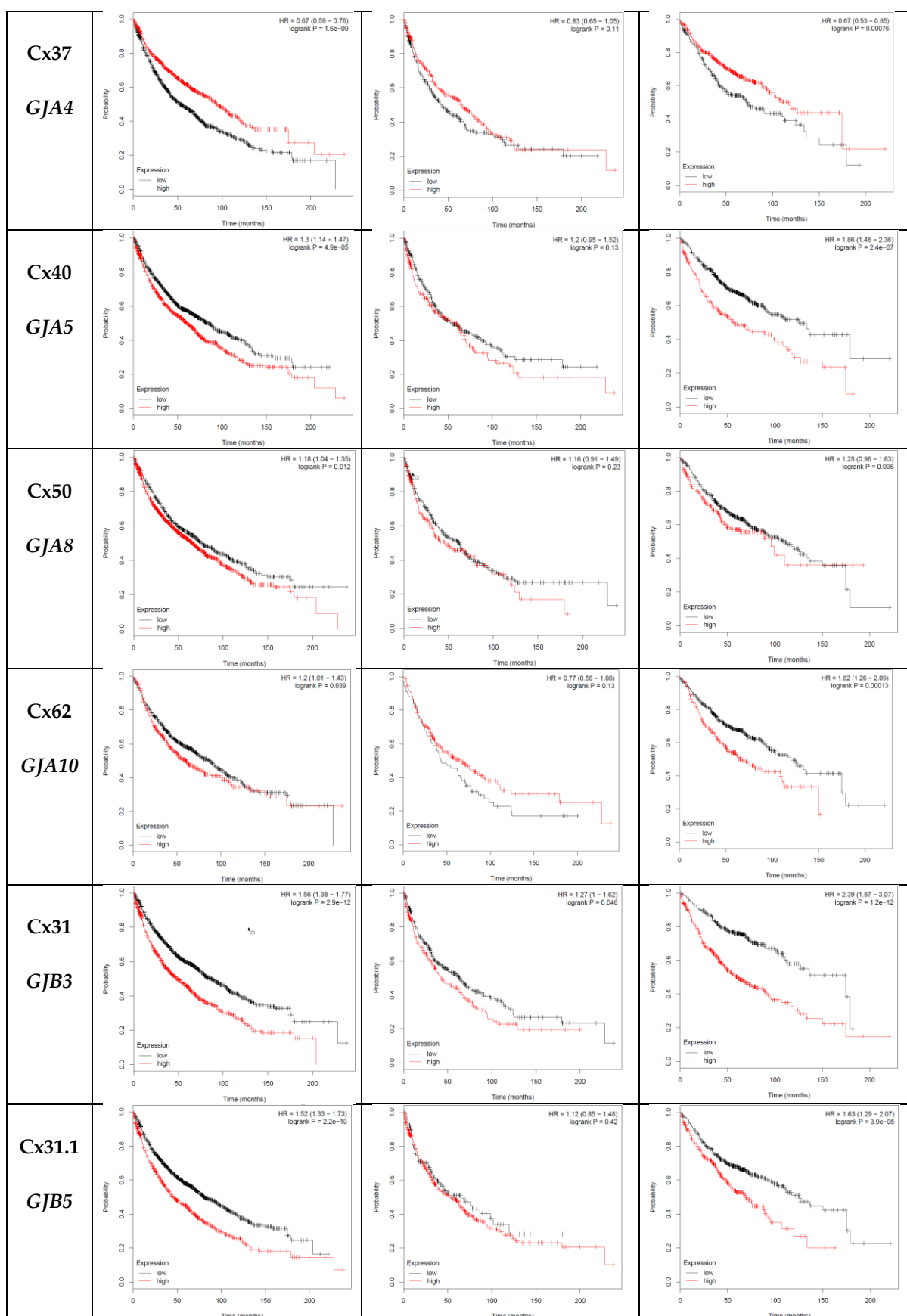


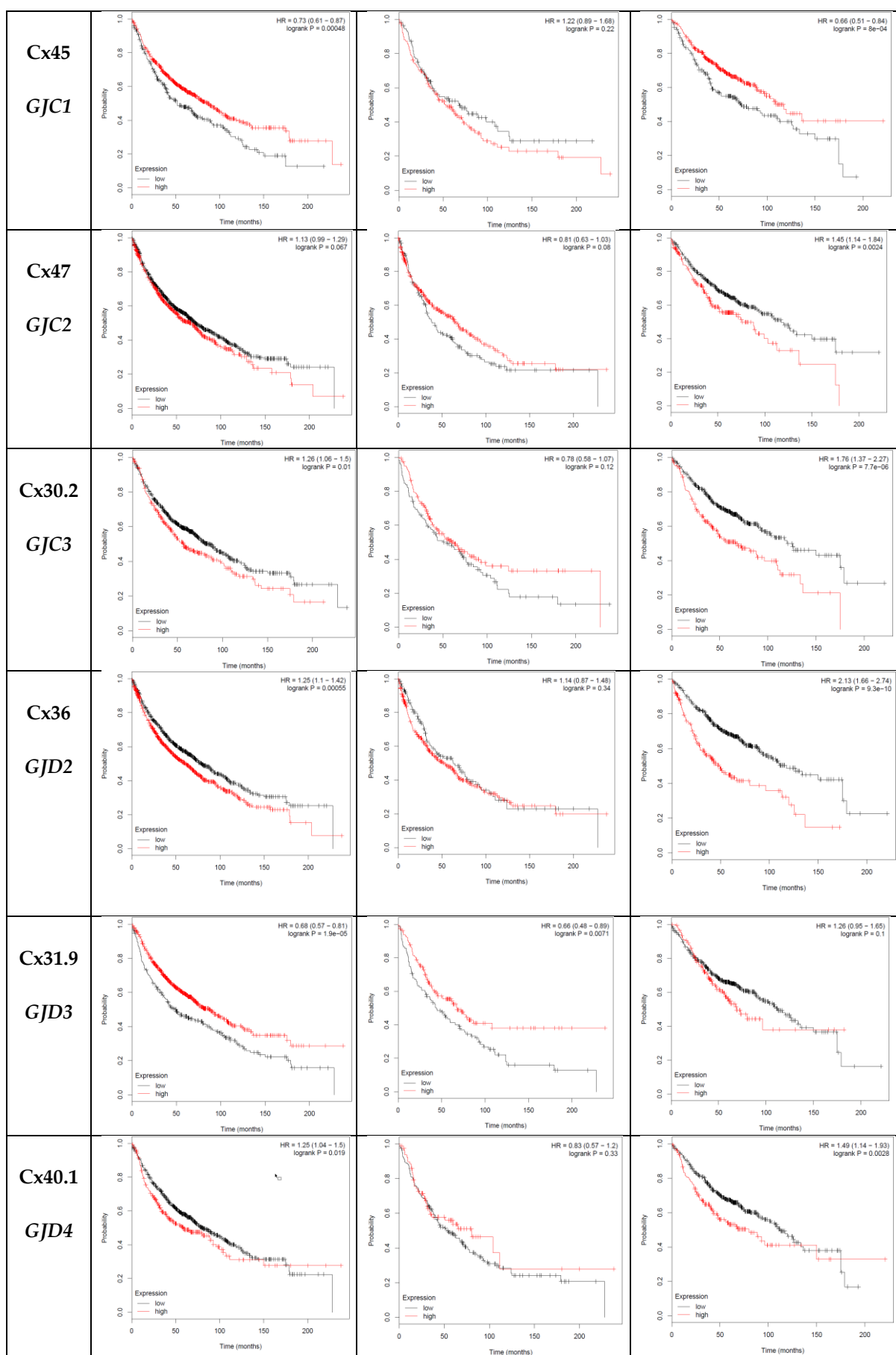


Supplementary Figure S3.

Kaplan-Meier curves of connexins known to drive lung tumorigenesis. The cohort expressing high levels of connexin mRNA is depicted in red, and the cohort with low connexin levels is in black. Probability refers to the likelihood of being alive at any time point. A hazard ratio (HR) below 1 suggests an association with better prognosis, whereas a HR above 1 suggests better prognosis (in the cohort expressing high levels of connexins).







Supplementary Figure S4.

Kaplan-Meier curves based on Cx43 expression patterns detected by immunohistochemistry of lung cancer samples. Tumours with IHC deemed significant are depicted in red and compared with the rest of the tumour samples (in blue). *p*-values refer to the log-rank test (Mantel-Cox analysis). Average survival times of the patient cohorts are listed.

