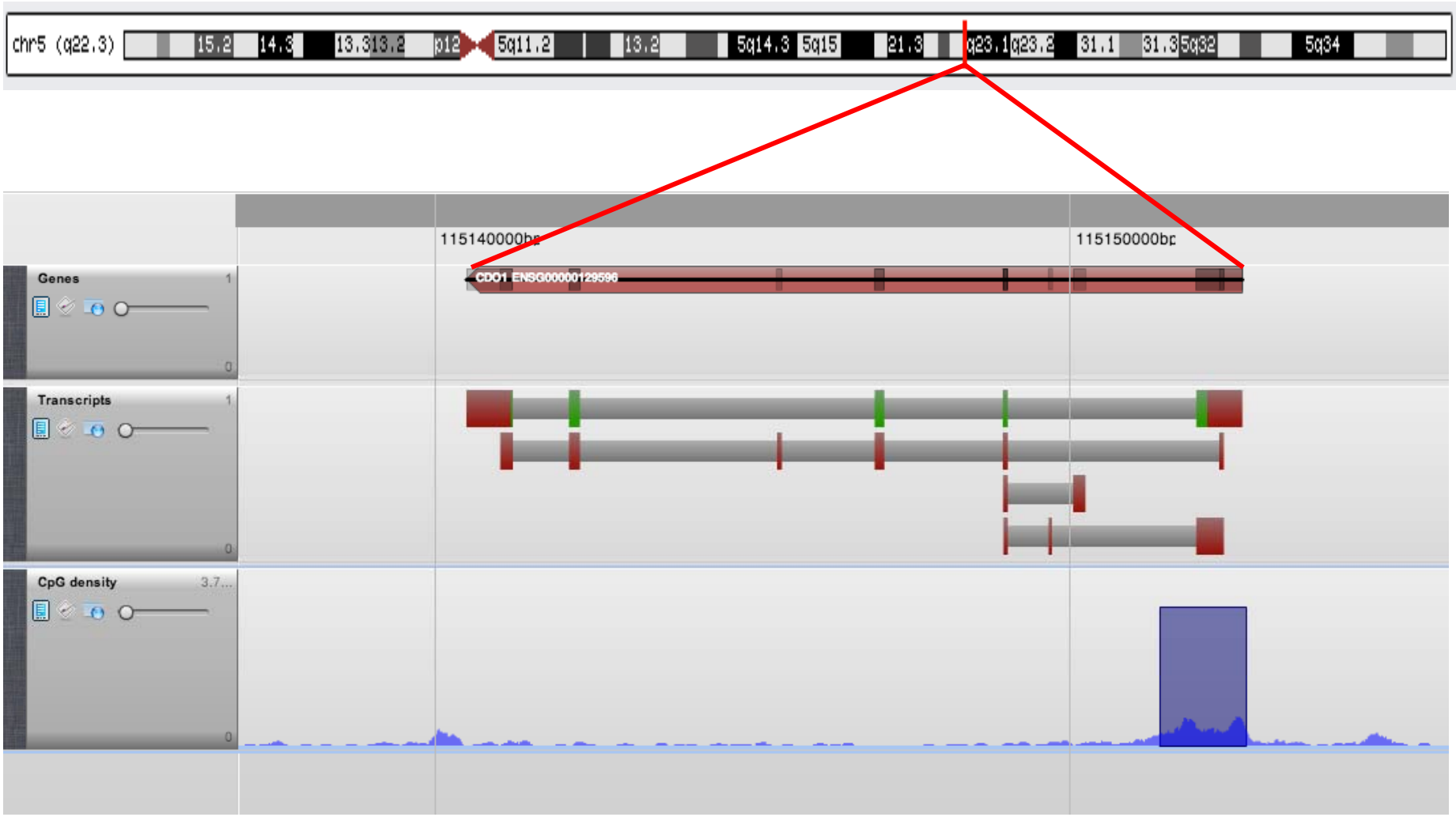
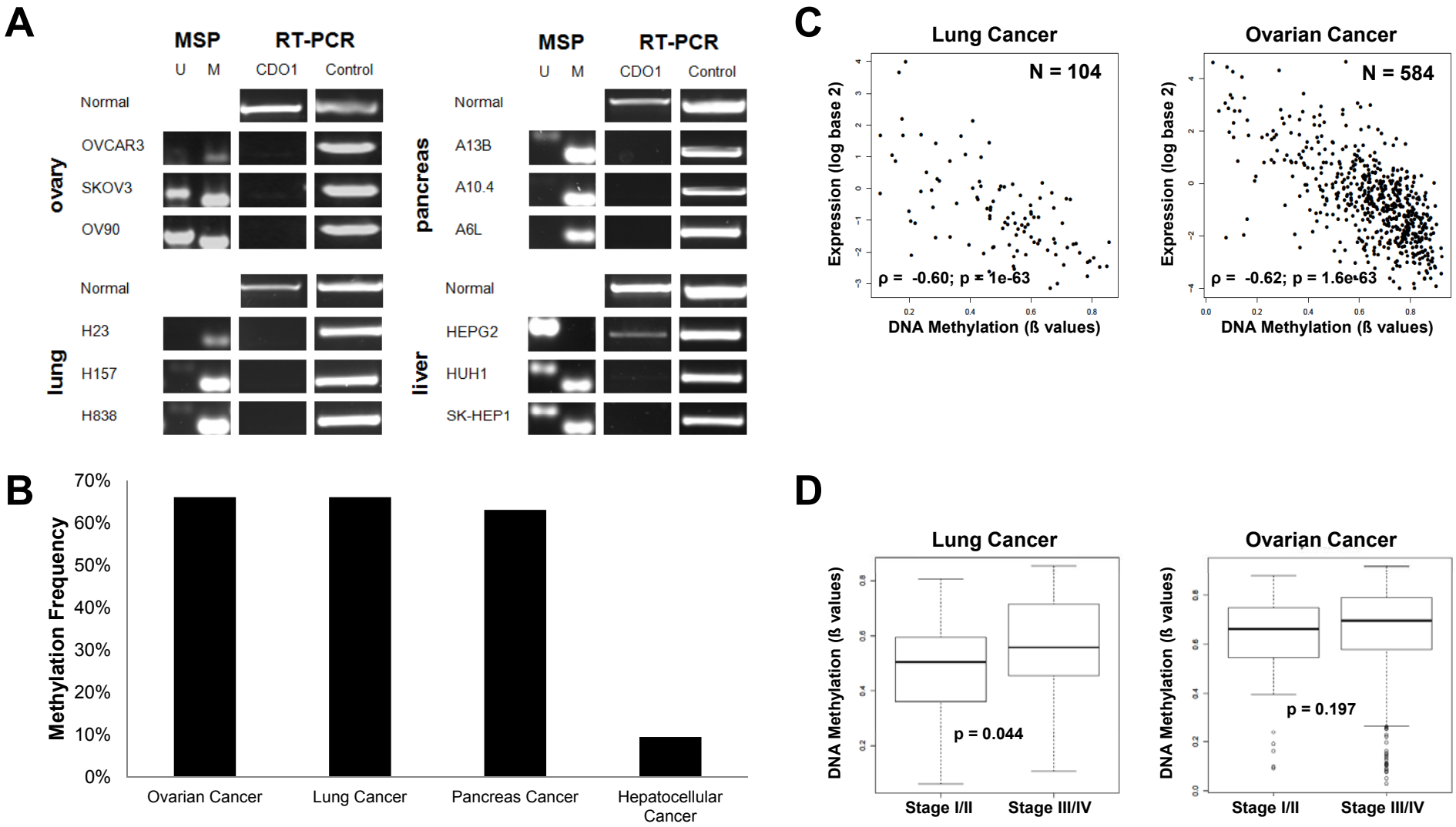
Supplementary Figure 1



Supplementary Figure 1- Genomic location, structure and CpG island of the *CDO1* gene.
The *CDO1* gene contains 5 exons dispersing over a length of about 15 kb on chromosome 5q23.2. The 5'-flanking region is GC rich (72%) and contains several putative regulatory elements including an antioxidant response element (ARE) and reactive oxygen intermediate target (CArG box)-like sequences, which mediate the transcriptional induction of genes involved in antioxidant defense and detoxification. *CDO1* encodes a protein of 200 amino acids with a molecular weight of 23 kDa. CDO1 is a non-heme iron-containing dioxygenase (EC 1.13.11.20) and the key enzyme in the homeostasis of cysteine and glutathione.

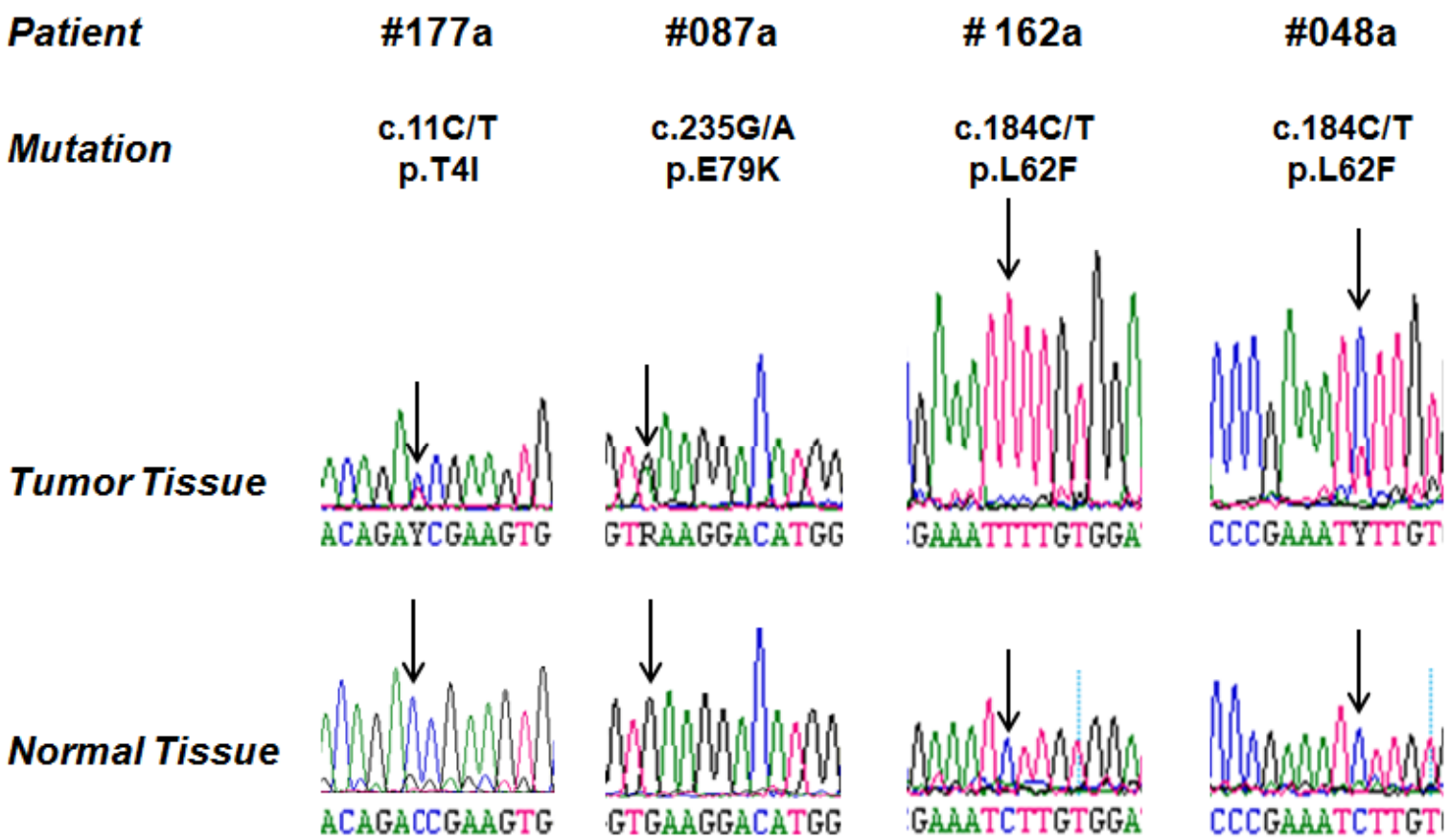
Supplementary Figure 2



Supplementary Figure 2- DNA methylation-associated silencing of *CDO1* occurs in multiple types of cancer

(A) DNA methylation and mRNA expression status of *CDO1*, assayed by MSP and RT-PCR, in three representative cell lines of each cancer type. GAPDH expression was assayed as control. Basal expression of *CDO1* was confirmed in normal tissue of each cancer type. **(B)** Overall DNA methylation frequency (in %) of *CDO1* in primary samples of ovarian (n = 65), lung (n = 65), pancreas (n = 30), and hepatocellular cancer (n = 21). **(C)** Scatter plots depicting correlation between expression log base 2 values (y-axis) (analyzed on Agilent 244K Custom Gene Expression G4502A-07 platform) and DNA methylation ß values (x-axis) (analyzed on Illumina HumanMethylation 27k platform) of *CDO1* in primary samples of lung (n = 104) and ovarian cancer (n = 584) from TCGA Data Portal. **(D)** Box plots demonstrating a statistically significant correlation between tumor stage and *CDO1* methylation frequency in TCGA lung but not in ovarian cancers . A $p < 0.05$ was considered statistically significant.

Supplementary Figure 3



Supplementary Figure 3- Tumor-specific point mutations within the *CDO1* gene.
Protein damaging missense mutations within the *CDO1* gene in primary breast tumor tissue of four patients. Arrows indicate the position of the mutation. Tumor-specificity of mutations was confirmed in non-tumor tissue of same patients.