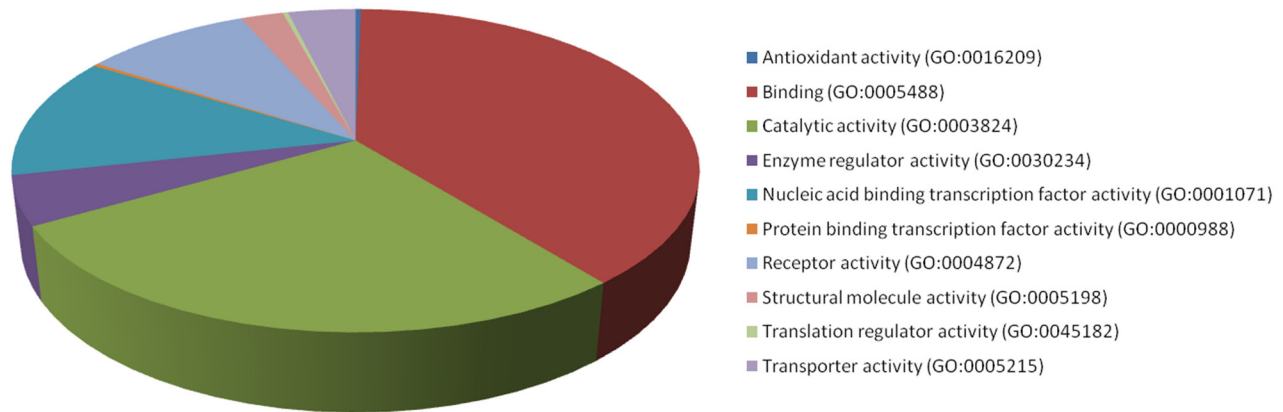


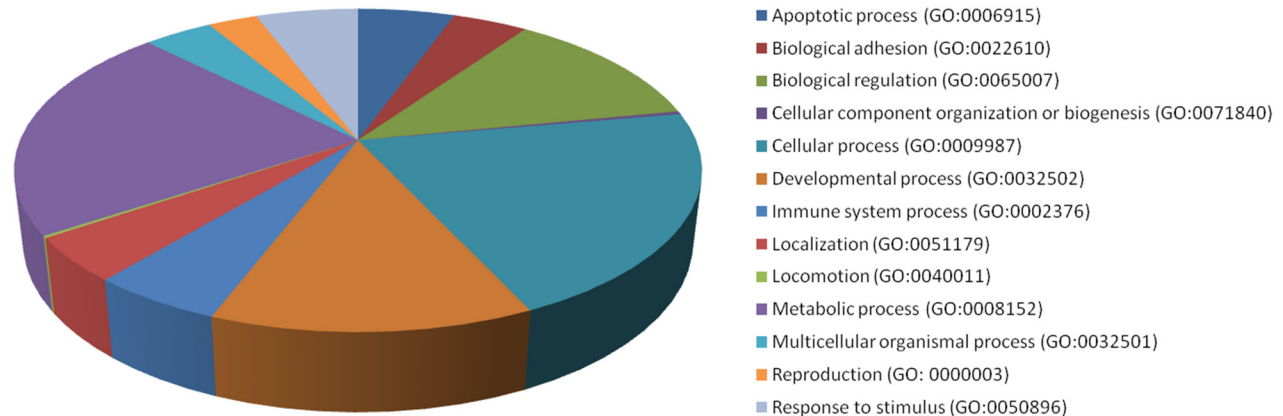
Impact of DLK1-DIO3 imprinted cluster hypomethylation in SMOKER patients with lung cancer

SUPPLEMENTARY FIGURES AND TABLES

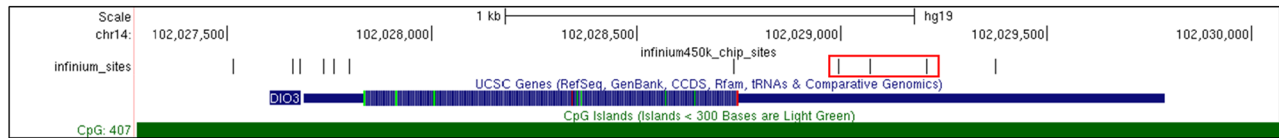
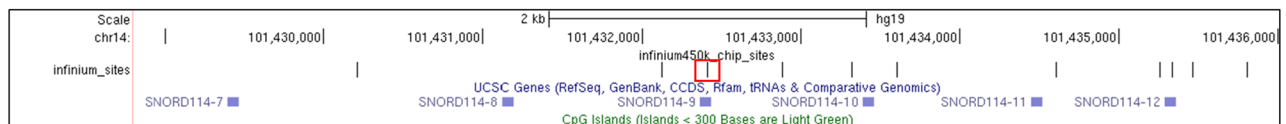
GO Molecular Function



GO Biological Process



Supplementary Figure S1: Classification of validated targets by gene ontology (GO) molecular function and biological processes. Summary of molecular functions and biological processes for validated target genes of miRNAs included in the *DLK1-DIO3* cluster. Approximately 39% of the genes were annotated to binding and more than 20% of the genes were involved in metabolic processes.

DIO3**miR-889****SNORD114-9**

Supplementary Figure S2: Genomic features of *DIO3*, *miR-889* and *SNORD114-9*. These schemes indicate the CpG islands present on the region. The red squares designate the genomic regions selected for 454 bisulfite sequencing.

Supplementary Table S1: The methylation levels in lung cancer versus mou-tumoral tissue.

See Supplementary File 1

Supplementary Table S2: Validated tumor suppressors of miRNAs included in the DLK1-DIO3 cluster.

See Supplementary File 2

Supplementary Table S3: Characteristics of the study cohort

	Patients (N=47)
Gender	
Male	76.6 (36)
Female	23.4 (11)
Age (years)	67 [60-73]
Smoking status	
Smokers	40.4 (19)
Ex-smokers	44.7 (21)
<i>Non-smoker</i>	14.9 (7)
Packs/year	41.0 [20.0-65.7]
Histology	
Lung adenocarcinoma	57.4 (27)
<i>Squamous cell carcinoma</i>	42.6 (20)
Staging	
Stage I	40.5 (19)
Stage II	38.3 (18)
Stage III-IV	21.2 (10)
Subjects with COPD	42.6 (20)

Continuous variables are expressed as the median [interquartile range (IQR)] and categorical variables are expressed as the number of cases (%).

Supplementary Table S4: Description of control cohort

	Controls (N=23)
Gender	
Male	87.0 (20)
Female	13.0 (3)
Age (years)	35 [21-62]
Smoking status	
Smokers	30.4 (7)
Ex-smokers	21.7 (5)
<i>Non-smoker</i>	47.8 (11)
Packs/year	2.0 [2.0-20.0]
Subjects with COPD	17.4 (4)

Continuous variables are expressed as the median [interquartile range (IQR)] and categorical variables are expressed as the number of cases (%).

Supplementary Table S5: Characteristics of the TCGA cohort.

See Supplementary File 3

Supplementary Table S6: List of primer sequences used for 454 bisulfite sequencing

454 Bisulfite Sequencing	
Primers	Sequences
F <i>DIO3</i>	TGTTTGGTTTATTGGAAATTTTTTT
R <i>DIO3</i>	AACAACAAAAAACCCCTCTC
F <i>mir-889</i>	TATTAGGGATTGTATTGGTTATG
R <i>mir-889</i>	TTTAAATACTAAAACAATAATTA
F <i>SNORD114-9</i>	TATTTAGGTTATTTTTGGGGTTTTT
R <i>SNORD114-9</i>	AACCATAAACAAATAAATTCTATATCTCTA