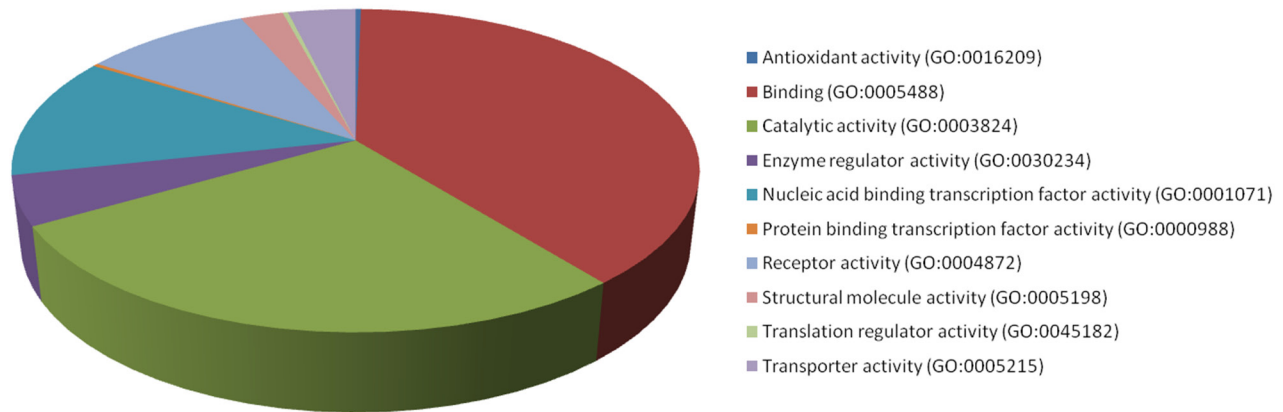


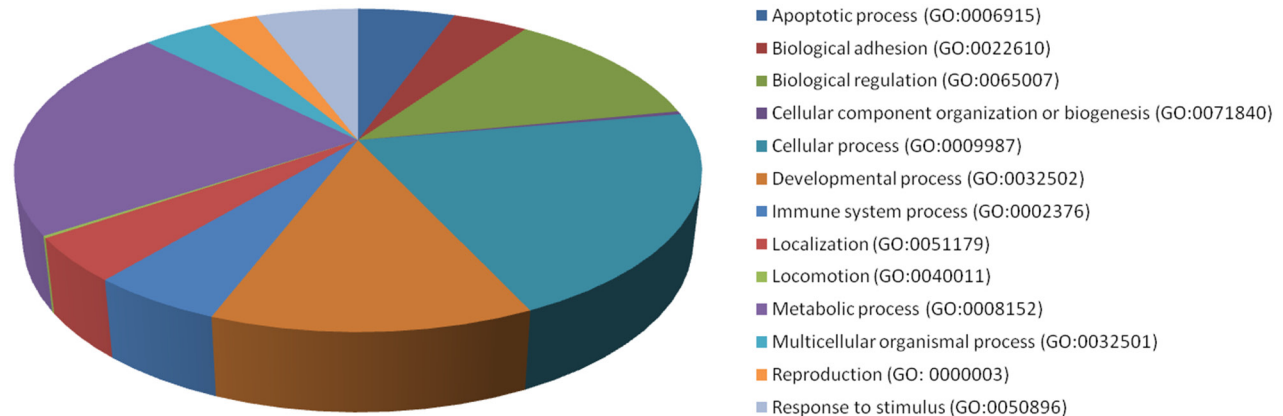
## Impact of DLK1-DIO3 imprinted cluster hypomethylation in SMOKER patients with lung cancer

### SUPPLEMENTARY FIGURES AND TABLES

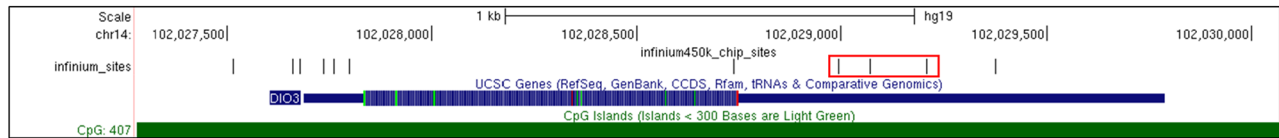
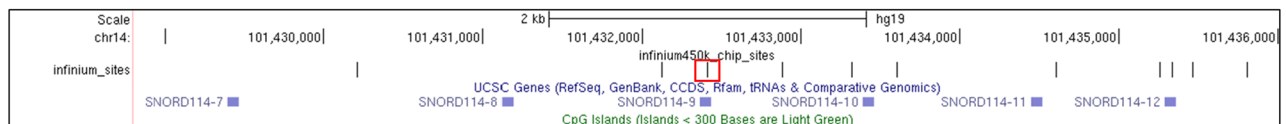
#### GO Molecular Function



#### 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)
<b>Gender</b>	
Male	76.6 (36)
Female	23.4 (11)
<b>Age (years)</b>	67 [60-73]
<b>Smoking status</b>	
Smokers	40.4 (19)
Ex-smokers	44.7 (21)
<i>Non-smoker</i>	14.9 (7)
<b>Packs/year</b>	41.0 [20.0-65.7]
<b>Histology</b>	
Lung adenocarcinoma	57.4 (27)
<i>Squamous cell carcinoma</i>	42.6 (20)
<b>Staging</b>	
Stage I	40.5 (19)
Stage II	38.3 (18)
Stage III-IV	21.2 (10)
<b>Subjects with COPD</b>	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)
<b>Gender</b>	
Male	87.0 (20)
Female	13.0 (3)
<b>Age (years)</b>	35 [21-62]
<b>Smoking status</b>	
Smokers	30.4 (7)
Ex-smokers	21.7 (5)
<i>Non-smoker</i>	47.8 (11)
<b>Packs/year</b>	2.0 [2.0-20.0]
<b>Subjects with COPD</b>	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>	TGTTTGGTTTATTGGAAATTTTTTTT
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