

## DESCRIPTION OF ADDITIONAL SUPPLEMENTARY FILES

### Supplementary Data 1.

This table contains the list of genes differentially regulated in the global transcriptomic profile of CDK12-OE vs. control EV MCF10A cells (MCF10A\_CDK12-OE\_vs\_EV sheet) and CDK12-KI/PyMT vs. WT/PyMT tumor cells (PyMT\_CDK12-KI\_vs\_PyMT\_WT sheet). For each entry, the following information is reported (from left to right):

- Gene symbol (gene symbol corresponding to HUGO nomenclature).
- $\log_2$ (fold change) of gene transcriptional levels in CDK12 cells compared to control samples;
- $\log$ CPM (average logarithm of counts per million reads);
- $P$  value for differential gene expression resulting from quasi-likelihood F-tests;
- FDR adjusted  $P$  value with Benjamini Hochberg method;
- gene type (i.e. coding, non-coding);
- descriptive gene name;
- Ensembl gene accession number;
- Entrez gene accession number.

Statistical analyses were performed using the edgeR package of R software.

### Supplementary Data 2.

This table contains the list of metabolites differentially regulated in the untargeted metabolomics analysis of CDK12-OE vs. control EV MCF10A cells by LC-MS. For each entry, the following information is reported (from left to right):

- Hit (metabolite name corresponding to KEGG nomenclature);
- T.stat (T-Statistics, cutoff > 1.5 for significantly higher metabolite abundance in CDK12-OE vs. EV MCF10A cell comparison, across all samples);
- $P$  value and  $-\log_{10}(P)$  (Negative of the base 10 logarithm of  $P$  values); FDR, False Discovery Rate (FDR-adjusted  $P$  value threshold to 0.25); Statistical analyses were performed using the MetaboAnalyst 3.0 tool.

### Supplementary Data 3. MFA flux analysis.