## SUPPLEMENTARY FIGURES



Supplemental Figure S1. Ingenuity Pathway Analysis (IPA) of proteomics data sets obtained from human breast cancer MCF7-Y537S cells. (A) Canonical pathways predicted to be altered in MCF7-Y537S Vs MCF7-EV-Lv105 are shown. As expected, certain canonical pathways were significantly altered by the differential protein expression in MCF7-Y537S respect MCF7-EV-Lv105. In particular in absence of 4-OHT (1  $\mu$ M), all the resulting pathways in MCF7-Y537S were up-regulated compared to MCF7-EV-Lv105, except for RhoGDI signaling and PTEN signaling pathways that were down-regulated. (B) In presence of 4-OHT (1  $\mu$ M), all the resulting pathways that were down-regulated. (B) In presence of 4-OHT (1  $\mu$ M), all the resulting pathways that were up-regulated. The pvalue (p < 0.05) for each pathway is indicated by the bar and is expressed as -1 times the log of the p-value. A positive z-score (Orange color; z-score > 2) represents the upregulation of a specific pathway, while a negative z-score (Blue color; z-score < 2) indicates the down-regulation of a pathway.





Supplementary Figure 2. Toxicity effects of differentially expressed proteins in MCF7-Y537S Vs MCF7-EV-Lv105. Ingenuity Pathway Analysis showed that certain toxicity functions are significantly enriched by the proteins differentially expressed in this comparative analysis (p < 0.05). In the Stacked Bar chart, the p-value for each pathway is indicated by the bar and is expressed as -1 times the log of the p-value (cutoff z-score ± 2).In red color the amount of the proteins up-regulated and in green color the amount of the proteins down-regulated in each patwhays.



Supplementary Figure 3. Toxicity effects of differentially expressed proteins in MCF7-Y537S Vs MCF7-EV-Lv105 in presence of 4-OHT (1  $\mu$ M). Ingenuity Pathway Analysis showed that certain toxicity functions are significantly enriched by the proteins differentially expressed in this comparative analysis (p < 0.05). In the Stacked Bar chart, the p-value for each pathway is indicated by the bar and is expressed as -1 times the log of the p-value (cutoff z-score ± 2).In red color the amount of the proteins up-regulated and in green color the amount of the proteins down-regulated in each patwhays.



Supplementary Figure 4. Ingenuity Pathway Analysis (IPA) of proteomics data sets obtained from human breast cancer MCF7-Y537S cells compared to MCF7-ESRI. Canonical pathways predicted to be altered in MCF7-Y537S Vs MCF7-ESRI in presence of 4-OHT (1  $\mu$ M) are shown. As expected, certain canonical pathways were significantly altered by the differential protein expression in MCF7-Y537S respect MCF7-ESRI. In particular, in presence of 4-OHT (1  $\mu$ M), all the resulting pathways in MCF7-Y537S were down-regulated compared to MCF7-ESRI, except for RhoGDI signaling pathway that was down-regulated.