Integrated analysis of microRNAs, transcription factors and target genes expression discloses a specific molecular architecture of hyperdiploid multiple myeloma

Supplementary Material

Fig. 1S A

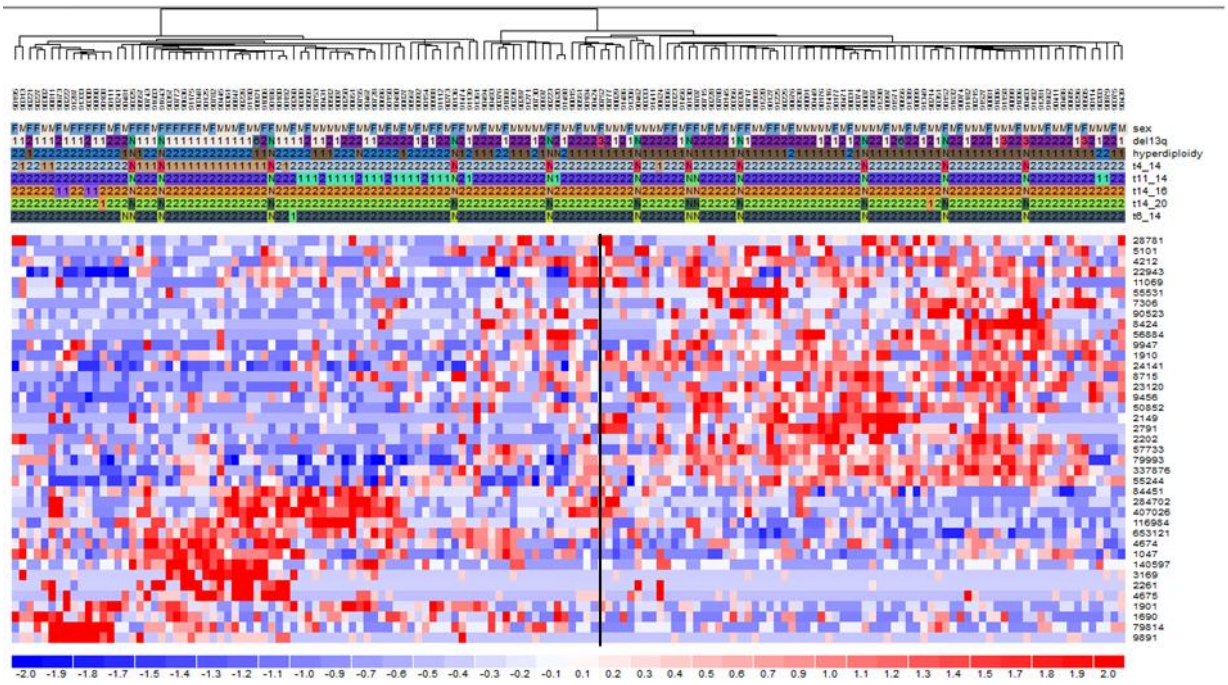


Fig. 1SB

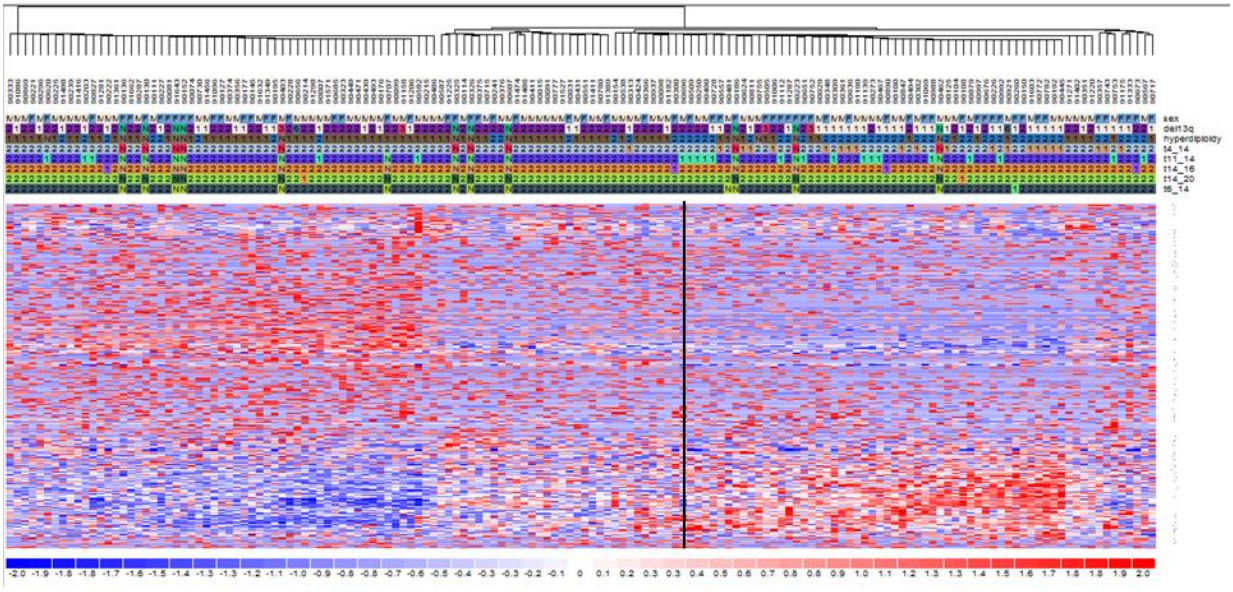


Figure 1S: Significant differential expressed genes and microRNA signatures for hyperdiploid MM classification.

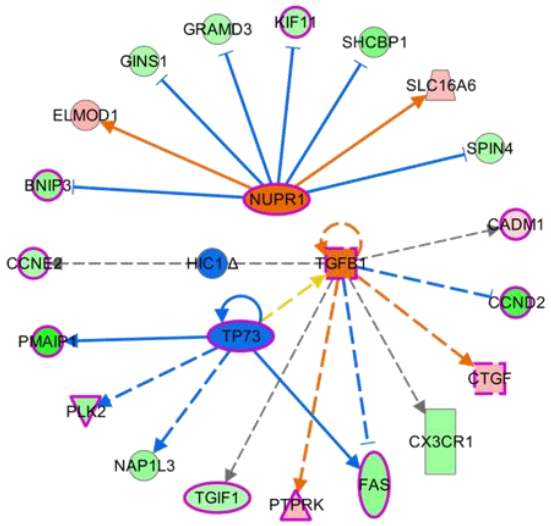
Heat maps showing the significant differential expressed mRNAs (39) or miRNAs (343) detected by using DChip Software. The genetics characteristics are reported including hyperdiploid status indicated as 1=HD-MM and 2=nHD-MM, N=not available and genetic alteration presence (1) or absence (2). Then standardized expression values (mean= 0, SD =1) for each molecule were analyzed through hierarchical clustering in DChip in order to show groups of mRNA and miRNA with similar expression changes. Clustering uses the Spearman correlation between genes and samples and serve as the basis for merging nodes and building hierarchical trees. Finally clustered data were visualized through heatmaps. Colors represent respectively the down-regulation (scales of blue) and the up-regolation (scales of red). The standardized expression values most likely fall within [-2, 2]. By default, DChip uses pure white to represent 0, pure red to represent 2 or higher, and pure blue to represent –2 or lower.

A)The top 39 significantly expressed and annotated mRNAs fall mainly into two main groups. Affymetrix probe_set ID were reported

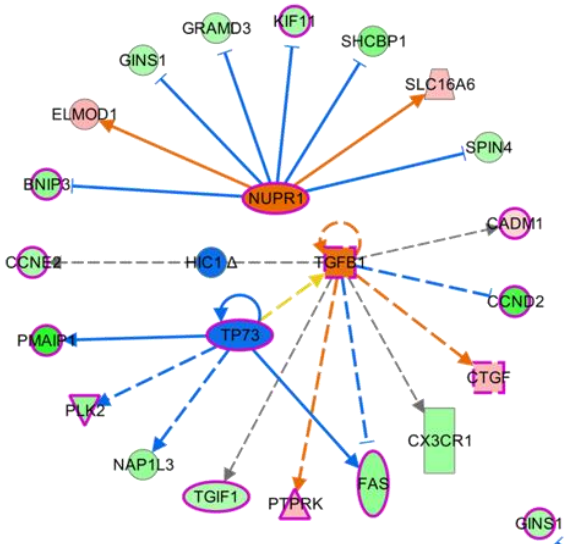
B)The 343 SDE-miRNAs reflects the mRNAs profile and cluster in the two subtype MM groups.

Fig.2S

A. Overlay with Cell Growth



B. Overlay with Cell Cycle Progression



C. Overlay with Tissue Development

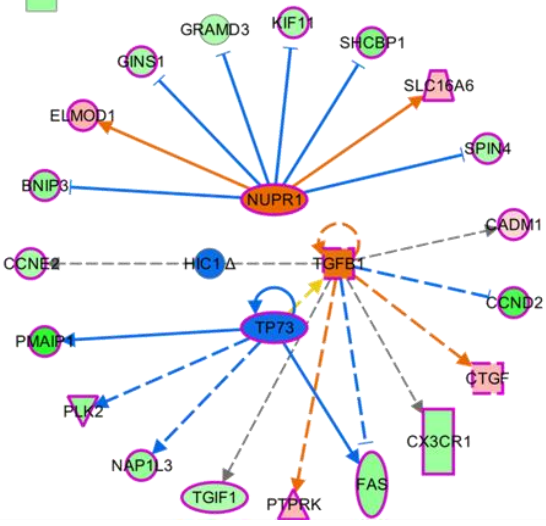
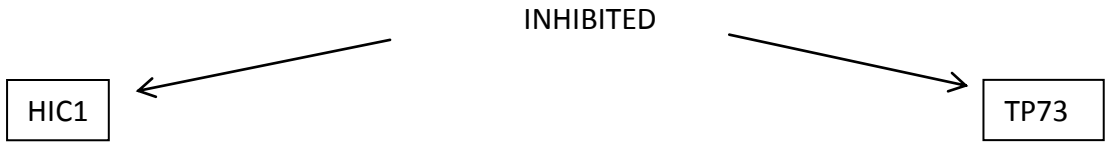


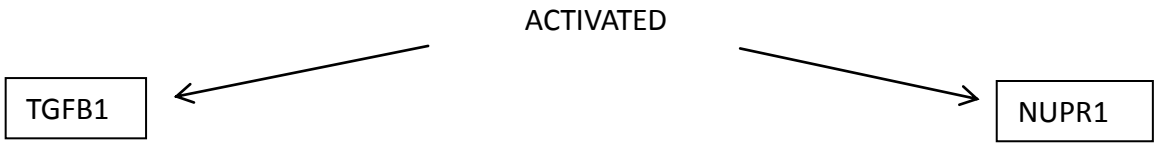
Figure 2S: Overlay of regulatory Networks and Biofunction.

This picture shows (evidenced with pink-painted borders) the overlay of bio-functions and of modulated genes involved in URA. This shows how the different regulation of this molecules may be related to different cell progression behavior and finally may explain the different progression of tumor in two groups. In each figure we represent a different enriched functions and we highlight corresponding molecules by evidencing them with a different border. Enriched functions are related to cell growth (A), cell cycle progression (B) and tissue development (C).

TABLE 1. Target molecules in the dataset



Genes in dataset	Prediction (based on expression direction)	Other	Findings	Genes in dataset	Prediction (based on expression direction)	Other	Findings
SPP1	Inhibited	-0,71	Upregulates	PLK2	Inhibited	-0,65	Upregulates
CCNE2	Inhibited	-0,54	Upregulates	NAP1L3	Inhibited	-0,66	Upregulates
CA2	Inhibited	-0,67	Upregulates	FAS	Inhibited	-0,69	Upregulates
AMIGO2	Inhibited	1,16	Downregulates	PMAIP1	Inhibited	-1,33	Downregulates



Genes in dataset	Prediction (based on expression direction)	Other	Findings	Genes in dataset	Prediction (based on expression direction)	Other	Findings
CTGF	Activated	0,86	Upregulates	SPIN4	Activated	-0,520	Downregulates
PTPRK	Activated	0,84	Upregulates	SLC16A6	Activated	0,780	Upregulates
CADM1	Affected	0,51	Regulates	SHCBP1	Activated	-0,790	Downregulates
TGIF1	Affected	-0,51	Regulates	KIF11	Activated	-0,550	Downregulates
CCNE2	Affected	-0,54	Regulates	GRAMD3	Activated	-0,520	Downregulates
CX3CR1	Affected	-0,62	Regulates	GINS1	Activated	-0,540	Downregulates
FAS	Activated	-0,69	Downregulates	ELMOD1	Activated	0,920	Upregulates
CCND2	Activated	-1,13	Downregulates	BNIP3	Activated	-0,690	Downregulates

In the table are reported the URAs results as inhibited or activated UR molecules. The downstream genes identified in the SDE-genes are reported with relative FC value. Findings assigned by IPA are reported as upregulated or downregulated according to IPA annotation, where regulated indicate the both activity, up and down described functions