



Differential expression of invasion promoting genes in childhood rhabdomyosarcoma

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Background

- Embryonal and alveolar histology
- Histological markers
- Specific translocations
- Fusion proteins in RMA



Molecular classification

- Gene expression analysis
- Single nucleotide polymorphism analysis
- Genomic hybridization



Gene expression analysis

- Subtyping
 - Targeted therapy
 - Analysis of specific biological processes
-



Aim

To identify and to evaluate the role of genes involved in invasion of RMS



Patients and Methods



Patients (n = 19)

- CWS 96 and 2002-P trials
- Mean age [yrs]: 6.4 (1 -15)
- RMA: 8
- RME: 11
- Metastatic disease: 10



Materials (Array analysis)

- RNA extraction (Rneasy Kit Qiagen)
 - RNA quality assessment
 - Affymetrix U133 plus 2.0 whole genome array
 - Analysis of genome array (Affymetrix Microarray Suite)
 - Ingenuity Pathway analysis
-



Materials (Cell culture)

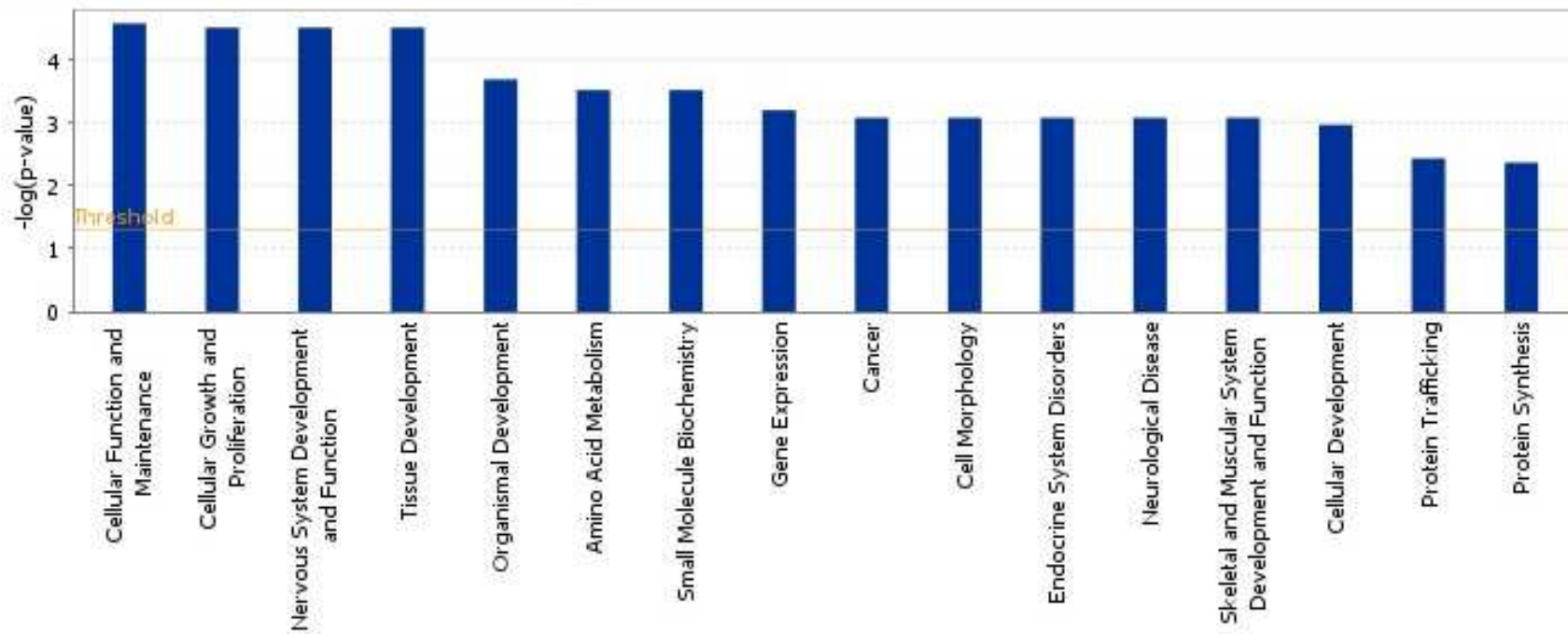
- Cell lines Rh30 (RMA) and RD (RME)
 - siRNA transfection (LMO4 and FOXF1)
 - Invasion assay
 - RT-PCR
-



Results



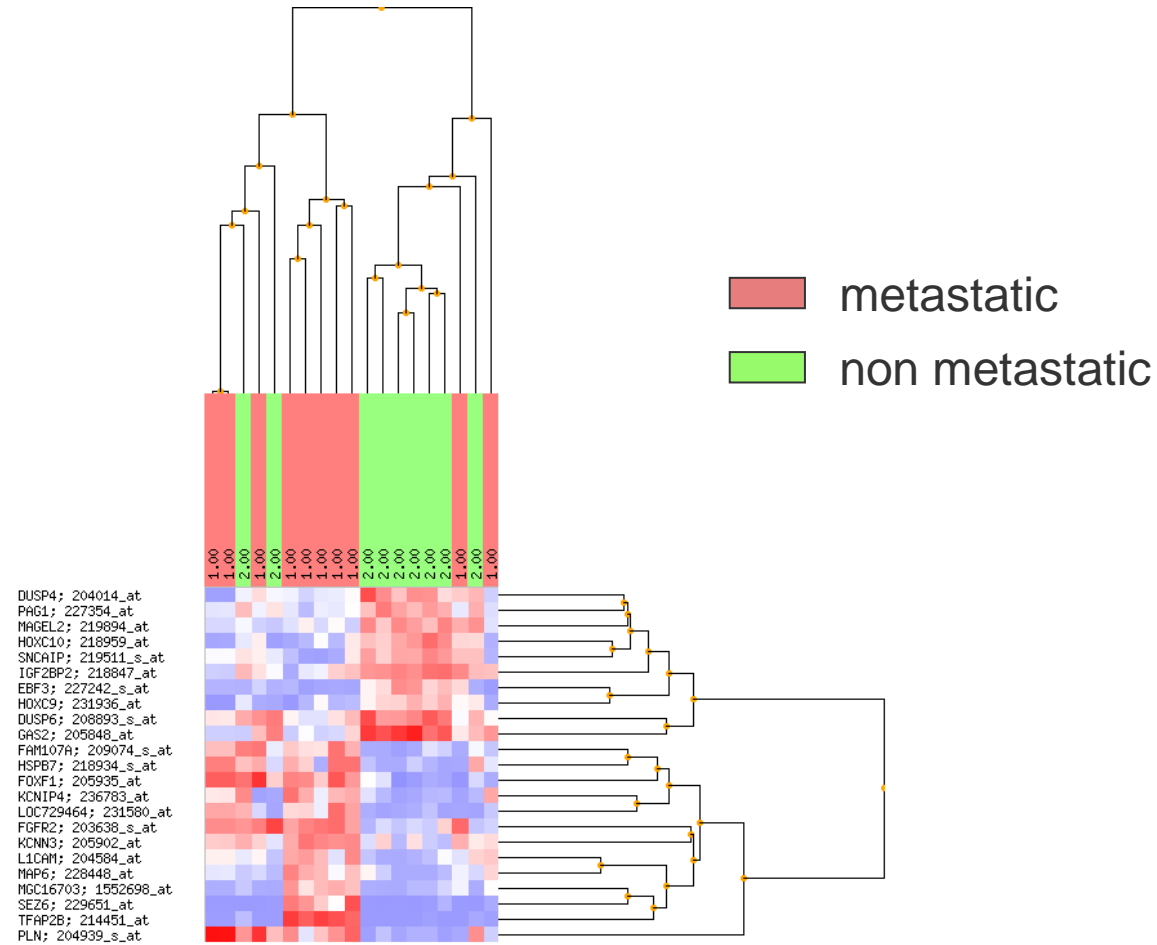
Gene expression RMA vs. RME



➔ Motility associated transcription factors FOXF1 and LMO4 ↑ in RMA

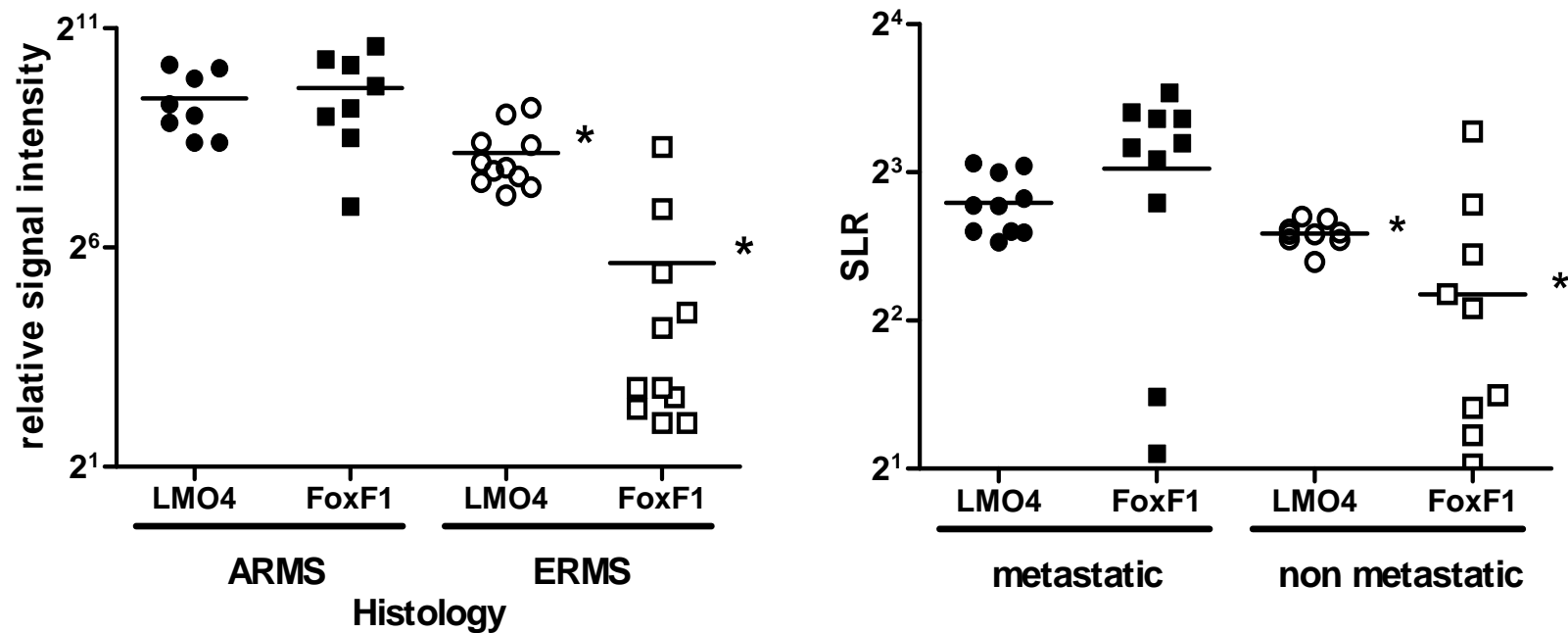


Clustering metastatic / non metastatic RMS





Role of FOXF1 and LMO4

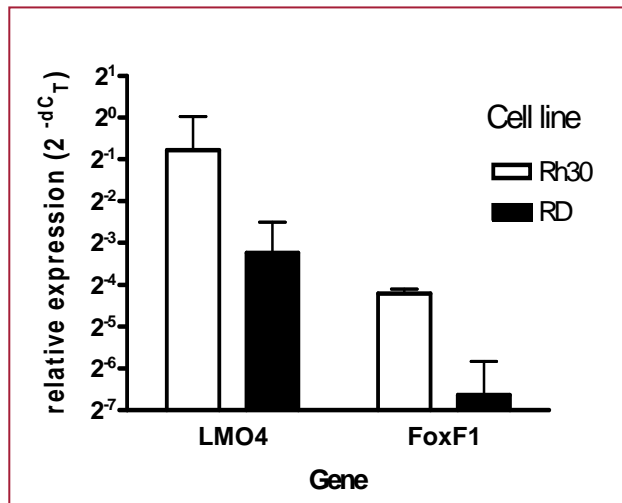


FOXF1 highly expressed in metastatic RMS

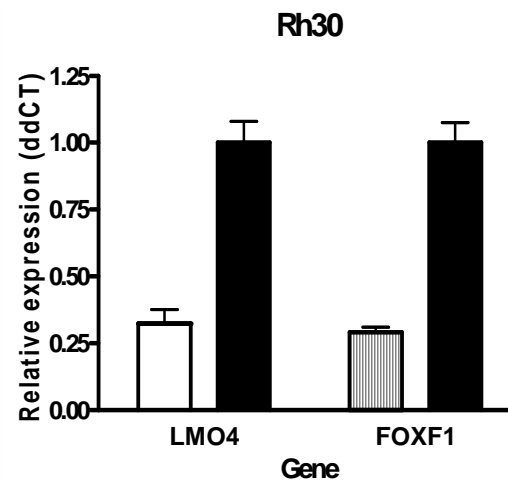
*:p < 0.05



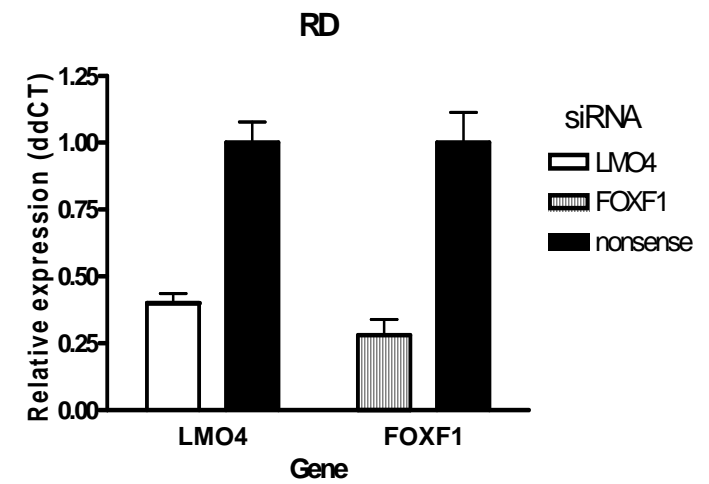
Effects of siRNA on gene expression



Gene expression
in cell lines



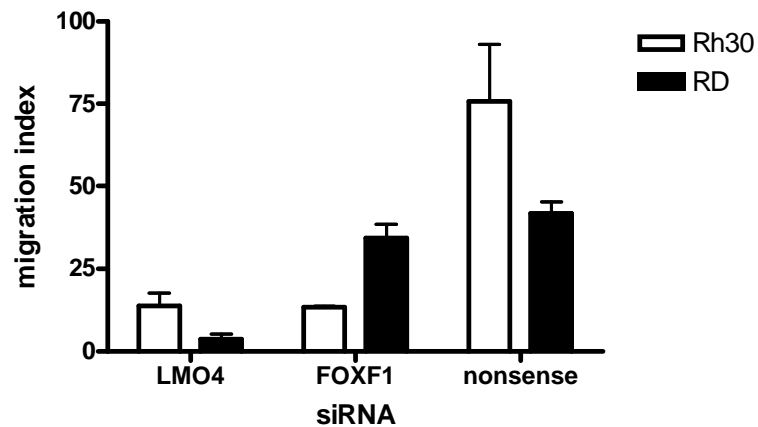
siRNA effects Rh30



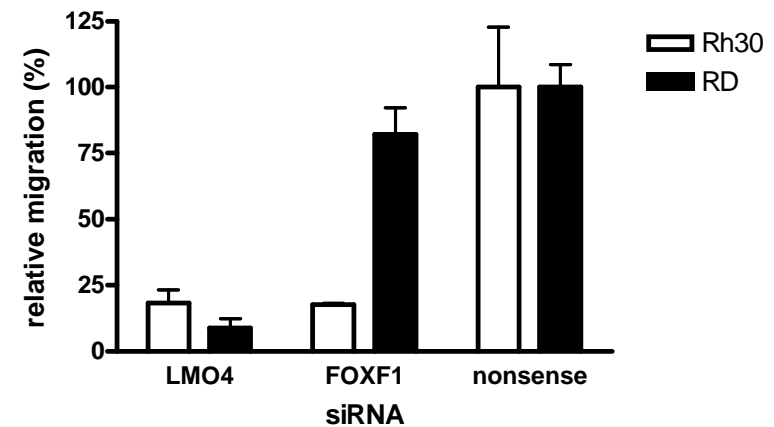
siRNA effects RD



Effects of siRNA on cell invasion



Migration index



Relative migration (%)



Conclusion

- Differential gene expression between RMA and RME
 - Differential gene expression between metastatic and non metastatic RMS
 - LMO4 and FOXF1 might contribute to metastatic invasion
 - Therapeutic option for metastatic RMS?
-

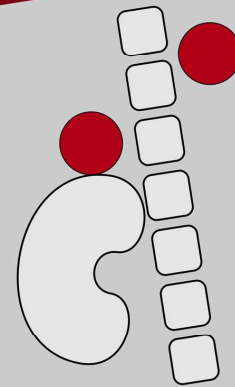


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