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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