miRNA in Tumor Tissues

An exploration of the article: MicroRNA Expression Signature of Human Sarcomas

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miRNA

- ≈22-nucleotide long non-coding RNA
- miRNAs control cell growth and death
- Used in this study instead of genes
 - researchers believe that there is a correlation between miRNA expression patterns and known sarcomas

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Tissue Types

- Tumors
 - RMS (Rhabdomyosarcoma)
 - 3 ARMS (Alveolar),1 ERMS (Embryonal), 2 PRMS (Pleiomorphic)
 - 1 DDLPS (Dedifferentiated Liposarcoma)
 - 8 GIST (Gastrointestinal Stromal Tumor)
 - 7 SS (Synovial Sarcoma)
 - 5 LMS (Leiomyosarcoma)
- Normal
 - 5 SM (Smooth Muscle)
 - 2 SKM (Skeletal Muscle)

The Arrays

- 34 Arrays
- 768 miRNA spotted in duplicate
 - 328 human known, 154 human unknown
 - Others from rats, mice, and control
- Reference Design experiment

Poor quality arrays!

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Out of 34 arrays, 19 stood out as being not very good, 7 stood out as being exceptionally poor

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Filtering and Normalization

- I did not want to throw out entire arrays, so I put lax restrictions on which data to keep
 - Only 87 (of 768) miRNA passed filtering criteria in the article
 - I kept most of the miRNA



Raw Data



Loess Normalized Data

Limma & SAM

- 2 of the 34 tissue samples had been misdiagnosed before the study
 - ARMS misd. as ERMS
 - PRMS misd. as GIST
- miRNA 133b: both the article and I found that this miRNA is significant in differentiating PRMS and GIST
- The article did not go in depth about ARMS vs ERMS

Dendrograms & PAM

- I focused on tumor vs non-tumor tissue
 - SAM's 100 most significant miRNA
 - Hierarchical clustering dendrogram
 - 1-abs(cor), complete method
 - Compare clustering of complete and PAM
- The article used SAM for significance testing and hierarchical clustering

Complete Method with spot #s

Dendrogram for significant miRNA



(+): logFC(normal-tumor)>0, (-): logFC(normal-tumor)<0

dist = 1-abs(cor), method = complete

PAM cluster names

Dendrogram for significant miRNA



dist = 1-abs(cor), method = complete

Conclusions

- The article threw out a lot more data
 I kept data that probably wasn't publishable
- Some miRNA are expressed differently under different tumor states.
- The article asserted that there were 5 groups, I said there were 9