GENETICS

ANOTHER LAYER OF COMPLEXITY IN GENE REGULATION

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Yesterday evening I attended an excellent presentation by Nikolaus Rajewksy about microRNAs, small noncoding RNAs that are thought to have a role in posttranscriptional regulation. Nikolaus just moved 3 months ago from New York to follow Jens Reich at MDC in Berlin). Basically, he talked about his recent "l(ou)sy" paper and the "SNP" paper after giving a rather detailed history about the development of the field. It started in 1950 with Jacob and Monod, 1960 Britten and Davidson, 1970 Haywood (who even quit science after being dissappointed), finally to 1990 when the Ambros and Ruvkun labs discovered nematode microRNAs. Current research is mainly done in the Tuschl, Batel, Cohen, Lander and Rajewsky labs who produce the bulk of the 800 papers or so published in 2006.
Approximately 30% of genes are influenced by microRNAs, the total number of microRNA sites is under heavy debate (~22,000) as well as the number of human microRNAs (328); each microRNA regulates ~200 genes. Unfortunately there is still no highthroughput technique to detect targets. There is also no good prediction by free energy and even mismatches in the 5 prime of mRNA are possible (individual predictions can be obtained at Pictar that uses a hidden Markov model).
If I understood that correctly, miRNA are the feedback mechanism on RNA level (with transcription factors at the DNA level). He mentioned 3 classes known so far in humans: oncomiRNA, miRNA 375 myotrophin, and miRNA 122 acting on cholesterol (quite interesting as being described recently in the NEJM. The experimental knockdown of liver specific mouse microRNA shows ~300 up- and ~300 down regulated genes. Upregulated genes have in approximately 50% of cases one miRNA nucleus, downregulated ones have even less than average binding sites. There is no overrepresented GO category in upregulated genes but cholesterol is highly significant in downregulated genes whatever that means. Action of miRNA seem to heavily context dependent giving us many more questions than answers. Yea, yea.