Application of Microarray Analysis in *Drosophila*

Microarray, also known as DNA array, is to have a collection (at least at a magnitude of thousand) of DNA fragments, whose sequences are known, being arrayed on a solid supporting substance, such as plastic or silicon chip. Usually those probes (i.e. the DNA fragments on microarray) are derived from genes of interest. Therefore, microarray is also called gene chip, or gene array. The basic idea of microarray evolved from Southern blotting. Researchers prepare their sample by labeling DNA molecules in query with substrate which is either fluorescent or radioactive, and then blot the microarray with labeled sample. DNA in query will hybridize to the matching probe on microarray, if there is, otherwise it will be washed away. After hybridization and washing, signals from the label of hybridized DNA will be detected and recorded by reader instruments such as photometer. And data will be compiled and analyzed by software finally.

The appearance of microarray allows us to do thousands of southern blotting in parallel. However, that doesn't mean the importance of this technique only limit to speeding up the way we do southern blotting. In fact, the capacity of microarray to test thousands of genes at once make it the most appropriate way to show gene expression profile at certain development stage, compare expression profile between cells in disease and healthy cells, and test the change in the transcription network controlled by certain transcription factor etc. While researcher taking advantages of this technique, they must be careful about its down side. One down side of microarray, which has been improved to some extent, is that mismatching between samples and probes leads to false-positive results. Another thing that researcher should be care of is that how they standardize and statistically analyze the data. Improper data processing will lead to misinterpretation of the data. At last but not least, microarray is still a relatively costly experiment. Proper design of experiment in ahead will avoid waste of money.

One year after White, K.P. *et al* published their work (White K.P. *et al.* 1999) of analysis of gene expression pattern in *Drosophila* during metamorphosis by microarray, a group of University of

California in San Francisco studied, by microarray, the genome-wide response of aging and oxidative stress in *Drosophila melanogaster* (Zou, S. *et al.* 2000). To monitor the change of expression pattern over aging, the authors collected male flies at different ages, and then compare the gene expression pattern of 3-day-old males to others of 10, 25, 30, 40, and 50 days old. Also they fed flies with paraquat, which is a free-radical generator, and compare their expression profile with that of non-fed flies, to test oxidative stress responses. From these experiments they discovered that the transcription level of genes involved in reproduction, metabolism, and protein turnover goes down with aging, while genes of detoxification and chaperones are up-regulation. More surprisingly, they also found that more than 60% of the age-regulated genes showed no response to oxidative stress, and 80% of the oxidative response genes showed no changes over aging, which are interesting and anti-intuition results.

An example of how researcher apply microarray in decipher transcription network came from a PNAS paper published by a Swiss group in 2003 (Beltran, S. *et al.* 2003). By comparing the transcription profile of *ash2*^{I1}, which is a mutant of transcription factor *ash2*, with WT by microarray, they attempted to identify putative target genes of *ash2*. 235 gene were identified, some of which are of great interest to the researches.

Microarray is the best way so far to monitor changes in transcription/expression levels. Without the microarray technique, the first paper would be impossible, and the second group would have input much more effect to achieve the same result. In the meanwhile, researches have also expanded the application of microarray into other areas, providing alternative to some conventional approaches. A paper published in 2003 (Sun, L.V. *et al.* 2003) used microarray to study protein-DNA interaction. The microarray they used is a little bit different from the ones used in first two papers. They were using genomic tiling microarray, which was constructed with genomic DNA fragment covering both coding and non-coding sequences. They set GAF as the query protein and identified 169 putative binding sites. Five of those binding sites as well as

seven non-binding sites were verified by ChIP, which is the conventional approach to study protein-DNA interaction (also is possible alternative way for this study). The results showed a good correspondence between the microarray data and ChIP data. The test set in verification seems not large enough to me though.

Recently, some other array, such as protein array and tissue array, also evolved, and have been applied into research. High false-positive rate is still a drawback of microarray technique.

Reference:

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