Expressions

Utility of RNAi Keeps Growing

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Company: GeneExpression Systems Inc.
Background: The company is a custom research organization that develops and markets gene expression-related products.

The "RNome" is the RNA equivalent of the proteome or genome. The subject of "RNomics" is a new emerging field that categorically studies the structure, function and processes of noncoding RNAs (ncRNAs). These are generally about 21 to 200 nucleotides in length (some are longer than 200) and have been involved in the processes of transcription, gene silencing, replication, RNA processing, modification, mRNA translation, protein stability and protein translocation.

The completion of whole-genome sequencing of humans and other organisms revealed a wealth of genomic information but opens new challenges for molecular biologists to decipher the complete list of protein-coding genes. In addition, transcriptional events such as RNA splicing and post-translational modifications made it difficult to predict the exact number of genes or proteins. With this degree of complexity, monitoring the entire proteome expression levels in order to elucidate their functions and develop them as drug targets is a challenging paradigm in the biotech industry. Despite the proteome sequencing efforts, the "RNome" also has to be studied in detail to fully understand and tally the number of genes encoded by a genome. The challenge for the future will be to identify the whole complement of ncRNAs and elucidate their functions in gene expression and regulation.

RNA interference

RNA interference (RNAi) is a process in which double-stranded RNA specifically inhibit expression of target protein by guiding the specific degradation of the coding target mRNA. In broad terms, "post-transcriptional gene silencing," "co-suppression," "quelling," and "siRNA" are collectively included in the phenomenon of "RNA interference."

The development of small interfering RNAs (siRNAs) is another step in the realization of the enormous potential of RNAi. This molecular tool will permit "loss-of-function" screens and rapid tests for genetic interactions in mammalian cells, which up to this point have been quite difficult to perform quickly. Some of its applications include:

1. Several essential genes for cell growth, cell cycle, cytoskeleton, kinases, and cell surface receptors have been characterized by siRNA-based methods in about 25 different mammalian cells.
2. "Whole-genome RNAi screening" strategy has been used in a high-throughput format to isolate phenotypes for several hundred genes that are involved in cell cycle, embryonic or germ-line development. The high-throughput capacity of RNAi makes it a particularly attractive method for rapid screening and validation of targets identified by microarray analyses, protein-protein interactions or *in silico* gene prediction.
3. Recently, several groups have applied the RNAi approach and specifically inhibited the replication of HIV by targeting viral (p24, vif, nef, tat and rev) or cellular genes (CD4, CXCR4, CCR5). This approach has been extended to block the infection of respiratory syncytial, human papilloma and polioviruses. Therefore, this particular area opens new avenues for gene-based therapeutics.
4. The ability to engineer vectors that can produce siRNAs to knock down the expression of several oncogenes, tumor suppressor and transcription factor genes will undoubtedly spark a firestorm of effort to assess their benefit as a cancer prevention method. Very recently, this reverse-genetics approach has been adopted to study polyglutamine, a neurodegenerative disorder.
5. RNAi may facilitate drug screening and development by identifying genes that can confer drug resistance, or genes whose mutant phenotypes are ameliorated by drug treatment, thereby providing information about modes of action for novel compounds.
6. One could generate high-throughput RNAi analysis for a set of genes by combining the "interactome" data with "phenome" mapping data.

We hope that all these approaches will help to develop new diagnostic reagents and novel molecular interventions for several human diseases. RNAi seems to be one of the breakthrough technologies of the 21st century, that will revolutionize molecular, cellular, and developmental biology and herald a new epoch in medicine.