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Positional Cloning, Transcription Mapping, and Whole Genome Gene Identification: The Choice is Yours!

In the last issue of *European Journal of Human Genetics,* Antonarakis [1] focused on the value of the exon trapping approach combined with EST database searching for gene identification and mapping. He named this approach 'mapping by sequence homology' (MSH), as the identification of sequence homology between trapped exons and ESTs allows one to map the corresponding cDNA to the region where the exon is trapped.

This is a valuable approach that takes advantage of current experimental and bioinformatic resources. However, it is important to note that the use of one versus another gene identification/mapping strategy depends very much on the specific goals of the project. Why look for genes? I can think of three main reasons: (1) to isolate a specific gene (e.g., positional cloning of a disease gene), (2) to build a transcription map of an entire chromosome or a large chromosomal region (e.g., by using the 'MSH' method), and (3) to contribute to the efforts aimed at the identification of all human genes. Any strategy which involves targeting at a specific chromosomal region, such as positional cloning and transcription mapping, is considerably less efficient than whole genome random approaches such as mapping ESTs.

While the justification for performing positional cloning is in some instances compelling, due to the medical relevance of disease gene identification, the motivation to construct whole chromosome transcription maps is, at least in my opinion, less clear. With the obvious exception of chromosome 21, which is involved in the most important human aneuploidy syndrome, and of some large chromosomal regions bearing major interest (e.g., regions involved in cancer, imprinting, and X inactivation), I cannot see a specific reason to favor transcription map versus whole genome gene identification approaches. On the contrary, I believe that gene identification efforts should focus primarily on the production and mapping of ESTs, isolation of full-length cDNAs, and large scale genomic sequencing.

Reference

1 Antonarakis SE: Mapping by sequence homology. Eur J Hum Genet 1996;4:247–249.

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