

Gene expression changes during murine postnatal brain development

ABSTRACT

A small percentage of the genes expressed in the postnatal developing brain show changes in expression level during the newborn to adult phase of development. It is likely that these developmentally regulated transcripts represent molecular markers for the complex developmental process occurring in the postnatal brain.

INTRODUCTION

Background For most vertebrate organs and tissues, the majority of development occurs during embryogenesis, and postnatal changes are primarily concerned with growth. The central nervous system (CNS) is unusual in that a considerable amount of morphological development, cell differentiation and acquisition of function takes place during postnatal development. As yet, the molecular mechanisms underlying these complex developmental processes are not well understood. We have recently completed a differential display (DDRT-PCR) analysis of genes expressed in the murine postnatal developing brain. This analysis formed the baseline for an ongoing study and produced a series of RNA fingerprints representing genes transcribed at specific stages of brain development. For our analysis we compared RNA fingerprints at four different timepoints during postnatal development: newborn (day 1), day 10, day 20 and adult (day 42). Incidental to our experimental objective, we also identified a large number of genes which were clearly developmentally regulated in the wild-type mouse brain. We submit this data principally to allow others to isolate specific transcripts with developmentally regulated expression in the postnatal brain without the necessity of performing extensive screening procedures. From a total of approximately 25,000 transcripts displayed, around 200-300 (approximately 1%) exhibited developmentally regulated expression profiles. Here we present groups of RNA fingerprints displaying a subset of these developmentally regulated genes, along with sufficient technical information to replicate specific fingerprints and recover selected cDNAs. The particular fingerprints presented here were selected on the basis that identical DDRT-PCR profiles were obtained with at least two separate batches of RNA, and that each fingerprint displayed at least three developmentally regulated transcripts. On each group of fingerprints we have indicated the position of at least three bands representing the more obviously developmentally regulated genes. We have assigned these marked transcripts into three broad categories as follows: genes for which mRNA levels increase during brain development; genes for which mRNA levels decrease during development; and genes exhibiting a peak in mRNA levels during this developmental period. To ensure that changes in DDRT-PCR profiles represent genuine changes in expression levels, two cDNA fragments were recovered and used in downstream expression analyses. The overall procedure followed is illustrated in Figure 1 (and see). The northern blot expression profiles of both transcripts accurately replicated the original DDRT-PCR expression profiles, confirming the validity of our approach.

CONCLUSION

Conclusions In the course of analyzing gene expression in the postnatal developing murine brain we have observed that approximately 1% of genes transcribed are developmentally regulated. The objective of this report is to permit those interested in such transcripts to selectively isolate

specific developmentally regulated transcripts without the necessity of performing an extensive screen. Here we present the RNA fingerprints containing a subset of these developmentally regulated transcripts and we include all the necessary information to permit individual transcripts to be isolated and identified. We have highlighted a total of 131 developmentally regulated transcripts in three broad categories of expression profiles. Of these, approximately 7% (9) fell into category C while the remainder were equally divided between categories A (61) and B (61). We also present confirmatory evidence that changing DDRT-PCR expression profiles represent genuine alterations in expression levels during brain development. It should be noted that changes in expression profile reflect changes in RNA level per microgram total RNA in whole brain and, given that the postnatal brain is not a uniform structure, expression profiles should be interpreted accordingly.