Lewy bodies (LB) are a pathological hallmark of Parkinson's disease (PD). Whether LBs are neuroprotective, cytotoxic, or an age-related epiphenomenon is still debated. In the present study, the genetic fingerprints of mesencephalic dopaminergic (DA) neurons containing LBs versus mesencephalic DA neurons not containing LBs were compared in five PD patients. Total RNA from single neurons of both neuronal subpopulations was obtained by immuno-laser capture microdissection. Subsequently, RNA arbitrarily primed PCR was employed to generate expression profiles from the extracted RNA. Differentially displayed polymorphic fragments were dissected from silver-stained polyacrylamide gels. Most of these expressed sequence tags (ESTs) were homologous to known human sequences (56/64, 87.5%). Based on the potential significance of individual ESTs in neurodegenerative disorders, 5 ESTs of interest were selected for further quantitative expression analysis by real-time quantitative reverse transcription PCR (rtq RT-PCR). DA neurons without LBs preferentially expressed molecules beneficial for cell survival, whereas genes preferentially expressed in DA neurons containing LBs may support a cytotoxic role of LBs. Thus, we favor the view that LB-positive DA neurons are sicker than their LB-negative counterparts, and that inhibition of LB formation may indeed represent a
therapeutic strategy in PD.