Commentary

Nestin immunoexpression in CNS tumours

The introduction of immunohistochemical techniques to demonstrate the expression of specific proteins has greatly increased our ability to properly identify various tumour types. Immunohistochemistry has also been able to demonstrate intermediate filament (IF) proteins, which are important components of the cytoskeleton\(^1,2\). This is of particular importance because it can serve as a marker to determine cellular derivation of the tumours, including those of the central nervous system (CNS)\(^3\). Studies have concluded that nestin is expressed in stem cells, cancer stem cells as well as neuroepithelial progenitor cells of the developing nervous system and can also be encountered in endothelial cells, immature skeletal muscle cells, activated hepatic stellate cells, cells of the neural crest, corpora lutea, gastrointestinal cells as wells as cells in the differentiating heart and testis, but very little is known about its function or regulation\(^4-7\).

There are more than 40 IF proteins that are divided into six main classes or types (I-IV) based on their molecular structure, with nestin belonging to type IV. Types I and II belong to acidic and basic keratins of epithelial cells. Type III is comprised of 4 proteins - desmin, glial fibrillary acidic protein (GFAP), peripherin and vimentin. These IF proteins may form homo- and heteropolymeric proteins. Type IV consists of neurofilaments -L, -M and -H, which are found in high concentrations along the axons of vertebrate neurons. These IFs are important because during axonal growth, new neurofilament subunits are incorporated all along the axon. The level of neurofilament gene expression seems to control axonal diameter, which in turn controls how fast the signals travel down the axon. Nestin is also classified as a type IV IF protein. It is not able to polymerize into filaments alone but is thought to require the presence of a type III or another type IV IF protein. Type V includes nuclear lamins.

Nestin (type IV), along with vimentin and GFAP (both type III) are members of the IF protein family that is abundantly detected in the developing CNS during the embryonic stage. Steinert and Liem\(^8\) found that changes within the spatial and temporal expression of IF proteins regulate remodeling of the cell cytoskeleton during development. It was also reported that in the CNS, IFs exhibit sequential expression whereby during differentiation, nestin becomes downregulated and is replaced by tissue-specific IF proteins, but it has been found to re-appear in adults during injury to the CNS or muscle.

In this issue, Sandhya Rani et al\(^9\) describe the results of their study on brain tumours of both neuronal and glial lineage as well as metastatic tumours. They demonstrated nestin expression and its co-expression with neuronal and glial intermediate filaments using immunohistochemical techniques. They were able to successfully localize nestin in brain tumours displaying various grades of malignancies as well as in mature dysplastic spinal motor neurons found adjacent to the tumour and in cerebellar Purkinje cells. The results of Sandhya Rani and associates and the interpretation of their findings are interesting. Further studies are, however, required to prove their concept.
References


