Neurofibromatosis Type 1 in Childhood.

Neurofibromatosis type 1 (NF1) is one of the most common single gene disorders and it presents many difficult management problems. Physicians who have to tackle these problems in children will be stimulated and helped by this book, which presents the experience of a dedicated, multidisciplinary, paediatric NF1 clinic. The book starts with a brief historical overview and a highly readable summary of what is known of the molecular pathology of NF1. However, the core of the text is in a series of research paper style chapters which present data on a series of 200 children seen at the clinic. These chapters include a very useful review of the clinical features found in the patient group, a study on cognitive function and academic performance in affected children, a description of the MRI findings in a relatively unbiased group of the children, and a review of the perinatally difficult problem of optic tract gliomas. A particularly intriguing chapter describes a significant (and controversial) association between MRI "unidentified bright objects" and cognitive impairment. Exploration of this area might provide some insight into the basic pathological mechanism of cognitive impairment in NF1. Last but not least, appendices contain a very useful clinical assessment protocol, and a very well written patient information sheet. Any doctor who is involved in the management of children with NF1 will find this book useful.

Evan Reid


In order fully to use the advantages subcellular compartmentalisation confers on an organism, the extensive obstacle of transporting proteins across lipid bilayers needs to be overcome. Protein targeting is the study of how newly synthesised proteins reach their designated cellular location for functionality and of the molecular conveyances used to do this. Targeting signals act as recognition motifs to permit the protein to bind to the protein targeting machinery on the relevant organelle. Parallel themes are echoed throughout protein targeting pathways, both at the signalling and at the molecular apparatus level. For instance, targeting signals in proteins which arise directly from primary structure, are either partly or totally responsible for directing proteins to the endoplasmic reticulum, nucleus, peroxisome, and mitochondrion. Tertiary structural motifs also exist, such as the tyrosine containing b-turns which are specific for the targeting plasma membrane proteins to coated vesicles. Once at the target organelle, protein recognition by the appropriate transport machinery for internalisation is necessary. This may occur by endocytosis (at the plasma membrane) or through some sort of "pore" (for example, nucleus and endoplasmic reticulum). To ensure vectorial and irreversible transport, targeting signals may be destroyed at the final location of the protein. Of course the situation is far more complicated if the protein has to traverse several different intracellular membranes before arriving at its final location, each having its own distinct signal. Lastly, we should not forget the vast support network of interacting proteins, such as molecular chaperones, which ensure correct folding and assembly of the newly targeted proteins. The understanding of protein targeting has many clinical applications, including the study of diseases which arise because of a fault in this mechanism and for elucidating molecular mechanisms of protein targeting pathways. A universal absence of protein targeting is incompatible with organelle biogenesis and therefore life, but defects in specific targeting signals which lead to disease are well characterised. For instance, in mucolipidosis II, newly synthesised lysosomal enzymes are targeted to the external environment, in familial hypercholesterolaemia, mutations in the low density lipoprotein (LDL) receptor reduce its endocytic ability, ultimately raising plasma LDL levels, and the commonest mutation reported in the cystic fibrosis transmembrane conductance regulator prevents it from leaving the endoplasmic reticulum for the cell surface, and therefore cystic fibrosis arises not so much from what the mutant protein is unable to do, but from the fact that it is now mistargeted. A short paragraph in each chapter updating the reader on the progress made on the medical relevance of their findings would have been welcome.

Overall, I recommend this book wholeheartedly and I am sure it will sit on the bookshelves of many cell biologists. It is an unusual scientific text in that you can actually read it rather than refer to it and it will certainly stimulate the desire for further reading.

Juliet A Ellis