INTRODUCTION

Electron microscopy has an important role in diagnostics

John W Stirling & Richard C Davey

Electron Microscope Unit, Anatomical Pathology, SouthPath, Flinders Medical Centre

Electron microscopy has an important role in our understanding of disease. Although immunohistostaining (IH) has replaced TEM in respect to the identification of tumours, TEM is still essential for the diagnosis of a wide range of diseases. The critical factor is resolution. The resolving power of the electron microscope (EM) is 0.2-0.3 nm, a thousand times better than the light microscope (LM) which has a resolution of 0.2 µm (200,000x). As a result, the EM has a significantly higher magnification range in comparison to the LM, allowing us to see cell and tissue components easily. This structural information gives us an insight into the cellular basis of disease and can provide important diagnostic information.

SELECTED EXAMPLES OF DIAGNOSTIC TEM

Renal disease

The use of TEM in the diagnosis of renal disease is standard practice. The method is most useful when light microscopy (LM) findings are equivocal or normal (Shillingford 2002). The location and structure of deposits and the texture, width, and thickness of the glomerular basement membrane (GBM) are the principal diagnostic features.

The location and structure of immune complex deposits

Example: Immunoglobulin G (IgG) deposits in the glomerular basement membrane (GBM) are usually comprised of fine granular electron-dense material. In immunostained glomerulonephritis (Fig 1), the deposits are Congo red-stained extracellular non-branched fibrils or tubules ranging from ~9 to >500nm in diameter (Shillingford & Woods 2002).

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Malignant tumours

Overall cell morphology and the range of cytoplasmic organelles and inclusions within a cell are indicators of differentiation. TEM can be used to identify tumours with variable differentiations (e.g. neuroepithelial tumours and Ewing's sarcoma) and tumour subtypes (e.g. the separation of gastrointestinal adenocarcinomas from gastrointestinal stromal tumours). A typical use of TEM in tumour diagnosis is the identification of mesothelioma when histological appearances and fibrillar labelling are helpful (Cotran 1997). In this instance, the presence of long thin stromal cell processes and long stromal collagen fibres (COL), an indicator of mesothelial differentiation, Meissner cell cytoplasm (C), Bar = 500 nm.

Skeletal muscle and myocardium: structural abnormalities and inclusions

A range of primary abnormalities occur in muscle diseases and as secondary events in various neurological diseases. Although a wide range of changes are seen in satellite cells, nuclei, cytoplasm, and mitochondrial (Fig 4), only a few of these alterations are specific and diagnostically significant.

Fibrils and crystalloidal inclusions

Based on their detailed and general morphology, fibrils, tubules, and crystalloids are usually identified by TEM. The principal applications in tumour diagnosis are the identification of amyloid, myofibrils, Z-discs and mitochondria (Fig 4), only a few of these alterations are specific and diagnostically significant.

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a recessively inherited disorder common in populations of European origin. The protein is a large, highly glycosylated multiple transmembrane protein mainly expressed in small vessels of the cerebral cortex. The principal defect is a genetically determined loss of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase leading to a reduction in electron transport chain activity with increased reactive oxygen species (ROS) formation. Of important note, the microvascular involvement appears to be caused by a failure in the formation of the pericyte-astrocyte complex in the perivascular space. CADASIL is a recently recognised cause of stroke and dementia. The type I CADASIL mutation, COL3A1, is the most common genetic cause of spontaneous intracerebral haemorrhage, the most frequent cause of death in CADASIL patients. The outer tubular pairs (arrow) lack both outer and inner densest bands. Bar = 100 nm.

REFERENCES


