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Editorial

Transmission Electron Microscope: A Diagnostic and Research Tool

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Tools and technology are key to research and development in material science as well as biomedical science. Even today, surgical pathology is based on the descriptive microscopic features of tissues and cells. Auxiliary techniques like immunohistochemistry (IHC), immunofluorescence (IF) and electron microscopy play a vital role in achieving an accurate diagnosis. The study of cellular and subcellular ultrastructural features is sometimes very essential investigation for the culmination of a perfect diagnosis. A variety of renal disorders, carcinomas, neuroendocrine tumors, viral infections and myopathies need electron microscopic exploration to ascertain the cause and pathological features of a diagnostic entity. Transmission electron microscopy has an edge over other optical technologies. In fact, anatomical laboratories are incomplete without Transmission Electron Microscope. Biomedical scientists have always been interested in the structure and function of organs and tissue components of experimental animal as well as human body to ascertain the normal and pathological status. Accurate structure size and special distribution of various tissue components and subcellular organelles can only be determined through ultrastructural image analysis and morphometry.

Ever since the invention of the first compound microscope in the early 17th century by Hans & Zaccharias Janssen, a vast array of optical microscopes have been developed to study the structural organization of living systems during health and disease in an effort to understand the disease process and cause. Unaided human eye has limited resolving power. The documented 'resolving power' of unaided human eye is around 200 µm. The entire logic of microscopy is to magnify any microstructure enough so as to fit into the resolving power of our eyes. The light microscope could resolve down to 200 nm with oil immersion objective lens. Practically the resolving power of light microscope is 1000 times better than human eye. Biologists found in early 20th Century that light microscope do have limitations, as subcellular components and cytoplasmic organelles could not be revealed with the light microscope. The limitations of light microscope led to the discovery of electron microscope (EM). The 'resolving power' (R) of a microscope is a ratio of 'wavelength (λ) of light' to the twice of 'numerical aperture (NA) of objective lens ($R=\lambda/_{2NA}$). The descriptive value of 'resolving power' of a light/compound microscope comes out to be 200 nm for 'oil immersion objective' (NA=1.25) with 'green light' of 500 nm wavelength ($R=^{500}/_{2x1.25}=200$). But with the electron microscope we could achieve a resolving power of 0.2 nm that is 1000x better than a light microscope or one million times better than unaided human eye. The core factor of improving 'resolving power' is the reduction in wavelength of light or source of illumination. The visible light and ultraviolet light have limitations of wavelength. The source of illumination used in the EM is high energy 'electron beam' derived from heated tungsten filament or the tip of lanthanum hexabromide (LaB_6) crystal. The lanthanum hexabromide (LaB_6) crystal is relatively better than tungsten filament as the electron source (tip) size of LaB_6 crystal is 20 µm as compared to 100 µm of tungsten filament. Electron optics is a vast subject and could be learnt separately for understanding the functioning of EM and trouble shooting.

The prototype of 'Transmission Electron Microscope' (TEM) was developed by Ruska & Knoll in 1931 however; the concept of focusing of electron beam by magnetic field was demonstrated by Hans Busch of the University of Jena (Germany) in 1923. During all these years, the electron microscopy science has undergone a great evolution and now we have very sophisticated TEMs with wider applications in biology, medicine and material science. The preparation of specimen to be viewed with an electron microscope also needs an expertise. Modern TEMs are operated through embedded system programs loaded in a personal computer (PC) and are equipped with 'digital cameras'. Real-time image analysis and morphometry is also possible for structure size, width or thickness, diameter etc. Multiple parameters like perimeter, partial-perimeter, circularity and area can be determined using a variety of 'image analysis software's on acquired and saved images, for better understanding of pathological changes. Statistical analysis of quantitative data of ultrastructural morphometric parameters would make the biomedical research more comprehensive, understandable and presentable.

Thin basement membrane disease (TBMD) of kidney needs accurate measurement of thickness of glomerular basement membrane (GBM) at-least at 50 orthogonal intercepts across the GBM at accurately enlarged electron micrographs, manually or through interactive measurements through software on digital images of ultrastructure of renal glomerulus at the original magnification of 20,000x. The diagnosis of Alport's Syndrome (a hereditary nephropathy) also needs electron microscopic study. Podocytopathy, thrombotic micro-angiopathy (TMA), lupus nephritis, Fabry's nephropathy, IgA nephropathy and renal amyloidosis need electron microscopic exploration of renal biopsies/tissues for an accurate diagnosis.

Mitochondrial distribution, accumulations, intramitochondrial inclusions, granules and degenerative changes could only be explored under TEM. Application of TEM in diagnoses of neuroendocrine tumors on the bases of cytoplasmic inclusions is well established.

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The quantification of ultrastructural components and assessment of percentage of subcellular components showing abnormality could only be accomplished through electron microscopic study of tissues for research as well diagnostic purpose. Pathological lesions of viral etiology should always be investigated by TEM to ascertain the direct evidence of viral particles. Transmission Electron Microscope is not only an instrument for structural study but a very powerful research cum diagnostic tool in the biomedical science. The Austin Journal of Pathology & Laboratory Medicine would be an open access source for the pathologists and researchers to publish and share their research work and expertise.

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