

Correlative light and electron microscopy (CLEM) with 3D microscopy rendering to visualise glomerular changes in the diabetic kidney

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Abstract:

Aim: The most striking ultrastructural change associated with diabetic nephropathy (Type 2) is thickening of the glomerular basement membrane (GBM) around capillary loops with corresponding thickening of the mesangial matrix. Normal GBM thickness is 250 to 350 nm while in diabetes this dimension can increase to 600 to 1,000 nm. As glomerular capillary function progressively declines, fine structural changes in the endothelial cell (EC) cytoplasm, mesangial matrix thickening and capillary luminal closure eventually give rise to the characteristic Kimmelstiel-Wilson nodule. The aim of the present study is to determine whether visualisation of early changes in EC ultrastructure, biomarkers and basement membrane changes by correlative 3D renderings can provide enhanced insight into the pathogenesis of diabetic nephropathy.

Methods: Correlative light and electron microscopy (CLEM) approaches allow simultaneous immunolocalization of specific biochemical biomarkers with corresponding ultrastructural context. By producing serial array sections this synergistic data can be rendered in 3D to obtain unprecedented insight into disease mechanisms and processes.

Results: The present work illustrates immunolabelling of glomerular structures and staining of basement membrane using a novel DAPI reagent followed by fluorescence imaging. This data can then either visualised in 3D or be used for overlay on ultrastructural maps for enhanced contextual information.

Conclusion: By visualising these changes in 3D it is more readily possible to establish whether or not a lesion focal or global and more accurately stage the disease process.



Biography:

Murray Killingsworth completed his PhD from the University of New South Wales, Sydney in 1989 followed by postdoctoral studies in ophthalmic retinal cell biology at Lidcombe Hospital in southwest Sydney. He is the director of the Correlative Microscopy Facility at the Ingham Institute for Applied Medical Research, a premier medical research institute of southwest Sydney and a Conjoint Associate Professor at the University of New South Wales, Sydney and Western Sydney University. He has published more than 95 papers dealing with ultrastructural characterisation of disease pathogenesis and is a Founding Fellow of the Faculty of Science in the Royal College of Pathologists of Australasia FFSc (RCPA).

[13th International Conference on Diabetes, Endocrinology & Metabolism](#); January 29-30, 2020, Sydney, Australia.

Abstract Citation:

Murray C. Killingsworth, Correlative light and electron microscopy (CLEM) with 3D microscopy rendering to visualise glomerular changes in the diabetic kidney, World Diabetes 2020, 13th International Conference on Diabetes, Endocrinology & Metabolism; January 29-30, 2020, Sydney, Australia.