Establishing a Normal Baseline for Immunohistochemical Studies of the Kidney

P.	Prabir	Roy-Chaudhury ^a
M.C.	Michael C.	Jones ^a
A.M.	Alison M.	MacLeod ^a
N.E.	Neva E.	Haite ^b
J.G.	John G.	Simpson ^c
D.A.	David A.	Power ^a

^aDepartment of Medicine and Therapeutics, ^bDepartment of Molecular and Cell Biology, and ^cDepartment of Pathology, University of Aberdeen, Foresterhill, Aberdeen, UK

Dr. Prabir Roy-Chaudhury, Department of Medicine and Therapeutics, University of Aberdeen, Foresterhill, Aberdeen, AB9 2ZD (UK)

Dear Sir,

The detection of cytokines and their receptors using immunohistochemical techniques is an essential step in understanding the pathogenesis of many disease states. A major problem with this approach is defining a normal baseline.

We have attempted to analyse the expression of epidermal growth factor receptor (EGF-R) in the normal and diseased human kidney. Researchers involved in similar experiments have suggested that the non-involved pole of tumour nephrectomy specimens can serve as an adequate baseline [1,2]. We believe that there may be a number of problems with this assumption: (1) In the analysis of cytokines and their receptors, histological normality does not necessarily correlate with normal cytokine expression. EGF-R for example, has been shown to be upregulated in renal cell carcinoma [3]. Minor degrees of upregulation could therefore also occur in the histologically normal portions of such kidneys. (2) We have found that tissue from the non-involved pole of tumour nephrectomy specimens often has an inflammatory infiltrate together with areas of interstitial fibrosis. This could lead to an altered cytokine expression in histologically normal glomeruli. (3) In our experience, there is a wide variation in the intensity of EGF-R expression within the apparently normal glomeruli of tumour nephrectomy specimens, ranging from 1 + (weak) to 3 + (strong).

A possible solution to these problems could be the use of a control panel of renal biopsies from patients with thin basement membrane nephropathy (TBMN).

TBMN has become a defined clinical condition only over the last few years [4]. Patients usually present with microscopic haematuria and have normal renal function. No abnormality is seen on light microscopy of the renal biopsy but electron microscopy shows diffuse thinning of the glomerular basement membrane. The prognosis of this condition is invariably good. Indeed, there is still some speculation as to whether TBMN is a definite clinico-pathological entity or merely a variant of normal.

Biopsies from patients with TBMN do not have any evidence of an inflammatory exudate or interstitial fibrosis. We also found that there was very little variation in the intensity of staining for EGF-R within this group.

The absence of interstitial abnormalities and the uniformity of the EGF-R expression suggest that biopsies from patients with TBMN are likely to be a more suitable normal baseline than the non-involved pole of tumour nephrectomy specimens. Such a protocol would have the added advantage of comparing renal biopsies with each other rather than with kidney tissue recovered at surgery.

We suggest that centres with access to biopsies from patients with TBMN should use these, rather than tumour nephrectomy specimens, to establish a normal baseline for the study of cytokines and their receptors in renal disease.

References

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