

## TUBULAR $\alpha$ -B-CRYSTALLIN IN RENAL PROTOCOL BIOPSIES: PREDICTIVE FOR LATE INTERSTITIAL FIBROSIS?

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**Objectives:**  $\alpha$ -B-crystallin (ABCRYS) is a small heat shock protein expressed in the kidney, functioning as a chaperone molecule in epithelial cells to stabilize actin and intermediate filaments of the cytoskeleton. In the liver, ABCRYS is induced in the stellate cells very early after a fibrogenic stimulus and is accompanied by a change in immunohistochemical ABCRYS staining pattern from cytoskeletal to perinuclear, co-localizing with alpha-smooth muscle actin (myofibroblastic transformation). To the best of our knowledge, no studies on ABCRYS in renal transplantation have been published. We questioned whether the expression of ABCRYS in the tubular epithelium would be associated with renal allograft fibrosis.

**Methods:** A total of 92 consecutive, adult, Caucasian renal allograft recipients (34 women/58 men, mean age 57.4 $\pm$ 13.0 years) underwent a protocol biopsy at both 3 and 12 months post-transplantation. All patients were treated with mycophenolate mofetil, tacrolimus and corticosteroids. Only patients having both protocol biopsies of at least marginal quality according to the Banff criteria and with high quality frozen tissue for the immunohistochemistry were included.

**Results:** Forty-four (47.8%) 3 months protocol biopsies were scored as pattern A (granular staining, mainly located in the apical pole of the epithelium of the proximal tubules (brushborder and terminal web)), 48 (52.2%) as pattern B (both apical and basal half of the proximal tubular epithelial cell clearly positive (granular)). Biopsies showing ABCRYS pattern B had a significantly higher increase in interstitial fibrosis between 3 and 12 months ( $\Delta$ ci>0) than biopsies showing ABCRYS pattern A ( $\Delta$ ci>0 in 23/48 (47.9%) vs. 10/44 (22.7%); p=0.0165). Of all population and transplantation characteristics only a higher mean number of HLA-DR mismatches correlated with ABCRYS pattern B at 3 months. Of all Banff parameters at 3 months post-transplantation, only a trend (p=0.0654) between the degree of tubulitis and a higher prevalence of ABCRYS pattern B was found.

**Conclusion:** In this preliminary study on renal protocol biopsies we demonstrate an association between the ABCRYS staining pattern at 3 months and the subclinical progression of interstitial fibrosis between 3 and 12 months post-transplantation. This suggests that ABCRYS could be used as an early marker of cellular activation, multifactorial in the transplantation setting but locally present as tubulitis, possibly in the process of epithelial-mesenchymal transformation. These results need to be validated in a larger series.