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Molecular pathology patterns in podocytopathy: a pilot study

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Objectives : This pilot study was focused to evaluate WT-1, β-catenin, desmin and vimentin glomerular expression patterns in early primary focal segmental glomerulosclerosis (FSGS).
Methods : We reviewed the histopathological and clinical data of patients with biopsy proven FSGS (N=14, experimental group), IgA nephropathy (N=12, positive control) without AKI, infectious diseases, heart failure, respiratory insufficiency, cancer pathology and immunosuppressive therapy. As a negative control, kidney samples without glomerulopathies (GP) taken from surgery for renal cancer were tested (N=12). Glomerulosclerosis was assessed as percentage of all glomeruli. Mesangial lesions were measured semi-quantitatively in scores (0-3). Glomerular WT-1, β-catenin, desmin, and vimentin expression was assessed by IHC-P with quantification of IHC-stained to glomerular area (QuPath, Orbit Image Analysis). Molecules' co-expression was analyzed by IF-p and confocal microscopy (Center for Collective Use, Pavlov Institute of Physiology).
Results : The comparison of clinical and histopathological data between GP groups shown in Table 1. An immunomorphological study showed lower WT-1 expression in both GP groups compared to the negative control (Figure 1a, d). B-catenin expression was significantly higher in IgA and did not differ between FSGS and negative control (Figure 1b, d). In FSGS, β-catenin expressed lesser vs. IgAN, and co-expressed with desmin occasionaly (Figure 1f). A trend towards to increase in the desmin+ glomerular area was also detected, however, no significant differences between IG groups were found; as well as for vimentin (Figure 1c, d). In IgAN, glomerular WT-1 and β-catenin co-expression was prevalent (Figure 1e). In FSGS, glomerular cells were predominantly desmin+ and negative to WT-1/ β-catenin; WT-1+cells mainly co-expressed desmin (Figure 1f).
Conclusions : A decrease in WT-1 is an early feature of both FSGS and IgA glomerulopathies. In contrast to IgA, which is characterized by an increase in beta-catenin expression, desmin expression may be an early pathognomonic feature of FSGS.

Figure 1.jpg

Table 1. Comparison of clinical and histopathological data in FSGS and IgA nephropathy groups

Variables	IgAN	FSGS	*p*
Age, years	40 (32-47)	49 (20-64)	0.46
Gender, M:F	6:6	8:6	0.49
Proteinuria, g/24h	1.2 (0.7-1.6)	9.3 (3.1-14.0)	<0.001
Serum albumin, g/l	39 (37-41)	22 (19-34)	<0.001
eGFR (CKD-EPI), ml/min/1.73 m^2	76 (52-87)	85 (53-103)	0.40
Global glomerulosclerosis, %	14.0 (8.0-22.0)	2.5 (0-7)	0.003
Segmental glomerulosclerosis, %	12.5 (7.0-19.5)	3.5 (0-21)	0.43
Mesangial proliferation, scores	1 (1-1)	0 (0-0)	0.001
Mesangial matrix expansion, scores	1 (1-1)	0.5 (0-1)	0.05

Figure 1.jpg

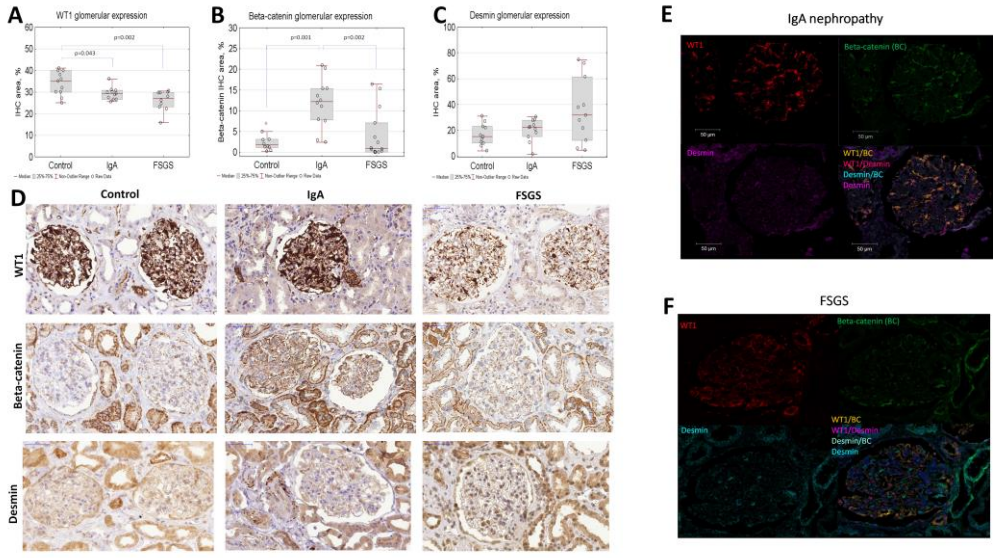

Figure 1 – Morphological study of kidney biopsies: quantitative morphometry of IHC-stained sections for WT1 (A), beta-catenin (B), and desmin (C) glomerular expression; representative pictures for IHC-staining in studied groups (D); and WT1, beta-catenin, desmin co-expression in IgAN (E) and FSGS (F) patients