Molecular markers in renal transplant biopsies

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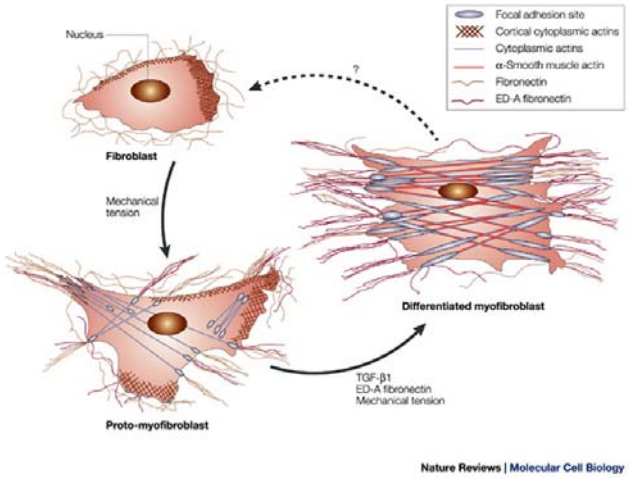
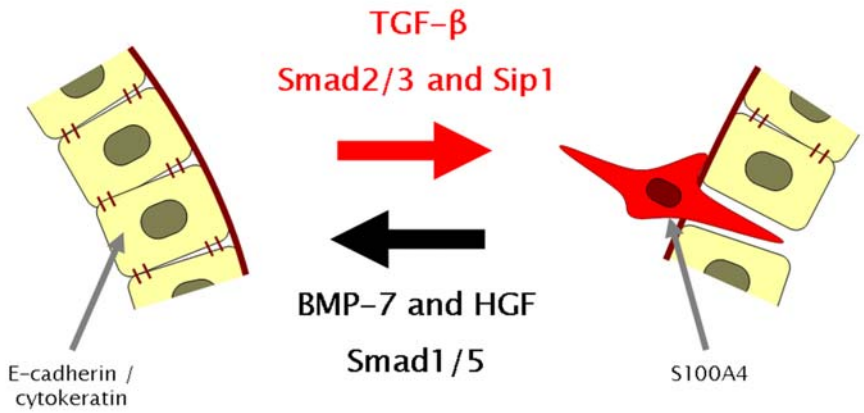
Appendix

Colour figures

Chapter 1: Figure 2. A two-stage model of myofibroblast differentiation. Fibroblasts evolve into proto-myofibroblasts due to changes in the microenvironment. Later, in the presence of growth factors and ECM molecules, the proto-myofibroblast differentiates into a myofibroblast. Printed with permission from Macmillan Publishers Ltd: Nat Rev Mol Cell Biol. Tomasek JJ, et al. Myofibroblasts and mechano-regulation of connective tissue remodelling. Nat Rev Mol Cell Biol 2002; 3(5):349-363, copyright 2002.



Chapter 1: Figure 3. Schematic drawing of epithelial to mesenchymal transition (EMT). During EMT the characteristic epithelial phenotype is lost and a mesenchymal phenotype is acquired. The mesenchymal phenotype is identified by S100A4 expression. TGF-β is the prime inducer of EMT through a Smad 2/3 and Sip1 pathway. This process can be reversed by BMP-7 through a Smad 1/5 dependent pathway and HGF.

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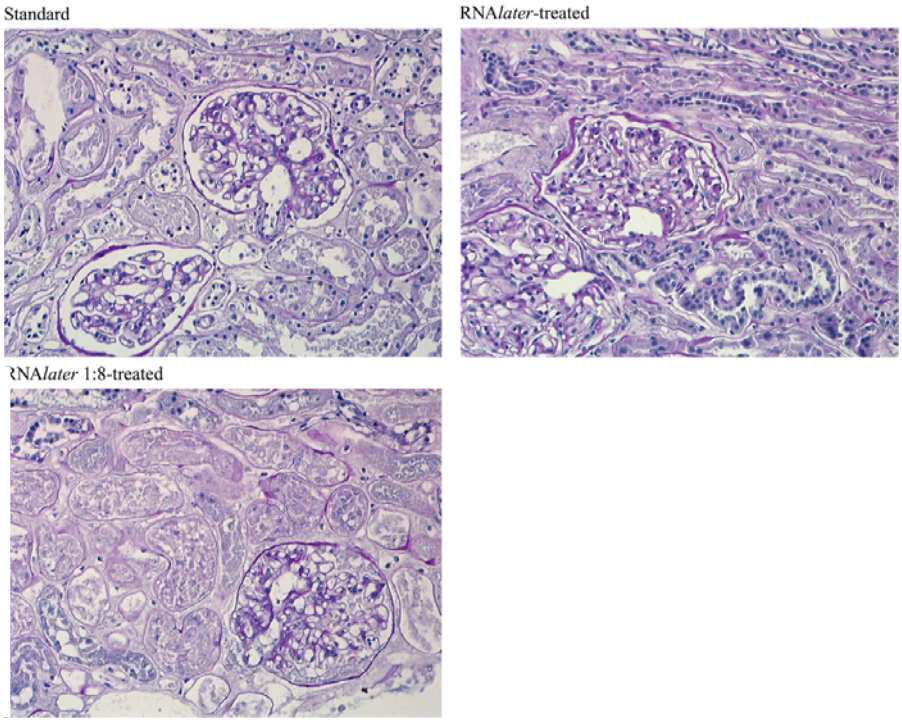
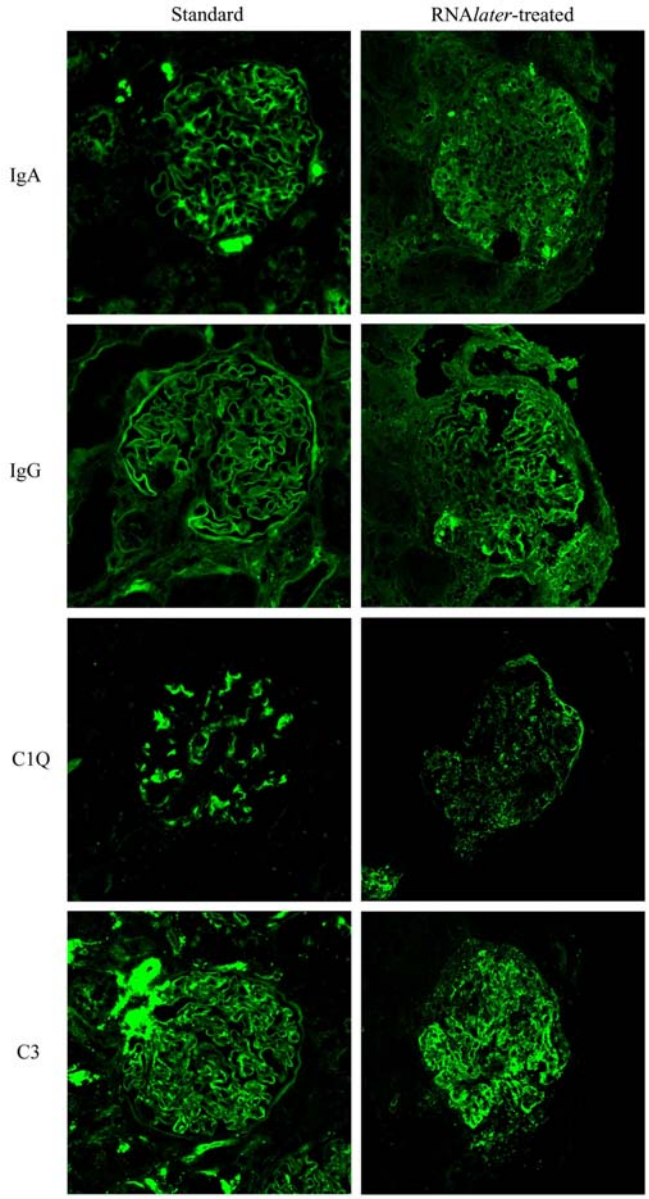


Chapter 2: Figure 8. PAS staining of the renal cortex. Histology of the renal cortex stored in either PBS, RNA*later* or RNA*later* 1:8 was compared through PAS stainings (magnification 40x). Glomerular morphology in RNA*later* treated tissue is altered, with the glomerular capsules appearing more wrinkled. Tissue treated with RNAlater 1:8 had dispersed cytoplasma, and the cell nuclei had disappeared.



Chapter 2: Figure 9. Immunofluorescence stainings for IgA, IgG, C1Q, and C3. The left panels represent stainings on renal cortex from a patient with lupus nephritis. Stainings were performed according to standard diagnostic practice. The renal cortex from a patient with lupus nephritis, which was stored in RNA*later* (right panels), displayed a dispersed staining pattern and a decreased intensity of the fluorescent signal.

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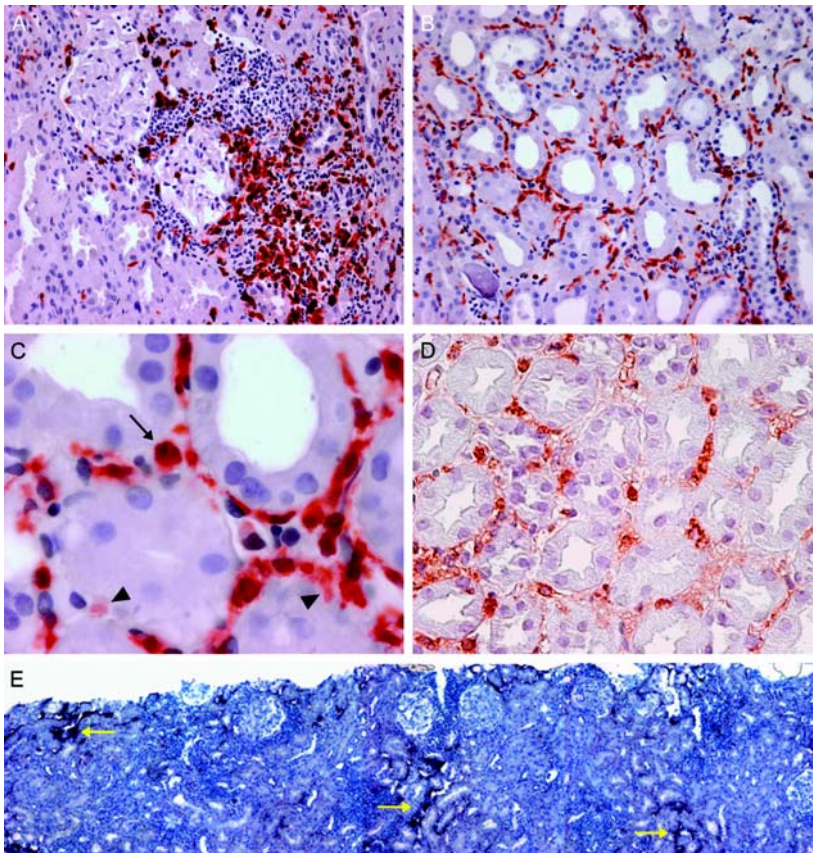
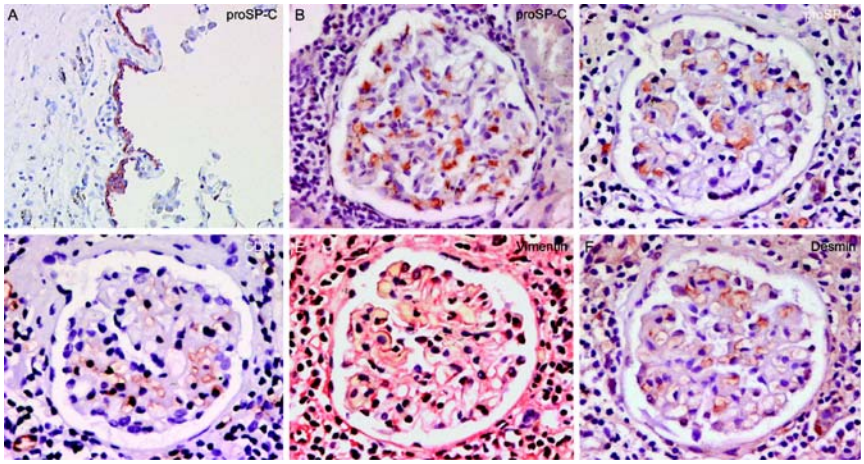
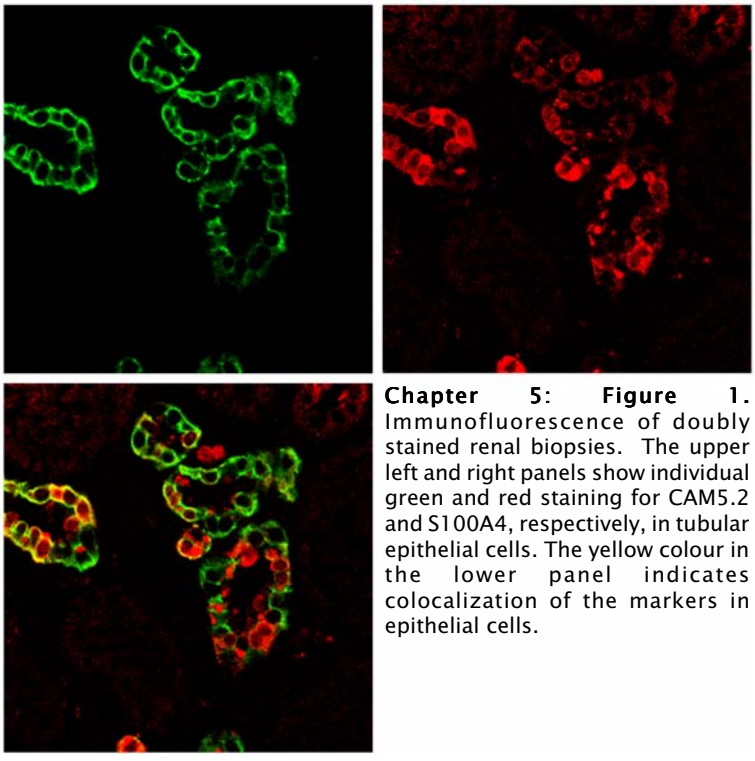


Chapter 3: Figure 4. Pattern of staining for S100A8 and S100A9 in patient biopsies with acute rejection. Staining for (A,B) the S100A8/A9 heterodimeric complex (Antibody 27E10) and (D) S100A9 was seen in focal infiltrates and in infiltrating cells between tubules. (C) Enlarged recording of tubulointerstitium showing positive signal for S100A8/A9 heterodimers. Arrow indicates a neutrophil granulocyte that is positive in the staining. S100A8/A9-dimeric protein complexes are presumably also deposited extracellularly (arrowheads). (E) Typical result for RNA *in situ* hybridization for S100A8 mRNA in a biopsy with acute rejection. Yellow arrows indicate positivity for S100A8 mRNA.



Chapter 3: Figure 7. Localization of proSP-C protein in acute rejection biopsies. (A) A typical beads-on-a-string staining pattern for proSP-C was observed in peripheral lung sections, which were used as positive controls. (B,C) ProSP-C protein was detected in glomeruli of sections from renal transplants with acute rejection. Sequential sections were stained for (C) proSP-C protein, (D) the endothelial marker CD31, and (E,F) the mesenchymal markers vimentin and desmin. The proSP-C staining pattern resembled the most that of desmin.



Chapter 5: Figure 1. Immunofluorescence of doubly stained renal biopsies. The upper left and right panels show individual green and red staining for CAM5.2 and S100A4, respectively, in tubular epithelial cells. The yellow colour in the lower panel indicates colocalization of the markers in epithelial cells.

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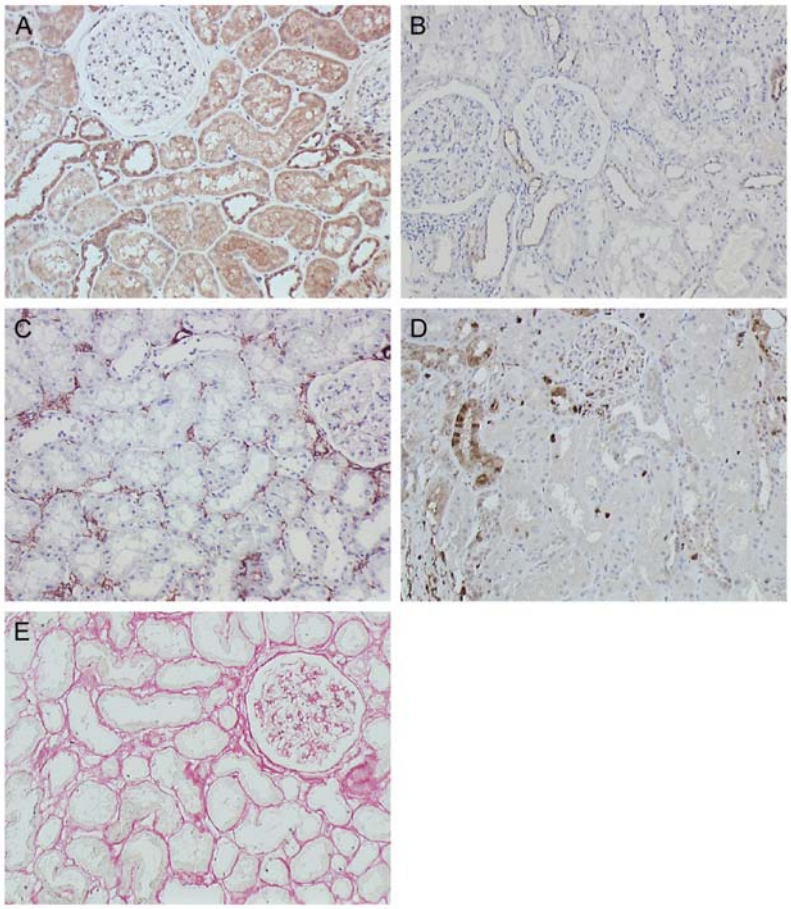
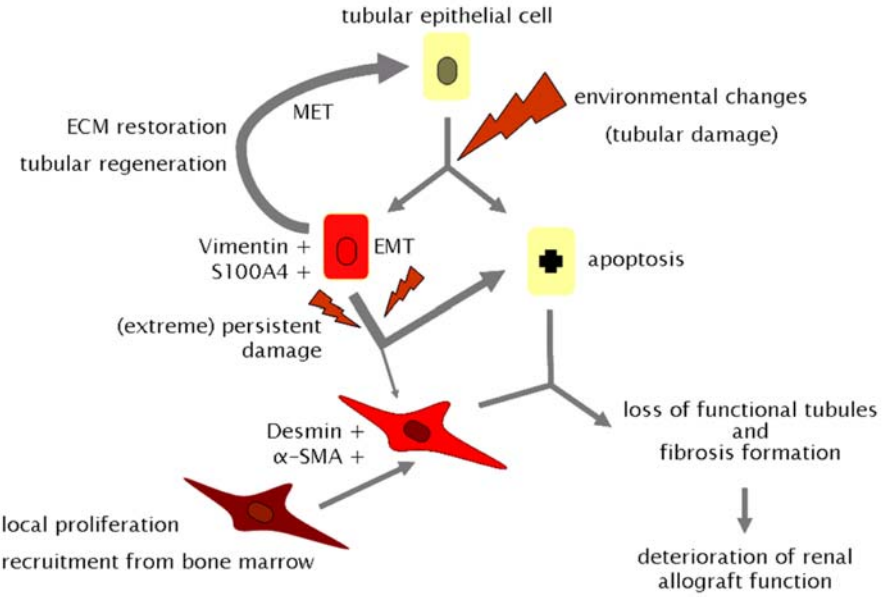


Chapter 5: **Figure 2.** Immunohistochemical stainings were performed for TGF-β, BMP-7, α-SMA and S100A4. Representative slides of immunohistochemical stains performed on renal transplant protocol biopsies. A: TGF-β staining was positive in tubular epithelial cells. B: BMP-7 staining was predominantly positive in distal tubules. C: α-SMA staining was mainly observed in the interstitial compartment and within arteries. D: S100A4 staining was positive in individual tubular epithelial cells. In addition, monocytes stained positively. E: Sirius red stained both collagen I and III and was predominantly positive in the interstitial compartment.



Chapter 7: Figure 1. Speculative schematic illustration of a possible role for EMT in the renal allograft.
ECM: extracellular matrix, EMT: epithelial to mesenchymal transition, MET: mesenchymal to epithelial transition, S100A4: human homologue to fibroblast specific protein-1, α-SMA: α-smooth muscle actin.

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