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OXFORD JOURNALS [Links](#)**Sirolimus ameliorates the enhanced expression of metalloproteinases in a rat model of autosomal dominant polycystic kidney disease.**[Berthier CC](#), [Wahl PR](#), [Le Hir M](#), [Marti HP](#), [Wagner U](#), [Rehrauer H](#), [Wüthrich RP](#), [Serra AL](#).

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BACKGROUND: Remodelling of matrix and tubular basement membranes (TBM) is a characteristic of polycystic kidney disease. We hypothesized that matrix and TBM degradation by metalloproteinases (MMPs) could promote cyst formation. We therefore investigated the renal expression of MMPs in the Han:SPRD rat model of autosomal dominant polycystic kidney disease (ADPKD) and examined the effect of sirolimus treatment on MMPs. **METHODS:** 5-week-old male heterozygous (Cy/+) and wild-type normal (+/+) rats were treated with sirolimus (2 mg/kg/day) through drinking water for 3 months. **RESULTS:** The mRNA and protein levels of MMP-2 and MMP-14 were markedly increased in the kidneys of heterozygous Cy/+ animals compared to wild-type +/+ as shown by RT-PCR and Western blot analyses for MMP-2 and MMP-14, and by zymography for MMP-2. Strong MMP-2 expression was detected by immunoperoxidase staining in cystic epithelial cells that also displayed an altered, thickened TBM. Tissue inhibitor of metalloproteinases-2 (TIMP-2) expression was not changed in Cy/+ kidneys. Sirolimus treatment leads to decreased protein expression of MMP-2 and MMP-14 in Cy/+, whereas MMP-2 and MMP-14 mRNA levels and TIMP-2 protein levels were not affected by sirolimus. **CONCLUSION:** In summary, in kidneys of the Han:SPRD rat model of ADPKD, there is a marked upregulation of MMP-2 and MMP-14. Sirolimus treatment was associated with a marked improvement of MMP-2 and MMP-14 overexpression, and this correlated also with less matrix and TBM alterations and milder cystic disease.

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