Role of renal urothelium proliferation in the onset of calcium oxalate stones


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Background
Most mice kidney stone models induce nephrocalcinosis rather than urolithiasis.

Materials and methods
C57B6 mice under vitamin D and water containing 4% hydroxyl-L-proline, ammonium chloride (0.28M) and calcium (0.25%) were follow up until day 42. A group receiving Fibroblast Growth Factor 7 (FGF7 i.p. once a week), a urothelial cell mitogen was compared to control group. Localization and identification of crystal deposits were performed with polarizing microscopy, infrared imager and Scanning Electron Microscopy. Urothelial and tubular phenotypes were studied by immunohistochemistry, immunofluorescence and RT PCR.

Results
Calcium oxalate monohydrate (COM) deposits in fornices were detected in all kidneys as soon as day 14 with very few crystals in tubules. On day 21, crystal number was increased in FGF7 compared to control group. Though osteopontin (OPN) was unregulated and detected in urothelial cells, de novo expression of CD44 (osteopontin receptor) receptor was induced only in proliferating urothelial cells either induced by FGF7 or by long standing urine crystal exposure altogether with a loss of apical uroplakines III expression.

Conclusion
Our model seems interesting to study in KO mice, in order to investigate the critical events leading to urolithiasis. Our data show that urothelial cells proliferation promotes renal crystal retention especially within fornices, probably through different processes involving specific and non-specific crystal adhesion, and thus appears per se as a relevant risk factor for stone formation.