Functional paracelular permeability of the colon in rats with kidney disease.

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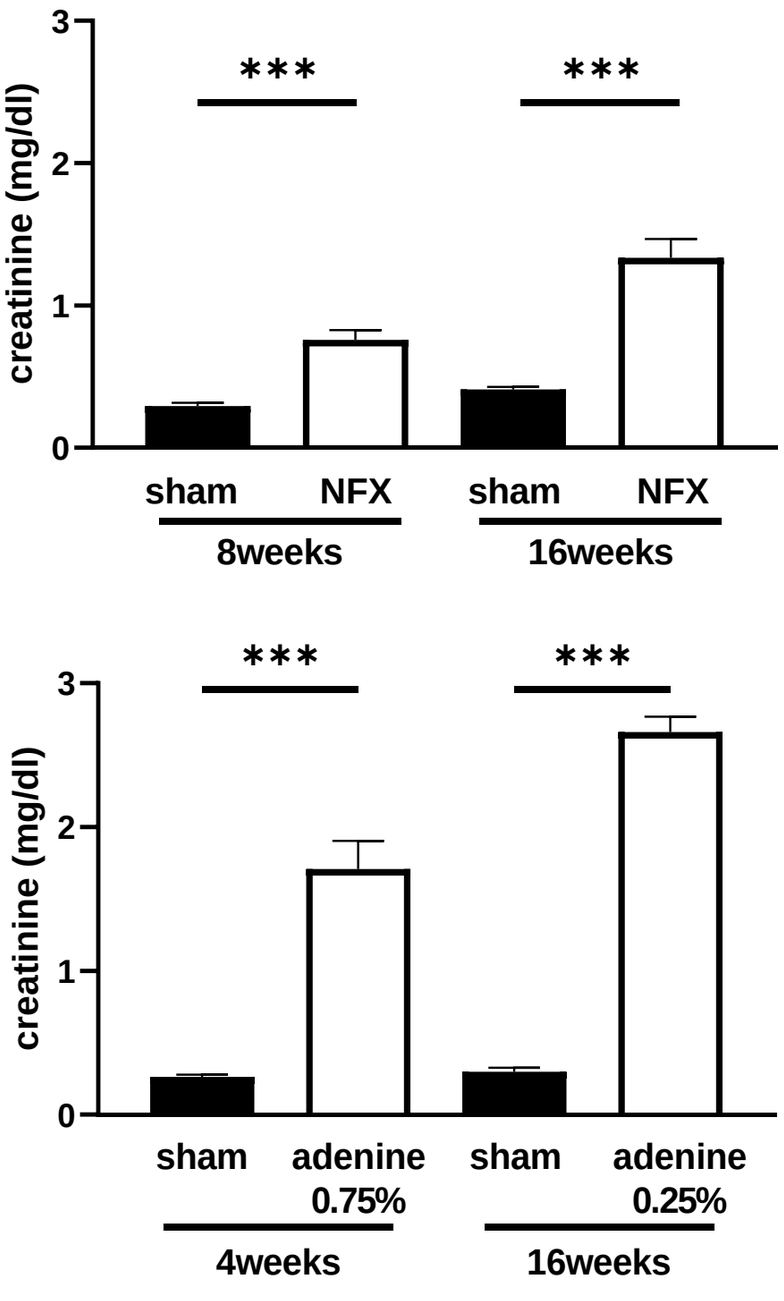
Objective

The intestinal barrier is the key regulator of the interactions between the gut content and the milieu intérieur of the host. To prevent paracellular flux of luminal solutes, the intestinal epithelial cells are sealed together by the tight junction proteins. These tight junction proteins allow passage of ions, small uncharged solutes, water and hydrophilic medium-sized (up to 10 KDa) molecules. We performed an animal study using three kidney disease models in rats to investigate discrepancies in colon permeability.

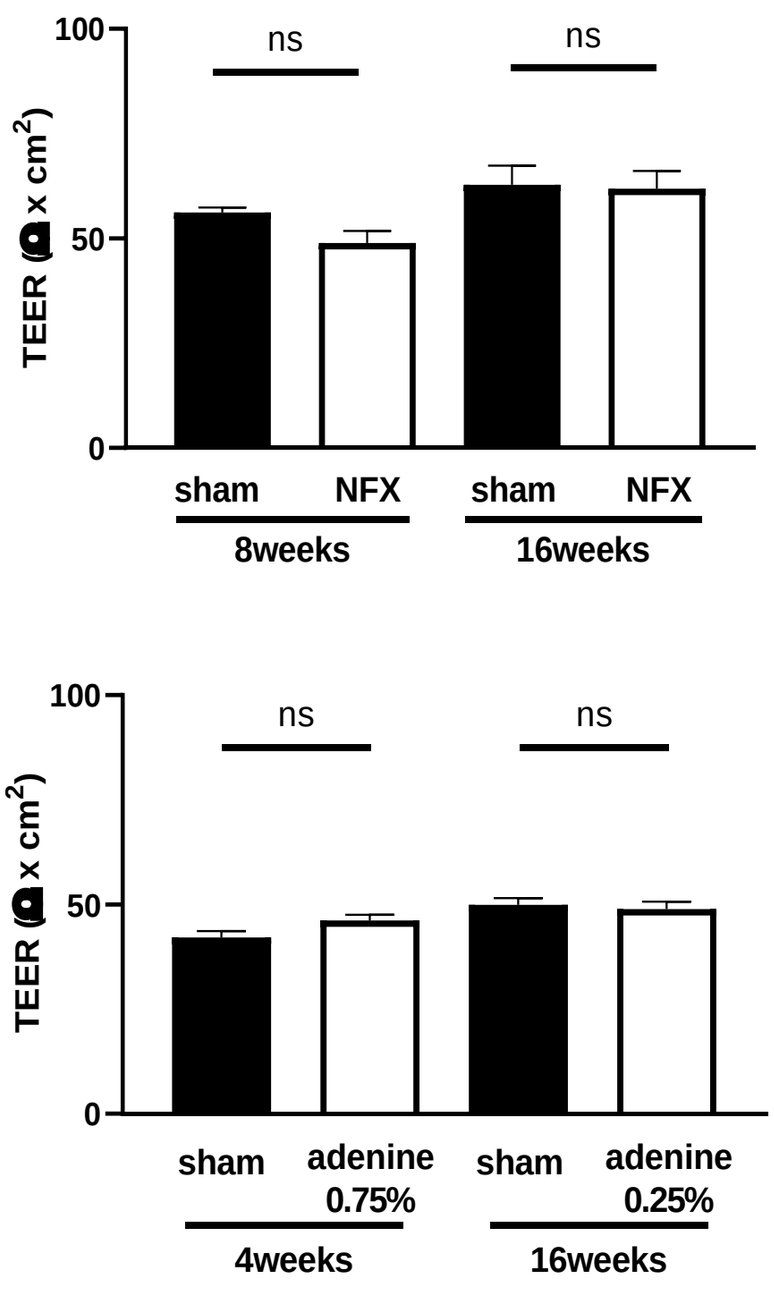
Methodology

Three rodent models of CKD were established (n > 7). Model 1 and 2 consist of low (0.25%) and high dose (0.75%) of adenine supplementation, resulting in chronic (16 weeks) and acute (4 weeks) kidney injury, respectively. Model 3 is a surgical model of 5/6th nephrectomy to mimic the progressive renal failure after loss of renal mass. For this model we used two timepoints, 8 and 16 weeks. Ussing chambers were used to assess the paracellular permeability functionally. Biopsy specimens were mounted in modified 3 mL chambers. Mucosal and serosal compartments were filled with Krebs buffer containing 10 mM mannitol and 10 mM of glucose respectively. Trans-epithelial electrical resistance (TEER) and passage of fluorescently labelled dextran (FITC-dx4; molecular mass=4000 Da, 1 mg/ml) were measured every 30 min over 2h.

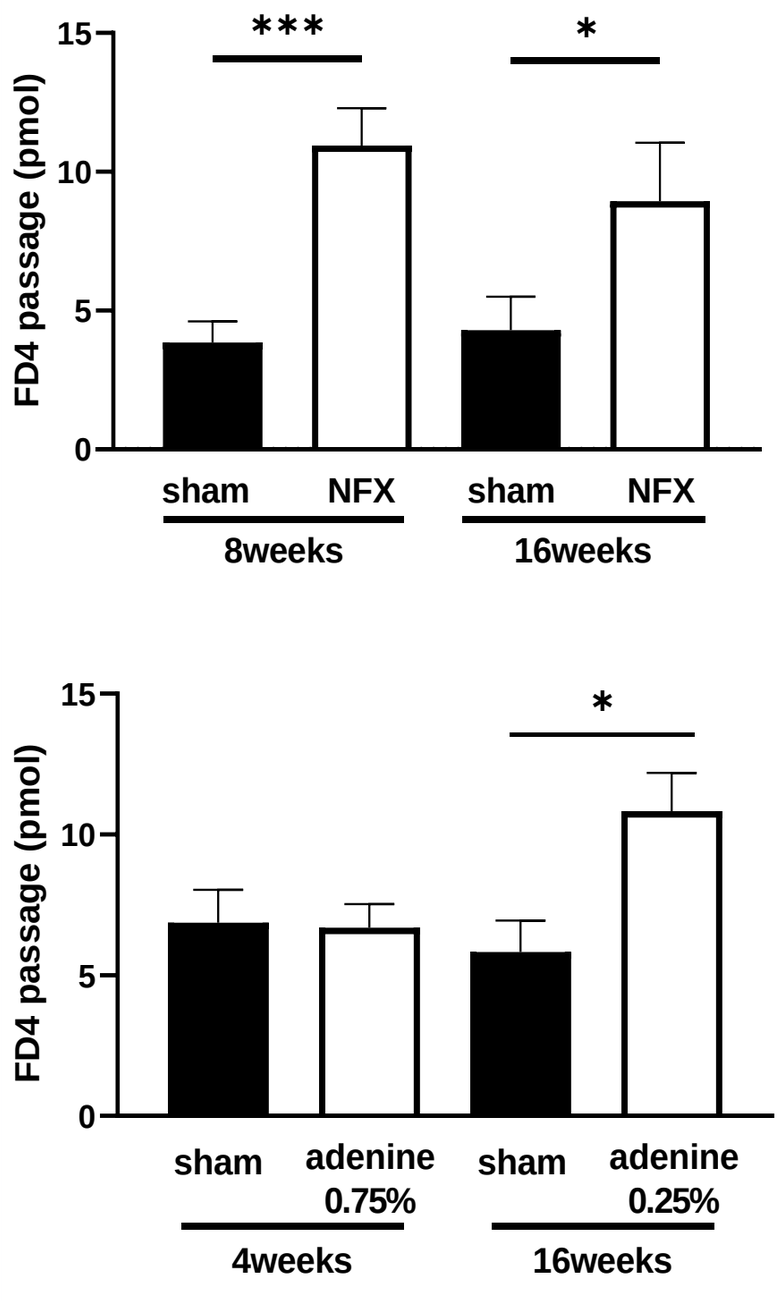
Results 1: kidney function



Results 2: TEER



Results 3: FITC-dx4 passage



Conclusion

We observed meaningful differences in FITC-dx4 passage in multiple rat groups with kidney disease. This difference suggests alterations in the colon after a decrease in kidney function, allowing higher passage of specific molecules through the paracelular tight junction complex. This is the first time that functional changes in intestinal permeability have been demonstrated. These findings strengthen the hypothesis of the gut-kidney interaction.