Oxalate Transport: Intestine

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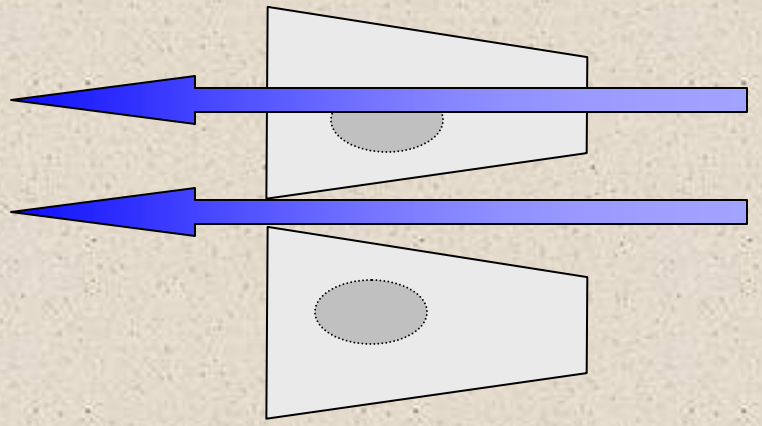
Intestinal Oxalate Transport

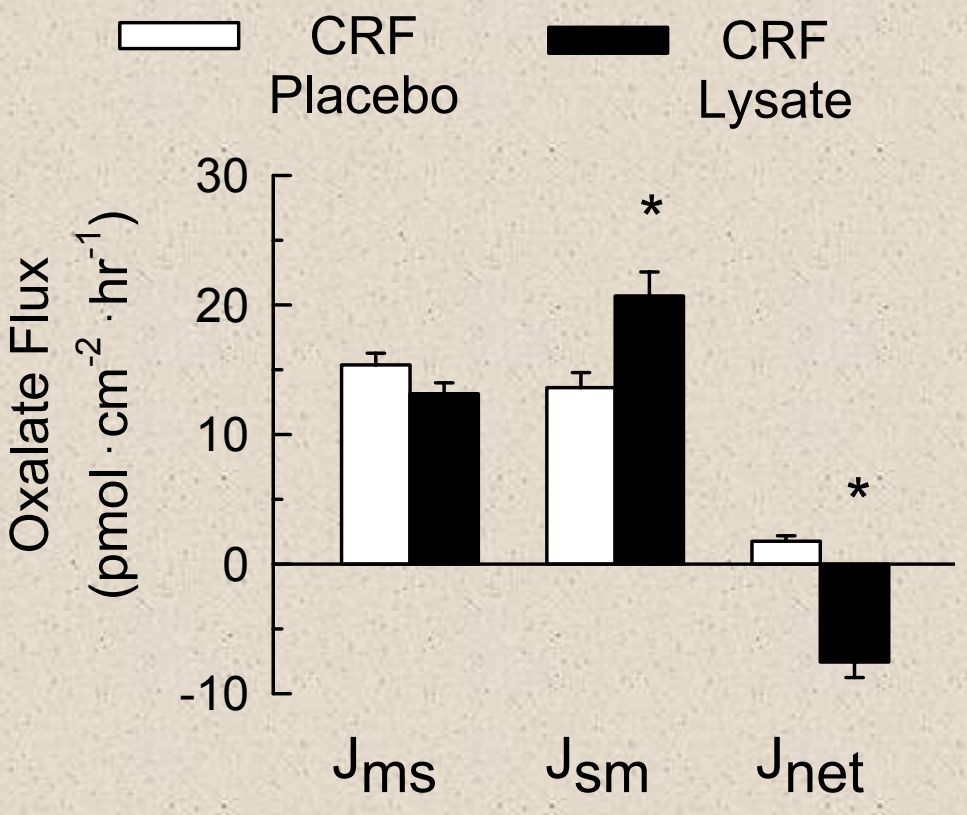
- Role of *Oxalobacter sp*.
- Oxalate transport studies
- Expression profiles for “candidate” transporters

Potential Role for Oxalobacter in the Intestinal Handling of Oxalate

- *Oxalobacter* may reduce intestinal absorption of oxalate by utilizing dietary sources of oxalate.
- *Oxalobacter* may derive oxalate from systemic sources, possibly by initiating or enhancing intestinal oxalate secretion.



Colonic Oxalate Transport in Hyperoxaluric CRF Rats Treated with Placebo or Encapsulated Oxalobacter Lysate

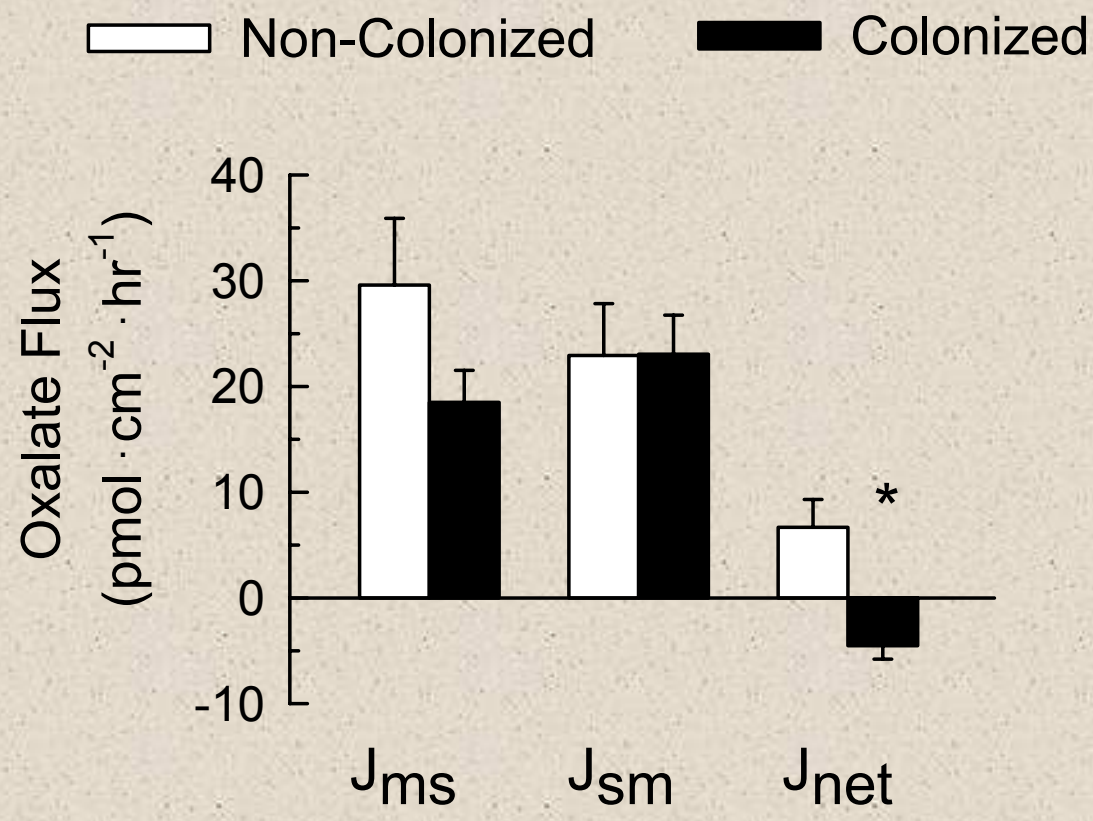


- Simultaneous treatment with 0.75% Et. Gly. in the drinking water and capsules, for 5 days, BID.
- Urinary oxalate is reduced 50% (102 ± 11 to 57 ± 8 µmol/24 h).
- *Oxalobacter* lysate treatment induced local oxalate secretion in the distal colon.

Recommendations and Directions for Future Investigations in 2000

- A laboratory rat that is naturally colonized with *Oxalobacter* is required.
- Factors involved in initiating and sustaining colonization with *Oxalobacter* should be elucidated.
- Definitive studies in animals are warranted to address the physiological interactions between *Oxalobacter* and the gut mucosa.
- Further investigations specifically directed at exploiting enteric secretory pathways for oxalate will most likely reveal the potential for alternative therapeutic approaches in reducing the burden of urinary oxalate excretion.

Colonic Oxalate Transport in Naturally Colonized Rats with Normal Renal Function



- Rats were colonized or not-colonized from birth by rearing with colonized (gavaged with OxWR) or non-colonized mother.
- Urinary oxalate was significantly lower in colonized rats (5.3 ± 0.5 µmol/24 hours) *vs.* rats not colonized (8.3 ± 0.8 µmol/24 hours).

Rationale for studies on intestinal oxalate secretion

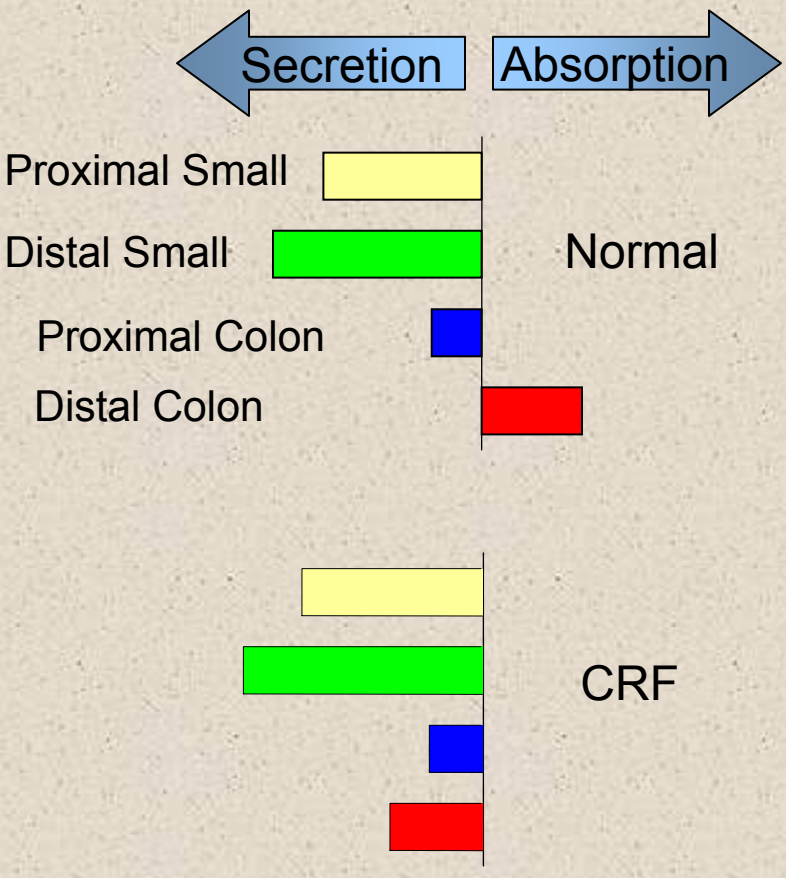
Our working hypothesis is that by maximizing enteric elimination of oxalate, the burden of oxalate excretion *via* the kidneys will be reduced and consequently the risk of hyperoxaluria, oxalosis and kidney failure may be mitigated.

Oxalate transport studies in Animal Models of Hyperoxaluria

- Experimental evidence in support of *adaptive* enteric oxalate excretion in rats with Chronic Renal Failure (CRF) and in oxalate-loaded rats.
- Identified ANG II-mediated oxalate secretory pathways in CRF with/without hyperoxaluria
- In oxalate-loaded rats with normal renal function, *adaptive* enteric oxalate excretion appears to be largely independent of ANG II mediation.

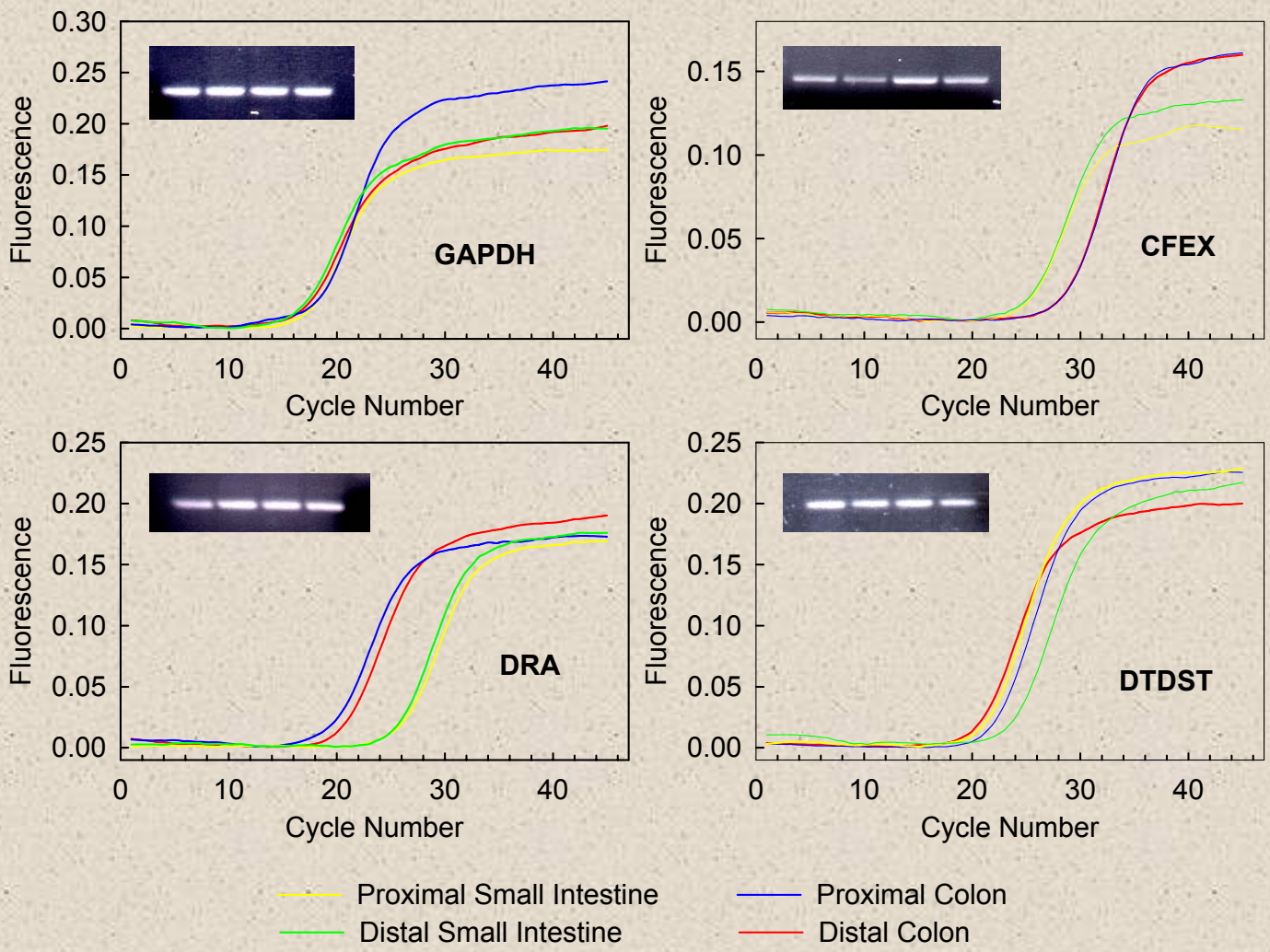
Heterogeneity in Oxalate Handling in Rat Intestine

Net Oxalate Flux *In Vitro*

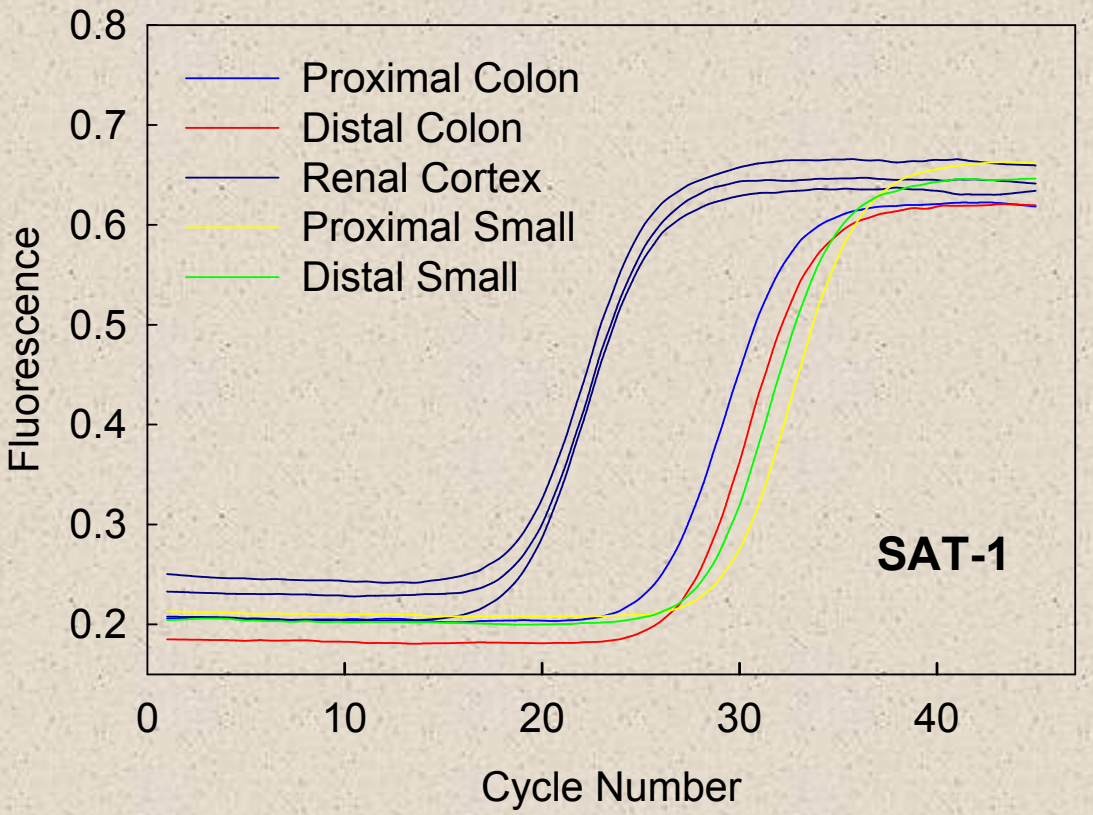


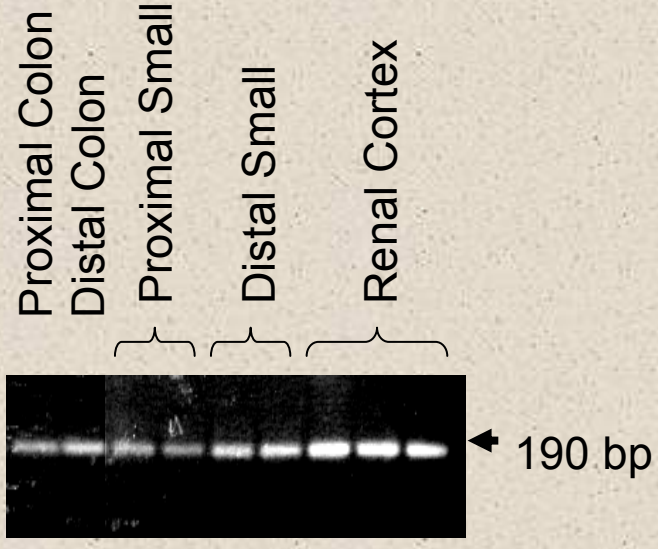
- Various proteins have been implicated in transepithelial oxalate and include those coded by genes of the SO_4-Anion (slc26 family), AE series, and even poorly selective anion channels.
- Can the expression patterns of genes encoding these putative oxalate transporters help explain segmental heterogeneity and provide a basis for understanding the nature of the adaptive processes attendant with oxalate diseases?

mRNA Expression Patterns along the Rat Intestinal Tract



SAT-1 mRNA Expression in Rat Kidney and Intestine





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