Kidney controls acid base by three mechanisms

- Reabsorption of filtered bicarbonate—mainly PCT, lesser extent DCT and thick AL
- Excretion of acids
- Denovo synthesis of bicarbonate (CD) and ammonium (PT)
Renal adaptation to metabolic acidosis

- Known that acid base disturbance modulate proton/bicarbonate transport in cortical collecting duct- fine tuning of Acid/base status
- α- intercalated cells secrete protons
  - apical H⁺-ATPase and basolateral anion exchangers
- β- intercalated cells secrete bicarbonate
  - apical anion exchangers (Pendrin) and basolateral H⁺-ATPase
β Intercalated cell  α Intercalated cell
Adaptation of metabolic acidosis and its recovery are associated with changes in anion exchanger distribution and expression in the cortical collecting duct.
Study methods

- Female New Zealand white rabbits
- Acid load with 100mmol/L NH₄CL/7.5% sucrose solution for 3 days
- Recovery done with 100mmol/NaHCO₃/7.5% sucrose for 12-18hrs
- pH and serum HCO₃ levels drawn and pH of urine collected from the bladder
Rabbit Acid Base status

![Graphs showing Urine pH and Serum bicarbonate levels during Normal, Acidosis, and Recovery phases. The graphs indicate significant differences with asterisks (* and **) for Acidosis and Recovery compared to Normal.](image-url)
Pendrin

- Apical chloride / bicarbonate exchanger expressed by β intercalated cells.
- Regulated by change in acid/base status- expression continuously vary with changes in acid base state
Pendrin Expression in CCD
Pendrin expression

**Graphs**

(b) Pendrin cap expression level
- Normal
- Acidosis
- Recovery

(d) Pendrin-positive cells
- Normal
- 3-day acid
- 7-day acid
- Recovery
β Intercalated cell  α Intercalated cell
Acidosis induced basolateral redistribution of AE1
Adaptive changes in the α-intercalated cells

- Acidosis induced a reversible redistribution of AE1 to the basolateral membrane and increased intensity of staining.
- This was reversed by administration of alkali.
Anion exchanger redistribution

![Graph showing relative intensity of AE1 positive cells in normal, acidosis, and recovery stages.](image)

- Basolateral intensity of AE1 positive cells
- Relative intensity
- Normal, Acidosis, Recovery

*Significant difference at the recovery stage.*
Reversal of ratio of staining

![Graph showing the percentage of total cell number for Basolateral/apical staining intensity under Normal, Acidosis, and Recovery conditions.](image-url)
Changes in distribution of AE1 and number of intercalated cells

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Region</th>
<th>Acid/base status</th>
<th>Rabbit N=</th>
<th>Sections, total no.</th>
<th>Image no.</th>
<th>No. of CDs</th>
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Abbreviations: Acid., acidosis; AE1, anion exchanger; AQP2, aquaporin 2; CD, collecting duct.
Pendrin mRNA expression is regulated by Acid Base status
H+ and HCO₃⁻ flux
Conclusion

- Pendrin expression level, cap size and number of cells all decreased with acidosis
- Pendrin expression shifted from apical membrane to presumed intracellular pool
- Increased α intercalated cells expressing AE1 to increase H⁺ secretion.
THANK YOU