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Adaptive Variation in SGLT1 and SGLT2

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Abstract: *Sodium–glucose co-transporters SGLT1 and SGLT2 are central components of intestinal nutrient handling and renal glucose conservation. Beyond their classical roles, these transporters exhibit complex regulatory behaviors shaped by circadian rhythms, nutrient sensing pathways, transcriptional control, and species-specific physiological adaptations. This review synthesizes experimental findings on SGLT1 and SGLT2 expression patterns, segmental distribution, and regulatory mechanisms. Particular attention is given to nutrient induced signaling through sweet taste receptors, post transcriptional modulation of transporter abundance, and the contrasting profiles observed across intestinal segments and species. Together, these findings highlight the diversity of regulatory inputs governing SGLT transporters and underscore their importance in maintaining glucose homeostasis across physiological contexts. Understanding these regulatory and species-specific features is essential for appreciating how SGLT1 and SGLT2 integrate environmental, dietary, and temporal cues to coordinate glucose absorption and reabsorption.*

• Introduction

SGLT1 and SGLT2 mediate glucose transport in the intestine and kidney, but their activity is shaped by a wider regulatory network influenced by circadian timing, nutrient status, transcriptional control, and intercellular signaling.

• Results and discussions

Table 1 summarizes the distribution of SGLT1 and SGLT2 gene expression across rats, mice, and pigs, together with the factors known to influence their regulation.

Table 1. Overview of SGLT1 and SGLT2 gene expression patterns and influencing factors in rats, mice, and pigs

Species	Rats		Mice		Pigs	
Transporter	SGLT1	SGLT2	SGLT1	SGLT2	SGLT1	SGLT2
Organ and segment of gene expression	Small intestine: jejunum seems to display the highest expression [Balakrishnan et al., 2010]	Kidney: localized only in the brush-border membrane of S1 and S2 renal tubule segments [Sabolić et al., 2012]	Small intestine: proximal segment (S1) shows highest expression (mRNA) [Nakamura Chisato et al., 2023]	Kidney: similar to rats [Sabolić et al., 2012]	Small intestine: jejunum (mid-intestine segment) shows higher expression [Moran et al., 2010, Herrmann et al., 2012]	SGLT2 mRNA abundant; detectable in whole kidney tissue [Aschenbach et al., 2002]
Gene expression influence factors	Increased expression in *ad libitum* fed rats [Sabino-Silva et al., 2010]; increased expression in the beginning of night (circadian rhythm influence) [Balakrishnan et al., 2010]	Females show significantly higher SGLT2 protein abundance than males [Sabolić et al., 2012]	High-glucose diet doesn't seem to change SGLT1 mRNA abundance, but might suppress proximal and mid-segment intestinal glucose transport activity [Nakamura Chisato et al., 2023]	Sex-opposite pattern of SGLT2 regulation, with males showing greater protein abundance and females showing greater mRNA expression [Sabolić et al., 2012]	High-carbohydrate diets (>50% carbohydrate) significantly increase SGLT1 mRNA, protein abundance, and glucose transport in proximal and mid-segments and not in the distal intestine [Moran et al., 2010]	Naturally higher basal abundance in pig kidney [Aschenbach et al., 2002]; scarce data

• Material and method

- Peer-reviewed studies were selected for gene expression, protein localization, regulatory mechanisms, comparative physiology.
- Windows Copilot assisted in identifying relevant sources and generating structured summaries.
- All AI-supported outputs were reviewed and validated by the authors.
- Zotero used to organize, annotate, and categorize all SGLT1/SGLT2 literature and maintain consistent citation.

• Conclusions

- SGLT1 and SGLT2 play central roles in the intestinal and renal tissues, with species-specific expression patterns.
- Certain factors like feeding patterns, circadian rhythm and sex have an impact on SGLT1 and SGLT2 gene expression. A lack of segment-specific SGLT expression data in the pig kidney can be noted.
- Post-transcriptional mechanisms shape functional SGLT1 and SGLT2 abundance .