SLC34A1 Gene

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solute carrier family 34 member 1

genes

1. Normal Function

The *SLC34A1* gene provides instructions for making a protein called sodium-dependent phosphate transporter 2A (NaPi-IIa), which plays a role in the regulation of phosphate levels in the body (phosphate homeostasis). Phosphate is needed for many functions including the breakdown of substances (metabolic processes), signaling between cells, and the production of DNA building blocks (nucleotides) and fats. The NaPi-IIa protein is located in the membrane surrounding kidney cells, where it transports phosphate across the cell membrane. NaPi-IIa reabsorbs phosphate from urine back into the body when more of the mineral is needed.

2. Health Conditions Related to Genetic Changes

2.1. Idiopathic infantile hypercalcemia

At least 14 mutations in the *SLC34A1* gene have been found to cause a type of idiopathic infantile hypercalcemia called infantile hypercalcemia 2, which is characterized by high levels of calcium in the blood (hypercalcemia) and urine (hypercalciuria) and deposits of calcium in the kidneys (nephrocalcinosis). Individuals with this form of idiopathic infantile hypercalcemia also have low levels of phosphate in the blood (hypophosphatemia). The hypercalcemia typically causes vomiting, poor feeding, and an inability to grow and gain weight at the expected rate (failure to thrive) in infancy, although some affected individuals do not develop signs and symptoms of the condition until adulthood. Features in affected adults, whether they had symptoms in infancy or not, typically include hypercalciuria, nephrocalcinosis, and kidney stones (nephrolithiasis).

The *SLC34A1* gene mutations that cause infantile hypercalcemia 2 lead to production of an altered NaPi-IIa channel that cannot transport phosphate across kidney cell membranes. As a result, phosphate reabsorption is reduced and phosphate levels in the body are low.

Phosphate homeostasis is also controlled by vitamin D. When turned on (active), this vitamin stimulates the absorption of both phosphate and calcium from the intestines into the bloodstream. In an effort to raise the low phosphate levels caused by the loss of functional NaPi-IIa channels, vitamin D is activated. Too much active

vitamin D increases calcium absorption into the bloodstream, causing hypercalcemia in affected individuals. The abnormal balance of calcium leads to high levels of the mineral in urine and can result in deposition of calcium in kidney tissue and the formation of kidney stones.

2.2. Other disorders

Mutations in the *SLC34A1* gene can cause several other health conditions with a variety of signs and symptoms related to hypophosphatemia. As in infantile hypercalcemia (described above), the gene mutations that cause these health conditions prevent the NaPi-IIa transporter from functioning, reducing phosphate absorption in the kidneys and causing hypophosphatemia. Some people with these mutations, diagnosed with hypophosphatemic nephrolithiasis/osteoporosis 1, have nephrolithiasis or low bone mineral density (osteoporosis). Others, diagnosed with Fanconi renotubular syndrome 2, develop problems with kidney function and hypophosphatemic rickets, a bone disorder that often causes bone pain and bowed legs. It is unclear why mutations in this gene lead to different sets of signs and symptoms.

3. Other Names for This Gene

- FRTS2
- HCINF2
- Na(+)-dependent phosphate cotransporter 2A
- Na(+)/Pi cotransporter 2A
- Na+-phosphate cotransporter type II
- naPi-2a
- NAPI-3
- NPHLOP1
- NPT2
- NPTIIa
- renal sodium-dependent phosphate transporter
- SLC11
- SLC17A2
- sodium-dependent phosphate transport protein 2A isoform 1
- sodium-dependent phosphate transport protein 2A isoform 2
- sodium-phosphate transport protein 2A
- sodium/phosphate co-transporter
- sodium/phosphate cotransporter 2A
- solute carrier family 17 (sodium phosphate), member 2
- solute carrier family 34 (sodium phosphate), member 1
- solute carrier family 34 (type II sodium/phosphate cotransporter), member 1

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