

# New Genes Discovered for Hereditary Forms of Rickets

Institute of Human Genetics

**R**ickets is a metabolic disturbance in children that is caused by vitamin D or phosphate deficiency. As a result of nowadays vitamin D prophylaxis, most of the rickets cases observed are caused by phosphate deficiency. Scientists from the GSF Institute of Human Genetics have now identified mutations in 2 genes, that cause specific forms of hereditary rickets which result from phosphate deficiency.

The mutations occur in a gene on chromosome 4 (*DMP1*) which is responsible for the production of dentin matrix protein, which is mainly found in the mineralised bone matrix (1). Mutations of this

gene lead to phosphate deficiency, hypophosphatemia. In this metabolic disease excretion of phosphate via the kidney is increased and phosphate is thus no longer available for bone development. The results so far show, however, that mutations in other genes can also lead to this disease. Mutations in another gene that is responsible for the formation of a renal phosphate transport protein have already been identified and thus contributes to the regulation of phosphate homeostasis (*SLC34A3*) (2). Interest focuses on a protein that apparently plays a central role in the regulation of phosphate homeostasis since its serum levels are altered in individuals with the relevant gene mutation.



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The results indicate that the identified genes are part of a yet unknown metabolic pathway which is essential for the balance in phosphate metabolism. This metabolic pathway could be the key to develop new approaches for the therapy of this disease. Further investigations of the scientists are focused on the elucidation of these molecular events.

## Literature:

- Lorenz-Depiereux, B. et al.:  
Nature Genetics 38, 1248-1250 (2006)
- Lorenz-Depiereux, B. et al.:  
American Journal of Human Genetics 78,  
193-201 (2006)



**Typical signs of rickets:**  
The X-ray of an 18 months old child shows bowing of the long bones of the lower extremities and widening of the metaphysis.