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Titel des Beitrags:
Recessive missense mutations in LAMB2 expand the clinical spectrum of LAMB2-associated disorders.

Abstract:
Congenital nephrotic syndrome is clinically and genetically heterogeneous. The majority of cases can be attributed to mutations in the genes NPHS1, NPHS2, and WT1. By homozygosity mapping in a consanguineous family with isolated congenital nephrotic syndrome, we identified a potential candidate region on chromosome 3p. The LAMB2 gene, which was recently reported as mutated in Pierson syndrome (microcoria-congenital nephrosis syndrome; OMIM #609049), was located in the linkage interval. Sequencing of all coding exons of LAMB2 revealed a novel homozygous missense mutation (R246Q) in both affected children. A different mutation at this codon (R246W), which is highly conserved through evolution, has recently been reported as causing Pierson syndrome. Subsequent LAMB2 mutational screening in six additional families with congenital nephrotic syndrome revealed compound heterozygosity for two novel missense mutations in one family with additional nonspecific ocular anomalies. These findings demonstrate that the spectrum of LAMB2-associated disorders is broader than previously anticipated and includes congenital nephrotic syndrome without eye anomalies or
with minor ocular changes different from those observed in Pierson syndrome. This phenotypic variability likely reflects specific genotypes. We conclude that mutational analysis in LAMB2 should be considered in congenital nephrotic syndrome, if no mutations are found in NPHS1, NPHS2, or WT1.