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View all screenshots 9 La Biblia. The proton-coupled equilibrative nucleoside transporter-1 (PCENT1) is essential for embryonic development and placental formation in mice. Nucleoside transporters (NTs) play important roles during embryogenesis, as well as in the formation of the placenta. The nucleoside transporter-1 (ENT1), which is abundant in placental trophoblasts, has been implicated in the transfer of nucleosides across the trophoblast barrier that separates maternal and fetal blood. However, the NTs expressed during embryogenesis are largely unknown. Here, we provide the first detailed analysis of the expression of nucleoside transporters during mouse embryogenesis.

Expression profiles of nucleoside transporters and other plasma membrane proteins in mouse embryonic stem cells were determined using a membrane-impermeable biotinylation method followed by subsequent immunoblotting analysis and cDNA array analysis. Proton-coupled equilibrative nucleoside transporters (PCENTs) PCENT1 and PCENT2 were expressed in embryonic stem cells and primary trophoblasts throughout mouse embryogenesis. In contrast, PCENT1 was expressed in female embryos but not in males. Antisense expression of PCENT1 in trophoblasts inhibited growth and induced apoptosis of trophoblasts in vitro, suggesting that PCENT1 is essential for both embryonic development and placental formation. Intriguingly, disruption of PCENT1 caused a complex teratogenic phenotype including cleft palate, bladder exstrophy, limb defects, and congenital heart defects in a high percentage of embryos. The specific disruption of the NT was confirmed by the molecular cloning of PCENT1 and PCENT2. PCENT1, which is essential for embryonic development, is the first identified nucleoside transporter that enables the transfer of nucleosides into trophoblasts.

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