

Publication

Agrin is highly expressed by chondrocytes and is required for normal growth

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Agrin is a heparan sulfate proteoglycan that is best known for its crucial involvement in the organization and maintenance of postsynaptic structures at the neuromuscular junction. Consistent with this role, mice deficient of agrin die at birth due to respiratory failure. Here we examined the early postnatal development of agrin-deficient mice in which perinatal death was prevented by transgenic expression of neural agrin in motor neurons. Such transgenic, agrin-deficient mice were born at Mendelian ratio but exhibited severe postnatal growth retardation. Growth plate morphology was markedly altered in these mice, with changes being most prominent in the hypertrophic zone. Compression of this zone was not caused by reduced viability of hypertrophic chondrocytes, as no differences in the apoptosis rates could be observed. Furthermore, deposition of the major cartilage matrix components collagen type II and aggrecan was slightly reduced in these mice. Consistent with a role for agrin in skeletal development, we show for the first time that agrin is highly expressed by chondrocytes and localizes to the growth plate in wild-type mice. Our data show that agrin is expressed in cartilage and that it plays a critical role in normal skeletal growth.

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