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[\[PDF \(559K\)\]](#) [\[References\]](#)**Hepatocyte growth factor regulates the proliferation and differentiation of cartilage in developing forelimb of mouse embryos in vitro**Ayumu KOBAYASHI<sup>1)2)</sup>, Osamu AMANO<sup>2)3)</sup>, Yuji TANI<sup>3)</sup>, Toshikazu NAKAMURA<sup>4)</sup>, Shoichi ISEKI<sup>2)</sup> and Katsuro TOMITA<sup>1)</sup>

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**ABSTRACT**

We examined the role of hepatocyte growth factor (HGF) in the chondrogenesis and endochondral ossification in the forelimbs of mouse embryos by use of immunohistochemistry and organ culture system. In the forelimbs of embryonic day 14 (E14) embryos, intense immunoreactivity for HGF was localized to the chondrocytes located in the proliferative and early hypertrophic zones, and moderate to weak immunoreactivity in the resting and late hypertrophic zones of bone anlagen. Immunoreactivity for the HGF receptor, c-Met, was also localized to the chondrocytes in the resting, proliferative and early hypertrophic zones. In the explants of forelimb buds from E10 embryos cultured for 8 days, exogenous HGF added to the culture media enhanced proliferation of chondrocytes in the forelimb bone anlagen. In contrast, the antisense oligodeoxyribonucleotide (ODN) for HGF as well as the specific HGF antagonist NK4 inhibited proliferation of chondrocytes and caused hypertrophic change and collagen X production, the signs of chondrocyte differentiation, in the arm bone anlagen. Furthermore, the antisense ODN and antagonists for HGF caused a complete lack in the formation of

cartilaginous hand and digital bone anlagen. These results suggested that HGF functions in stimulating chondrogenesis and preventing endochondral ossification in the forelimbs of mouse embryos.

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