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Poster presentation

Therapeutic potential of CNP for skeletal dysplasias

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Background

We had revealed that C-type natriuretic peptide (CNP) is a potent stimulator of endochondral bone growth by using transgenic and knockout mice: transgenic mice with targeted overexpression of CNP in cartilage develop prominent skeletal overgrowth [1], whereas mice depleted with CNP exhibit impaired endochondral bone growth [2]. We planned to translate this effect of CNP into the therapy for skeletal dysplasias, of which the effective drug therapy is not established yet. Here we investigated the effect of CNP on the impaired bone growth of mice model of achondroplasia, the most common form of skeletal dysplasias.

Results

First, we investigated the effects of plasma CNP on impaired bone growth in achondroplastic mice that specifically overexpress CNP in the liver under the control of human serum amyloid P component promoter. Increased plasma CNP stimulated the impaired growth of achondroplastic bones, and they grew almost comparable to those of wild type mice at the age of 6 weeks. Then we treated achondroplastic mice with continuous intravenous infusion of CNP at the dose of 1 μg/kg/min, and successfully rescued the shortness of most bones formed endochondral ossification at the end of 3-week experimental period. Figures 1 and 2.

Conclusion

Our results indicate that treatment with CNP is a potential therapeutic strategy for skeletal dysplasias, including achondroplasia, in humans.

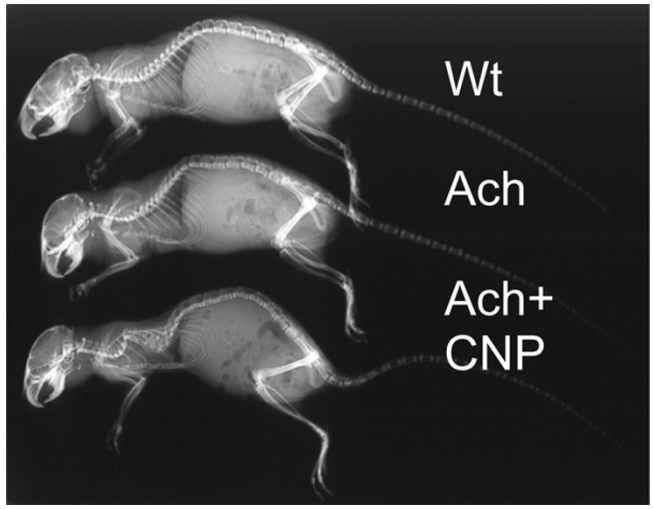

Figure 1
Soft x-ray picture of wild type mice (Wt), achondroplastic model mice (Ach), and achondroplastic model mice treated with CNP at the dose of 1 μg/kg/min.

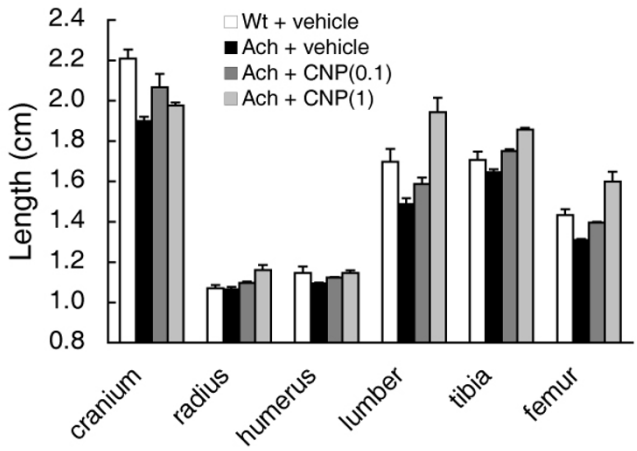

Figure 2
Lengths of bones measured on soft x-ray film.

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