Identification of novel cell growth-differentiation factors and elucidation of their roles in morphogenesis

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Elucidation of mechanism in morphogenesis and identification of novel cell growth-differentiation factors are expected to contribute to not only developmental biology and but also drug discovery and regenerative medicine. Many secreted proteins play crucial roles as cell growth-differentiation factors in morphogenesis. Therefore, identification of novel secreted proteins genes playing roles in morphogenesis is expected to greatly contribute to our understanding of mechanism in morphogenesis.

Fgfs are multipotential growth factors playing roles in morphogenesis. By homology-based PCR and homology-based in silico analysis of nucleotide sequence databases, we identified nine novel Fgf genes including Fgf10, Fgf16, Fgf17, Fgf18, Fgf19, Fgf20, Fgf21, Fgf22 and Fgf23. We examined their roles in morphogenesis by analyzing phenotypes of their knockout mice and knockdown zebrafish. These Fgfs were found to play crucial roles as cell growth-differentiation factors in morphogenesis including limb, lung, heart, adipose tissue, brain, bone and blood cell formation. By secreted signal-targeted in silico analysis of cDNA databases, we also identified five novel genes encoding novel secreted proteins including Neudesin, Ectodin, Fibin, Neuclin and Brolin. Ectodin and Brolin are novel Bmp antagonists. Neuclin is a novel Wnt antagonist. We also examined their roles in morphogenesis by analyzing phenotypes of their knockout mice and knockdown zebrafish. The novel secreted proteins were found to play crucial roles as cell growth-differentiation factors in morphogenesis including brain, tooth and limb formation. These findings have revealed novel mechanisms in morphogenesis in vertebrates and will provide new insights into drug discovery and regenerative medicine.