Impairment of endochondral ossification by Hoxa2 overexpression: A plausible molecular explanation of idiopathic proportionate short stature

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Introduction. Using transgenic mice ectopically expressing Hoxa2 all along chondrogenesis, we showed that Hoxa2 exerts a negative influence in the earliest stage of endochondral ossification (1,2) and demonstrated that this effect was due to a significant decrease in the number of mesenchymal cells entering chondrogenic differentiation. Furthermore, this endochondral ossification impairment was associated with an overall size reduction phenotype (Fig. 1) which could be referred to human idiopathic proportionate short stature (PSS).

Materials and methods. In our transgenic mice (Col2a1/Hoxa2-lacZ; Fig. 2), Hoxa2 expression was induced in Col2a1 expressing territories and maintained thereafter, i.e. all over the endochondral bone elements. Mice bearing the h8-actin-lacZ-STOP-lac-Hoxa2-lacZ transgene only (85-Hoxa2-lacZ) were considered controls.

Using immunohistochemistry and Western blotting, we compared the protein levels of Bapx1, Runx2, Sox5, Sox6, Bmp1a, Foxc2, β1-integrin, Bmp7, Gdf10, Gdf5, Ihh, Wnt5a, Gdf3, Bmp4, Fgf4, Gdf6, Meox1, Meox2, Pax1, Phtr3, Msx1, Msx2, Osteopontin, Pax9, S-100 and Sox9 in E13.5, E15.5 and E16.5 transgenic and control mice. Immunohistochemistry was performed on sagittal paraffin sections through the spine.

References