Abstract

Sprouty proteins play the role of negative regulators of receptor tyrosine kinases (RTKs), including the fibroblast growth factor (FGF) signaling pathway. During embryonic development, this pathway is essential for the regulation of cell proliferation, migration, differentiation and apoptosis, and its activity is crucial for normal limb development. An integral part of this pathway are also FGF receptors (FGFR), of which, for example, FGFR3 significantly affects chondrocytes in the growth plate and its mutations lead to the development of chondrodysplastic syndromes.

Sprouty proteins play important roles during the formation of body tissues in the process of organogenesis. It has been shown that Sprouty2 and Sprouty4 are involved in the formation of many organs, such as the brain, lungs, teeth, but also in the formation of limbs. Sprouty2 is a regulator of enchondral ossification, modulates signaling in osteoblasts and chondrocytes and is essential for normal chondrocyte proliferation and differentiation. *Sprouty4* is expressed in the progress zone of the limb bud. Disruption of *Sprouty2* and *Sprouty4* gene expression leads to limb defects, which has been demonstrated, for example, in mouse or chicken embryos.

In the presented work we deal with the development of the limbs of transgenic mice with Sprouty2/Sprouty4 deficiency, in which, among other defects, pathologies of the forelimbs were detected in a preliminary study. The aim of this work is to monitor the longitudinal development of limbs in Sprouty2/Sprouty4 deficient mice with a focus on anatomical-morphological evaluation of phenotypic manifestations of Sprouty2 and/or Sprouty 4 protein deficiency on the anterior limb autopodium, evaluation of limb pathology in prenatal individuals and possible comparison of developmental differences of pathologies in individuals with different genotypes reflecting different dosages of both proteins (*Sprouty2*+/- *Sprouty4*-/- and *Sprouty2*+/+ *Sprouty4*-/-).

Key words: Sprouty2, Sprouty4, FGF signalling pathway, limb pathogenesis, hand cleft