Abstract

Although the RING finger protein 121 (RNF121) is a highly conserved E3 ubiquitin ligase from *Caenorhabditis elegans* to human, its function is poorly understood and in higher eukaryotes it has been studied only at *in vitro* level. RNF121 has been described to have various functions: i) it was ascribed to function as a broad regulator of NF-κB activation, ii) it was shown to control intracellular trafficking of various membrane proteins, and iii) its downregulation leads to apoptosis. Moreover, RNF121 might have a role in cancer as its expression was found to be 16.4-fold higher in patients suffering from Barrett esophagus (precancerous lesion of esophageal adenocarcinoma) and was even more increased in esophageal adenocarcinoma comparing to healthy population. In addition, *RNF121* gene is localized in the candidate region containing breast cancer susceptibility genes.

To gain insight into physiological functions of RNF121, *Rnf121* knockout mice (*Rnf121*$^{tm1b(EUCOMM)Hmgu}$) were generated in the Czech Centre for Phenogenomics and further studied in our laboratory. *Rnf121*$^{+/-}$ intercross breedings showed a prenatal lethal phenotype of *Rnf121*$^{-/-}$embryos, which were dying prior embryonic day (E) 11.5. Preliminary experiments carried out in our laboratory showed numerous vascular defects in null mutant embryo, yolk sac and placenta. This diploma thesis aimed to investigate function of murine RNF121 in the embryonic development with focus on the placenta forming and vascularization. It was found out that RNF121 plays an important role in placenta development since in *Rnf121*$^{-/-}$ placenta smaller trophoblast and underdeveloped labyrinth were observed. Besides this, it was confirmed that RNF121 participates in the activation of the NF-κB pathway on *Rnf121*$^{-/-}$ mouse embryonic fibroblasts.

Key words: E3 ligase, ubiquitin, ring-finger, NF-κB, mouse knockout, placenta, vascularization