The zebrafish *nhlrc2* is indispensable for normal embryonic development

NHL repeat containing 2 (NHLRC2) is widely conserved, ubiquitously expressed gene with unknown function and mechanism of action. In humans, pathogenic variations in *NHLRC2* cause fibrosis, neurodegeneration and cerebral angiomatosis (FINCA), a severe childhood-onset multiorgan disease. In addition to FINCA, studies have connected *NHLRC2* to several cellular functions, e. g. deficient phagocytosis, apoptosis and formation of fibrosis. *NHLRC2* is required during early development, as it has been connected to viability of oocytes, embryonic lethality and developmental deformations in mammals.

In zebrafish, *nhlrc2* is expressed from 2-cell stage onwards. To study further the essential role of *nhlrc2*, we generated *nhlrc2* knockout zebrafish model. According to our results, *nhlrc2* expression is required for normal zebrafish development as *nhlrc2*$^{-/-}$ zebrafish larvae die during the early development. More moderate decrease in gene expression appears to be tolerated as *nhlrc2*$^{+/-}$ larvae develop normally, reaching adulthood. *nhlrc2*$^{-/-}$ phenotype includes changes in the swim bladder and head area, reiterating anatomical locations of clinical findings in FINCA patients (incl. interstitial fibrosis of the lungs and neuropathological changes).

By performing a rescue experiment, we were able to verify the connection between genotype and *nhlrc2*$^{-/-}$ mutant phenotype, as *in vitro* transcribed *nhlrc2* mRNA injected into single-cell stage zebrafish embryos delayed the onset of mutant phenotype as well as relieved its severity. Our findings support the conclusion of the crucial role of *nhlrc2* during the early development, and suitability of zebrafish model in resolving the function of *nhlrc2*. We hope that this will provide means for better treatment of FINCA patients.

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