Abstract

Differentiation of the head ectoderm is crucial for the evolutionary diversification of vertebrates. Expression of the genes responsible for this process is orchestrated troughout complex gene regulatory networks that are induced and modulated by Wnt, FGF and BMP signaling pathways. In addition, Wnt/β-catenin signaling, in combination with expression of the Wnt antagonists from the rostral-most part of the head ectoderm, represent a key source of information for the regionalization of the tissue along the antero-posterior axis. This allows the differentiation of the anterior ectoderm that gives rise to the anterior neural fold (ANF) and anterior part of the presumptive placodal region (PPR), and more posterior ectoderm where higher levels of active Wnt/β-catenin signaling promote differentiation into the neural crest (NC) and posterior PPR. Although the requirement of Wnt/β-catenin signalling for ANF, PPR and NC development has been intensively studied in non-mammalian vertebrate model organisms, we lack a clear picture about the situation in mammals. Furthermore, current knowledge in mammals has been gathered via experiments on the level of β-catenin and very little is known about the individual roles of the Tcf/Lef transcription factors. Thereby, we decided to manipulate the Tcf7l1, member of the Tcf/Lef family with unique ability to act as a strong transcriptional repressor even in the presence of β-catenin. Through conditional deletion of the *Tcf7l1* gene in neural plate border of developing mouse embryo, we managed to describe function of the Tcf7l1 protein as well as the role of the Wnt/β-catenin signaling in the process of mammalian head ectoderm specification. Absence of Tcf7l1 led to aberrant activation of the Wnt/β-catenin signaling in the anterior neuroectoderm and its conversion into the NC. As a result, cell populations of the developing prosencephalon and anterior PPR were restrained. Importantly, this phenotype was not accompanied by changes of the anterior-posterior neural character. Thus, Tcf7l1 defines the border between the region of prospective forebrain and anterior placodes on one hand and the neural crest on the other, via restriction of the Wnt/β-catenin signaling gradient.