Abstract

Somitogenesis is the key developmental process, which divides the vertebrate body axis into segmentally repeated structures. These structures are called somites. Somites derive from the unsegmented presomitic mesoderm (PSM) that flanks the notochord to both sides. A prepatterning process, taking place in the PSM, is necessary to allow the exact spatial and temporal formation of the somites. The prepatterning is achieved by a clock and wavefront mechanism. The clock consists of the Delta-Notch (D-N) pathway, building up a genetic circuit with several cyclically expressed *h/E(spl)/hey*-related genes while the wave front is created by a FGF gradient, showing its highest expression in the posterior PSM. Disturbance of the clock or the mediator of the wavefront (*her13.2*) results in a disruption of cyclic gene expression and posterior somite border formation, while anterior somites are still formed. On the level of Delta-Notch signalling it is not clear if the escaped anterior somites are formed due to redundancy, since there are at least four *notch* and four *delta* homologues in zebrafish. Furthermore it is not known if Notch signalling is transmitted via the canonical way through *Su(H)* during somitogenesis or if an alternative way is used.

Since there appears to be only one complete *Su(H)* homologue in zebrafish, the function of this gene was analyzed using morpholino oligonucleotides. The knockdown of *Su(H)* leads to a clear disruption of cyclic gene expression, comparable to effects in previously described D-N mutants. Beyond this, posterior somite defects were detected while anterior somites were still formed, implying that their formation is not due to redundancy between different *delta* or *notch* genes. Performing the *Su(H)* knockdown in the *fss/tbx24* mutant it could be shown that D-N signalling is necessary for the creation and synchronization of cyclic gene expression. These results clearly suggest that the canonical way of Notch signalling is used during somitogenesis.

To further specify the prepatterning process two newly identified *her* genes, *her11* and *her12*, were analyzed during somitogenesis. It turned out that both genes are dynamically expressed in the PSM and are differentially regulated by D-N signalling. Functional studies suggest that *her11* interacts with *her1* and *her7* and is involved in the fine tuning of cyclic gene expression while *her12* seems to be involved in somite border formation and cyclic gene expression.

It was recently shown that the D-N driven Her1 protein and the FGF activated Her13.2 protein form heterodimers in vitro. To proof a combinatorial function also in vivo, both genes were knocked down individually and in combination. The combined knockdown leads to distinct additional effects, namely the break down of cyclic gene expression right

from the start and a disruption of anterior somite formation. This suggests clearly a combinatorial role for both genes in vivo during early somitogenesis.