RFX3 governs growth and beating efficiency of motile cilia in mouse and controls the expression of genes involved in human ciliopathies

EL ZEIN, Loubna, et al.

Abstract

Cilia are cellular organelles that play essential physiological and developmental functions in various organisms. They can be classified into two categories, primary cilia and motile cilia, on the basis of their axonemal architecture. Regulatory factor X (RFX) transcription factors have been shown to be involved in the assembly of primary cilia in Caenorhabditis elegans, Drosophila and mice. Here, we have taken advantage of a novel primary-cell culture system derived from mouse brain to show that RFX3 is also necessary for biogenesis of motile cilia. We found that the growth and beating efficiencies of motile cilia are impaired in multiciliated Rfx3(-/-) cells. RFX3 was required for optimal expression of the FOXJ1 transcription factor, a key player in the differentiation program of motile cilia. Furthermore, we demonstrate for the first time that RFX3 regulates the expression of axonemal dyneins involved in ciliary motility by binding directly to the promoters of their genes. In conclusion, RFX proteins not only regulate genes involved in ciliary assembly, but also genes that are involved in ciliary motility and that are ...

Reference


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Table S1. Primers sequences used for ChIP.

<table>
<thead>
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<th>Gene (position)</th>
<th>orientation</th>
<th>sequence (5’ to 3’)</th>
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<td>Dync2lic (Promoter)</td>
<td>forward</td>
<td>GCCGAAGGTGGGAGAAGACTAC</td>
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<tr>
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<td>reverse</td>
<td>AGTTGGGAGCAGAATGCG</td>
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<tr>
<td>Dync2lic (downstream)</td>
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<td>AAC TCC GGC TAC TCT TCC</td>
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<tr>
<td></td>
<td>reverse</td>
<td>AGGGCTTCTGATCCCTTTG</td>
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<tr>
<td>Bbs4 (Promoter)</td>
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<td></td>
<td>reverse</td>
<td>ACCATCCCAAGCTTACACTTC</td>
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<td>Bbs4 (downstream)</td>
<td>forward</td>
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<td>reverse</td>
<td>CCAGGACAACCAGGACTACAC</td>
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