CFAP53 regulates mammalian cilia-type motility patterns through differential localization and recruitment of axonemal dynein components

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Abstract

Motile cilia can beat with distinct patterns, but how motility variations are regulated remain obscure. Here, we have studied the role of the coiled-coil protein CFAP53 in the motility of different cilia-types in the mouse. While node (9+0) cilia of *Cfap53* mutants were immotile, tracheal and ependymal (9+2) cilia retained motility, albeit with an altered beat pattern. In node cilia, CFAP53 mainly localized at the base (centriolar satellites), whereas it was also present along the entire axoneme in tracheal cilia. CFAP53 associated tightly with microtubules and interacted with axonemal dyneins and TTC25, a dynein docking complex component. TTC25 and outer dynein arms (ODAs) were lost from node cilia, but were largely maintained in tracheal cilia of *Cfap53*$^{-/-}$ mice. Thus, CFAP53 at the base of node cilia facilitates axonemal transport of TTC25 and dyneins, while axonemal CFAP53 in 9+2 cilia stabilizes dynein binding to microtubules. Our study establishes how differential localization and function of CFAP53 contributes to the unique motion patterns of two important mammalian cilia-types.

Figure

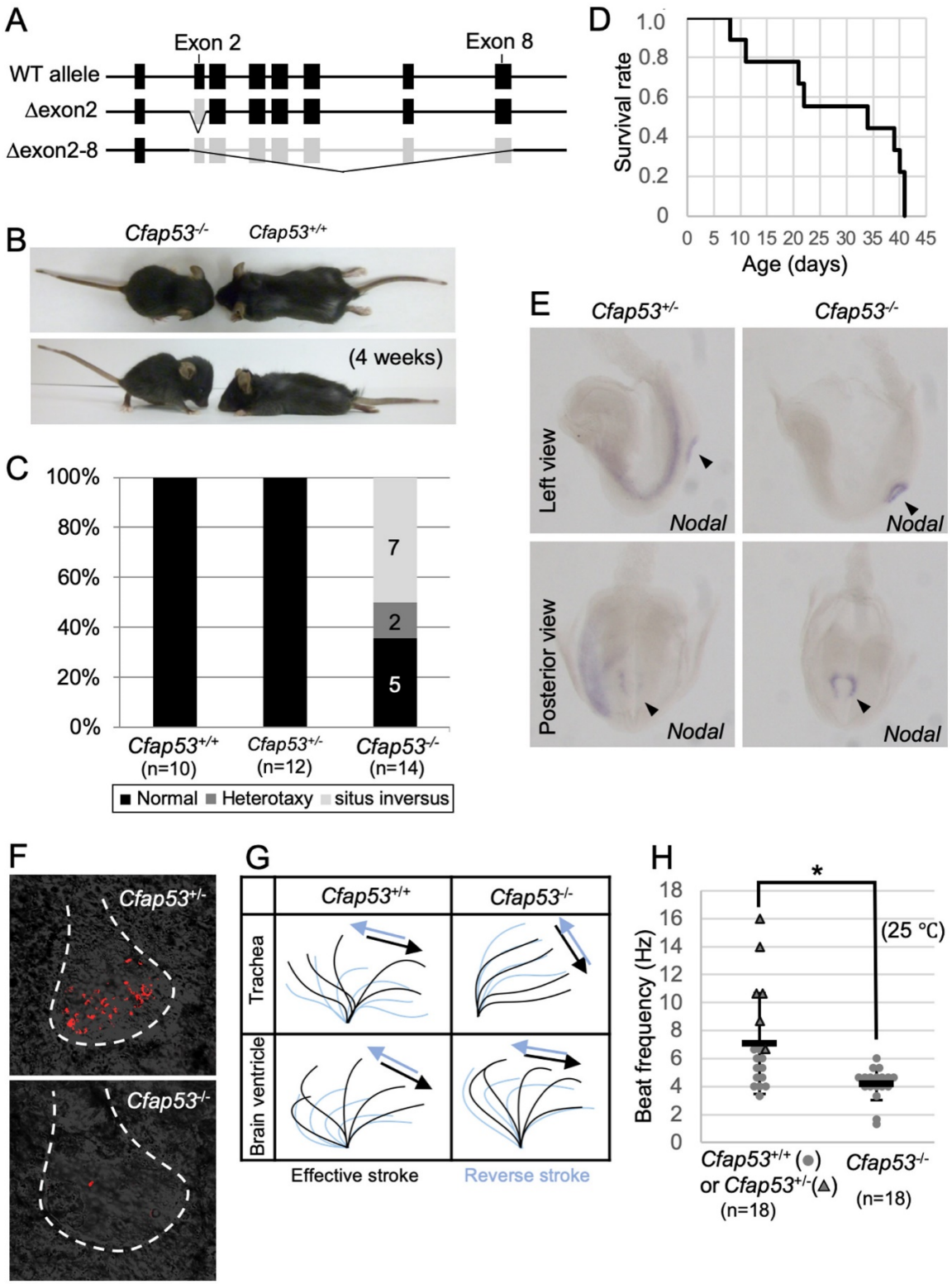

Figure legend: Laterality defects, hydrocephalus, and ciliary motion defects in *Cfap53* mutant mice

(A) Genetic structure of the wild-type mouse *Cfap53* locus and the generation of two types of knockout alleles lacking either exon 2 or exons 2 to 8. (B) Smaller body size and development of hydrocephalus in *Cfap53*$^{-/-}$mice at 4 weeks of age. (C) Laterality defects of *Cfap53*$^{-/-}$mice. (D) Survival curve for *Cfap53*$^{-/-}$mice (n = 14), with all animals dying by 6 weeks of age. (E) *In situ* hybridization analysis of *Nodal* expression in *Cfap53*$^{+/-}$and *Cfap53*$^{-/-}$mice at E8.0. *Nodal* expression was missing in the LPM of *Cfap53*$^{-/-}$embryos. Arrowheads indicate the node. (F) Immotility of node cilia in *Cfap53*$^{-/-}$embryos at E8.0. Red signals for the *Cfap53*$^{+/-}$embryo indicate motion trajectory in the corresponding movie. The red signal for the *Cfap53*$^{-/-}$embryo reflects the trajectory of a bubble. Dashed lines indicate the outline of the node. (G) Wave forms of tracheal and brain ventricle cilia. (H) Beat frequency for tracheal cilia of *Cfap53*$^{-/-}$and control mice (dots and triangles indicate *Cfap53*$^{+/+}$ and *Cfap53*$^{-/-}$ mice, respectively) determined at 25°C. Data are presented as mean ± SD (n = 18 independent experiments); two tailed Student's t-test (*p = 0.0041).