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Structural insight into the function of the spliceosomal helicase Aquarius

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Beyond participating in splicing, some spliceosomal components from higher eukaryotes play pivotal roles in coupling splicing to other RNA-processing events. The massive spliceosomal helicase Aquarius (170 kDa) is loaded at a specific location on the intron, where it acts as a molecular linker between splicing, the deposition of the exon-junction complex on the mRNA and the formation of snoRNPs from intronic segments. We have determined the crystal structures of the full-length Aquarius in complex with a non-hydrolysable ATP analog as well as with a single-stranded RNA. The structure reveals a complex molecular architecture, with a central core that resembles the RNA helicase Upf1 surrounded by several specific domains. Among them we identify an ARM-repeat domain, plus three other domains that were not observed in helicases. We could evidence that Aquarius possesses motor activity in vitro and that, strikingly, it exhibits opposite unwinding polarity versus Upf1. Crystal structure of Aquarius in complex with RNA revealed a novel mode of RNA binding by a helicase and led to the identification of structural adaptations underlying the reversal of directionality. Overall, the structure-function analysis brings insightful implications into the manner how two helicases have diverged from a common ancestor as a mean to achieve opposite polarities of translocation. Furthermore, we demonstrate that Aquarius is recruited to the spliceosome in complex with four other splicing factors and that the ARM domain is essential for the integrity of the complex. Moreover,the ARM domain makes contacts in the spliceosomal core, providing insight into the molecular basis underlying the accurate positioning of Aquarius on the intron. Following the line of these findings, we finally show that Aquarius plays an important role for the occurrence of splicing per se.

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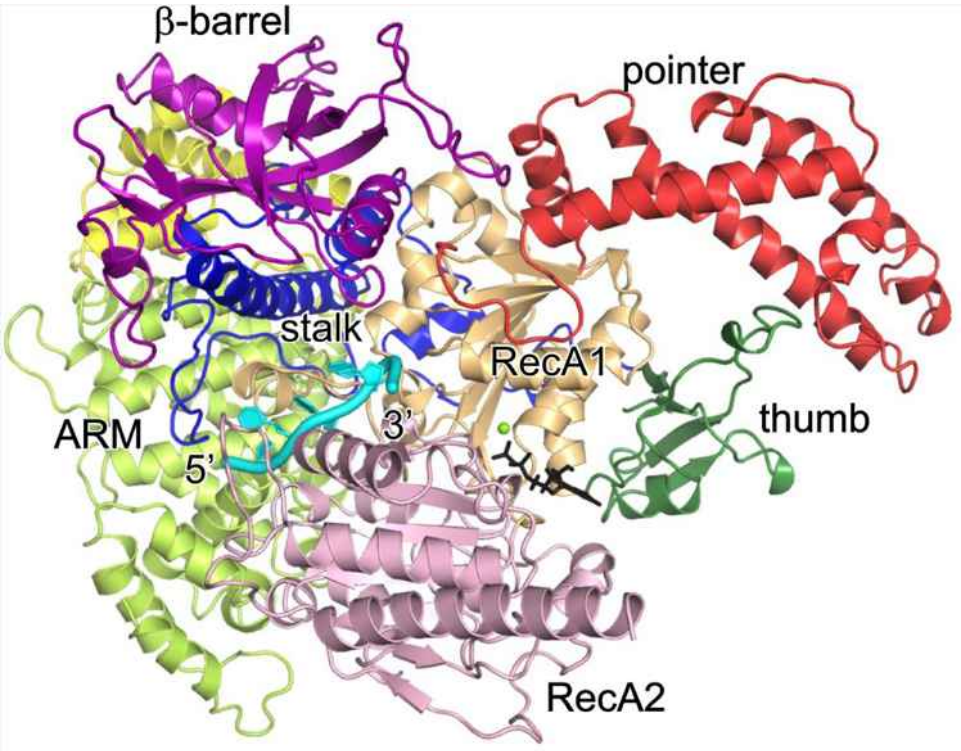

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