

RESEARCH ARTICLE

Ran GTPase, an eukaryotic gene novelty, is involved in amphioxus mitosis

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Abstract

Ran (ras-related nuclear protein) is a small GTPase belonging to the RAS superfamily that is specialized in nuclear trafficking. Through different accessory proteins, Ran plays key roles in several processes including nuclear import-export, mitotic progression and spindle assembly. Consequently, Ran dysfunction has been linked to several human pathologies. This work illustrates the high degree of amino acid conservation of Ran orthologues across evolution, reflected in its conserved role in nuclear trafficking. Moreover, we studied the evolutionary scenario of the pre-metazoan genetic linkage between *Ran* and *Stx*, and we hypothesized that chromosomal proximity of these two genes across metazoans could be related to a regulatory logic or a functional linkage. We studied, for the first time, *Ran* expression during amphioxus development and reported its presence in the neural vesicle, mouth, gill slits and gut corresponding to body regions involved in active cell division.

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Introduction

Ras-related nuclear protein (Ran) is an eukaryotic evolutionary conserved small GTPase representing the sole Ras superfamily member active in nucleus and traditionally considered a master regulator of nuclear trafficking [1,2]. Like other Ras proteins, it interacts with many cellular proteins comprising GTPase-activating protein (RanGAP), guanine-nucleotide-exchange factor (RanGEF) and GTP-Ran binding proteins, such as RanBP1 [3]. RanGEF catalyzes the GDP/GTP exchange while RanGAP promotes the GTP hydrolysis of Ran protein. In contrast, the cytoplasmic RanBP1 is an accessory protein that accelerates GTP hydrolysis carried out by RanGAP when other GTP-Ran binding proteins are absent [4]. A further relevant Ran accessory protein implicated in GTP hydrolysis is the importin β 3, also named RanBP5, able to bind nuclear pore complexes [5]. Ran activity is crucial for nuclear import-export, and the presence of a GTP-Ran gradient across the nuclear envelope has been implicated in nucleocytoplasmic transport [6]. In addition, RanBP1 overexpression in murine fibroblasts and *Xenopus laevis* egg extracts has demonstrated the involvement of Ran pathway in mitotic progression [7,8]. The decrease of GTP-Ran levels in frog eggs resulted in disrupted spindle