SHORT COMMUNICATION

Extra-Ribosomal Functions of the Ribosomal Protein, RPS3 as Predicted by In Silico Analysis

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ABSTRACT

Products of ribosomal protein (RP) genes have been found to play extra-ribosomal roles that range from DNA repair to RNA splicing. Their association with congenital disorders or cancers has also been widely documented. However, the relatively large number of different RPs, each with perhaps unique biological roles, has compounded the comprehensive elucidation of the physiological functions of each RPs. Experimental functional studies on the many and variegated RPs are labour intensive, time-consuming and costly. Moreover, experimental studies unguided by theoretically insights entail inaccurate results. Therefore, knowledge on the actual roles of these proteins remains largely undefined. A valid alternative is the use of bioinformatics resources to computationally predict functional roles of these biomolecules. Findings from such in silico studies of the RPS3 are reported herein. We reveal an array of possible extra-ribosomal functions that includes regulation of transcription (including via NF-κB-mediated, POK-induced and DNA-dependent), regulation of p53 activities and its stabilisation, inflammatory immune response, modulation of nNOS activities, and anti-oxidative capabilities. Our findings provide computational prediction of de novo extra-ribosomal functions of RPS3. These results will enhance the theoretical basis for designing future experimental studies on elucidating its definitive physiological roles.

Keywords: Protein models, RPS3, structural neighbours

The classical understanding of ribosomal proteins (RPs) is often confined to their functions as essential components of the ribosomes important for cellular ribosome-mediated protein synthesis. Nevertheless, since the mid-90s, their roles beyond ribosome-mediated protein biosynthesis (extra-ribosomal roles) such as association with cellular development, congenital diseases, and even cancers have been described (Wool, 1996; Noara, 1999). For example, RPS4 and RPL6 have been linked to Turner and Noonan syndromes respectively (Fisher et al., 1990; Kenmochi et al., 2000). In fact, many of the cancer-related studies demonstrated dysregulated expression of RP genes in diseased cases. Single and multiple RP genes were found to be over-expressed in leukaemic and solid tumours cells (Bassoe et al., 1998; Ruggero & Pandolfi, 2003), and in nasopharyngeal carcinoma cells (Sim et al., 2010). Aberrant expressions of RP genes have been linked to a wide range of cancer-types including carcinomas of colorectum (Pogue-Geile et al., 1991; Kasai et al., 2003; Sim et al., 2006), breast (Henry et al., 1993), prostate (Vaaara et al., 1998), uterine cervix (Cheng et al., 2002), esophagus (Wang et al., 2001), liver (Kim et al., 2004), nasopharynx (Sim et al., 2008) and in glioblastoma and multiform brain tumours (Lopez et al., 2002).

Despite the widely documented association between deregulated expression of RP genes and cancers, conclusive understanding on the definitive functional roles of these genes in organogenesis and oncogenesis is unclear. In the case of RPS3, even though higher expression levels were observed in tissues of colon adenocarcinomas and adenomatous polyps compared to those of adjacent normal colonic mucosa (Pogue-Geile et al., 1991) their actual roles in colorectal tumourigenesis hitherto are not fully understood. Access to information on extra-ribosomal functions of the product encoded by RPS3 and other RP genes

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