Structure-to-Function Computational Prediction of a Subset of Ribosomal Proteins for the Small Ribosome Subunit

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Abstract: Extra-ribosomal functions of ribosomal proteins have been widely accepted albeit an incomplete understanding of these roles. Standard experimental studies have limited usefulness in defining the complete biological significance of ribosomal proteins. An alternative strategy is via *in silico* analysis. Here, we sought a sequence-to-structure-to-function approach to computationally predict the extra-ribosomal functions of a subset of ribosomal proteins of the small ribosome subunit, namely RPS12, RPS19, RPS20 and RPS24. Three-dimensional structure constructed from amino acid sequence was precisely matched with structural neighbours to extrapolate possible functions. Our analysis reveals new logical roles for these ribosomal proteins, of which represent important information for planning experimental and further *in silico* studies to elucidate their physiological roles.

Key words: Extra-ribosomal functions, RPS12, RPS19, RPS20, RPS24, structural neighbours, 3D modelling.

1. Introduction

Ribosomal proteins (RPs) are originally construed as only essential components of the ribosomes involved in protein biosynthesis. However, since the 1990s, their extra-ribosomal roles have been discussed revealing their association with congenital diseases and a wide range of cancers [1], [2]. For instance, over-expression of *RPS12* has been observed in tissues of colon adenocarcinomas and adenomatous polyps [3], squamous cell carcinoma of the human uterine cervix [4], and gastric cancer [5]. The expression of *RPS19* was also found to be up-regulated in colon carcinoma [6], and is commonly mutated in patients with the congenital disorder of Diamond-Blackfan Anemia [7]. Truncating germline mutations in *RPS20* predispose individuals to hereditary nonpolyposis colorectal carcinoma [8], and *RPS24* showed significant differential expression between tissues of hepatocellular carcinoma and normal controls [9]. Despite these findings, knowledge on the definitive and complete functional roles of the proteins encoded by these genes remains vague. This is because their mutation status or expression behaviours in cancers alone do not provide sufficient information on their actual functions in the context of cellular development and differentiation.

Access to information on extra-ribosomal functions of these ribosomal proteins is largely hindered by the fact that existing studies focus on their expression profiles rather than biological functions. This is partly because the complete experimental characterization of RPs is laborious, time-consuming and costly. Then