Human Ribosomal Proteins RPeL27, RPeL43 and RPeL41 are Up-regulated in Nasopharyngeal Carcinoma Cell Lines

ABSTRACT
Apart from their canonical role in ribosome biogenesis, there is increasing evidence of ribosomal protein genes’ involvement in various cancers. A previous study by us revealed significant differential expression of three ribosomal protein genes (RPeL27, RPeL41 and RPeL43) between cell lines derived from tumor and normal nasopharyngeal epithelium. However, the results therein were based on a semi-quantitative assay, thus preliminary in nature. Herein, we provide findings of a deeper analysis of these three genes in the context to nasopharyngeal carcinoma (NPC) tumorigenesis. Their expression patterns were analyzed in a more quantitative manner at transcript level. Their protein expression levels were also investigated. We showed results that are contrary to previous report. Rather than down-regulation, these genes were significantly overexpressed in NPC cell lines compared to normal control at both transcript and protein levels. Nevertheless, their association with NPC has been established. Immunoprecipitation pulldown assays indicate the plausible interaction of either RPeL27 or RPeL43 with POTEET/TUBA1A and ACTB/ACTBL2 complexes. In addition, RPeL43 is shown to bind with MRAS and EIF2S1 proteins in a NPC cell line (HK1). Our findings support RPeL27, RPeL41 and RPeL43 as potential markers of NPC, and provide insights into the interaction targets of RPeL27 and RPeL43 proteins.

INTRODUCTION
Ribosomal proteins (RPs) are primarily known for their functions in ribosome biogenesis, and play a central role in translational processes. In fact, the highly coordinated processes of ribosome biogenesis are also tightly connected to events of cellular growth and development. Dysregulation in these processes could relate to occurrence of diseases that include cancers. It is also an established fact that the phenotypic effects RP genes extend beyond their canonical ribosomal involvement into extra-ribosomal functions such as DNA replication, transcription, DNA repair, DNA splicing and modification, apoptosis and many others [1]. In particular, differential expression of ribosomal proteins (RPs) have also been related to cancers [2, 3]. Recently all ribosomal protein genes have been accorded new nomenclature [4], and this is used in this paper will provide, but the old names are provided at their first mention in the text.

Nasopharyngeal carcinoma (NPC), a malignancy arising from epithelial cells of the nasopharynx is a cancer that has been extensively studied with respect to genetic susceptibility and involvement. Early evidence of RP genes involvement in NPC were limited to RPeS26 (RPS26), RPeS27 (RPS27), RPuS19 (RPS15), RPeL27 (RPL27), RPeL43 (RPL37a) and RPeL41 (RPL41) [5-7]. Albeit providing information on NPC-associated RP genes, these preliminary findings are largely speculative due to analysis that are semi-quantitative in nature and/or confined to assessment at transcript level. Indeed, inconsistent results of RPeS26 and RPeS27 in another study [8] nullified the verity of these two RP genes as NPC-associated factors. The case of RPuS19, although identified from a large list of differential expressed genes (via microarray assay) between NPC and non-cancerous nasopharyngeal tissue samples [6], was not subsequently selected for validation via conventional or quantitative RT-PCR analysis. Its’ up-regulation in NPC samples was also not evaluated at protein level. The three RP genes, RPeL27, RPeL43and RPeL41 were identified to be associated with NPC from a study that employed semi-quantitative RT-PCR assay of all RP genes encoding products for the large ribosome subunit [7]. Their under-