

Mitochondrial Ribosomal Proteins

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Mammalian mitochondrial ribosomes translate 13 proteins encoded by mitochondrial genes, all of which play roles in the mitochondrial respiratory chain. After a long period of reconstruction, mitochondrial ribosomes are the most protein-rich ribosomes. Mitochondrial ribosomal proteins (MRPs) are encoded by nuclear genes, synthesized in the cytoplasm and then, transported to the mitochondria to be assembled into mitochondrial ribosomes. MRPs not only play a role in mitochondrial oxidative phosphorylation (OXPHOS). Moreover, they participate in the regulation of cell state as apoptosis inducing factors. Abnormal expressions of MRPs will lead to mitochondrial metabolism disorder, cell dysfunction, etc. Many researches have demonstrated the abnormal expression of MRPs in various tumors.

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Mitochondrial Ribosome

tumor

1. Introduction

Ribosome is the ribonucleoprotein particle, which is an organelle for protein synthesis in cells, and its function is to synthesize the polypeptide chain efficiently and accurately according to the information of mRNA. Ribosomes can be found in almost all cells and even the smallest and simplest mycoplasma cell contains hundreds of them. At present, only mammalian mature red blood cells have no ribosomes, therefore, ribosomes are an indispensable structure of most cells. Mitochondria and chloroplasts contain ribosomes that synthesize their own proteins, which may be related to the origin of mitochondria and chloroplasts. The accepted endosymbiotic origin theory holds that mitochondria and chloroplasts originated from symbiotic bacteria and cyanobacteria in primitive eukaryotic, respectively. Therefore, mitochondrial ribosomes are more similar to the bacterial ribosomes than to cytoplasmic ribosomes. Mitochondrial ribosomal proteins (MRPs) are encoded by nuclear genes and synthesized by the cytoplasm 80S ribosomes, after specific targeting, sorting, transporting to mitochondria, and then assembling into mitochondrial ribosome small and large subunits with two rRNAs encoded by mitochondrial DNA (mt-DNA).

2. MRPs Associated with Diseases

With the research on MRPs, their names have changed ^[1], as shown in Table 1. The table also shows the changes of MRPs in tumor tissues reported in the past 5 years.

Table 1. Summary of the relationship between abnormal expression of mitochondrial ribosomal proteins and their encoding genes with diseases in recent 5 years.

Old Name	New Name	Cancer	Other Diseases
Mitochondrial ribosomal large subunit (mt-LSU) genes and proteins.			
MRPL1	uL1m	Lung cancer [2]	
MRPL3	uL3m		Neurodegeneration and memory impairment [3] , Hypertrophic cardiomyopathy [4] [5] , Prognosis [6] , Acute mountain disease [7]
MRPL9	bL9m	Breast cancer [8]	
MRPL10	uL10m		Early age-related macular degeneration [9]
MRPL11	uL11m		Mitochondrial encephalopathy [10] ↓
MRPL12/L7	bL12m	Breast cancer [11] ↑, Colorectal cancer [12]	
MRPL13	uL13m	Liver cancer [13] ↓, Breast cancer [13] [14] [15] ↑	
MRPL15	uL15m	Breast cancer [16] ↑	
MRPL16	uL16m		Septic cardiomyopathy [17] ↑
MRPL17	bL17m	Lung cancer [18] ↑	
MRPL19	bL19m	Endometrial cancer [19] [20] , Diffuse non-Hodgkin lymphoma [21] , Melanoma [22]	
MRPL21	bL21m	Acute myeloid leukemia [23] ↑	
MRPL23	uL23m	Oral squamous cell carcinoma [24] ↓, Glioblastoma multiforme [25]	
MRPL24	uL24m		Cerebellar atrophy, intellectual disability [26] ↓
MRPL28	bL28m	Gastric cancer [27]	
MRPL33	bL33m	Breast cancer [28] ↑, Lung cancer, colon cancer [29] ↑, Gastric cancer [30] , Acute myeloid leukemia and neuroblastoma [31] ↑, Human papillomavirus associated oropharyngeal squamous cell carcinoma [32] ↑	

Old Name	New Name	Cancer	Other Diseases
MRPL34	bL34m		Cardiomyocyte hypertrophy [33] ↓
MRPL35	bL35m	Glioblastoma multiforme [34] ↑, Colorectal cancer [35] ↑	
MRPL36	bL36m		Cri-du-chat syndrome [36]
MRPL37	mL37		Venous thromboembolism [37]
MRPL38	mL38	Liver cancer [38]	
MRPL39	mL39	Gastric cancer [39] ↓	
MRPL40	mL40		Schizophrenia [40] [41] [42] ↓
MRPL42	mL42	Glioma [43] ↑	
MRPL43	mL43	Gastric cancer [44] ↑	
MRPL44	mL44		Mitochondrial encephalopathy [10] ↓, Cardiomyopathy [45] [46] , Hemiplegia migraine, pigmentary retinopathy, renal insufficiency, Leigh-like lesions on brain MRI [47] , Asthma and allergy-related traits [48]
MRPL46	mL46	Ovarian cancer [49]	
MRPL47	mL47	Acute lymphoblastic leukemia [50]	
MRPL50	mL50		Cardiomyocyte hypertrophy [33] ↑
MRPL51	mL51	Lung cancer [51] ↑	
MRPL52	mL52	Colorectal cancer [52] ↓	
MRPL54	mL54	Breast cancer [53]	
CRIF1	mL64	Hepatocellular carcinoma [54] ↓, T-cell leukemia [55]	Acute radiation syndrome [56] , Endothelial inflammation [57] [58] ↓, Autoimmune arthritis [59] ↑
MRPS18-A	mL66	Liver cancer [60] ↑, Cholangiocarcinoma [61] ↑	
Mitochondrial ribosomal small subunit (mt-SSU) genes and proteins			

Old Name	New Name	Cancer	Other Diseases
MRPS2	uS2m	Glioblastoma multiforme [25]	Cardiomyocyte hypertrophy [33] ↑
MRPS5	uS5m		Noise-induced hearing loss and anxiety related behavior changes [62] ↑
MRPS7	uS7m	Osteosarcoma [63] ↑	Primary hypogonadism, primary adrenal failure [64] ↓
MRPS11	uS11m	Uveal melanoma [65] ↑	
MRPS12	uS12m	Glioblastoma multiforme [25]	
MRPS14	uS14m		Perinatal hypertrophic cardiomyopathy [66] ↑
MRPS18-B	mS40	Prostate cancer [67] ↑, Colorectal carcinoma [68]	Tuberculosis [69]
MRPS18-C	bS18m	Breast cancer [70] ↑	Epileptic encephalopathy [71]
MRPS21	bS21m		Cardiomyocyte hypertrophy [33] ↑
MRPS22	mS22		Epicanthus inversus syndrome [72] , Hypertrophic cardiomyopathy and fallopian tube lesions [73] ↓, Primary ovarian insufficiency [74] [75] [76]
MRPS23	mS23	Hepatocellular carcinoma [77] ↑	
MRPS34	mS34	Glioblastoma multiforme [25]	Cardiomyocyte hypertrophy [33] ↓
MRPS37	mS37	Acute lymphoblastic leukemia [23] ↑	
MRPS39	mS39		Leigh syndrome [78]

Legend: Prefix “u”: Genes and proteins are present in all kingdoms of life (for universal); prefix “u”: Genes and proteins are bacterial in origin and do not have an eukaryotic (or archaeal) homolog; prefix “m”: Genes and proteins are mitochondrion-specific. “↑” Upregulation in that disease; “↓” downregulation in that disease. This table only lists the MRPs (mitochondrial ribosomal proteins) that appear in this article.

3. Conclusions and Perspectives

The development of a high-precision analysis technology of cryo-electron microscopy enables us to identify the structure of mitochondrial ribosomal proteins with a scale of 0.1 nm. Each of the 80 MRPs is essential for the mitochondrial ribosome composition, which plays an irreplaceable role in the assembly and translation of

mitochondrial DNA. At present, studies of the relationship between MRPs and cell apoptosis are few. Although the apoptotic mechanisms of MRPS29, MRPL41 and MRPL65 have not been fully elucidated, they at least provide us with useful information to deeply study the apoptotic mechanisms of MRPs. We can further explore the changes of MRPs function or pathway-activating role in the process of inducing apoptosis, based on the analysis of the MRPs structure. Additionally, specific mechanisms can be clarified in the future.

The abnormal expression of MRPs and their encoding genes is closely associated with a variety of cancer and mitochondrial related diseases. Multiple MRPs are important predictors of disease diagnosis. However, the specific mechanisms of inducing the development of diseases are little known.

In the future, on the one hand, it is very important to strengthen the research on the relationship between the abnormal expression of MRPs, lack of their encoding genes, and diseases. On the other hand, some MRPs such as MRPS22, MRPL44 and MRPL28 that have been clarified as key factors in the development of cancer, which can be as biological targets to deeply study their specific pathways of influence, in order to lay a theoretical foundation for a targeted diagnosis and therapy of cancer in our research.

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