Review Letter

HIGH MOLECULAR MASS AMINO ACYL-tRNA SYNTHETASE COMPLEXES IN EUKARYOTES

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1. Introduction

Aminoacyl-tRNA synthetases (AARS) are enzymes which play an indispensable role in protein biosynthesis by catalyzing the formation of aminoacyl-tRNA from amino acid, the cognate tRNA, and ATP by highly selective intermolecular interactions [57]. Joachimiak and Barciszewski [41] have provided an extensive compilation of the properties of the aminoacyl-tRNA synthetases; however, information on the eukaryotic high M_r (HM_r) complexes of aminoacyl-tRNA synthetases was lacking. Here, we intend to fill this void by providing a summary of the properties of the eukaryotic aminoacyl-tRNA synthetase complexes.

Eukaryotic aminoacyl-tRNA synthetases may occur as complexes with M_r-values of $>10^6$ in contrast to the prokaryotic counterparts which have M_r-values of $\leqslant 250\,000$. These eukaryotic HM_r–AARS complexes appear ubiquitous in a wide spectrum of cell types from yeast to human placenta as shown in table 1. Although not all 20 aminoacyl-tRNA synthetases were examined in each case shown in table 1, it appears that the AARS commonly associated with M_r complexes are those specific for Arg, Gln, Glu, Ile, Leu, Lys and Met. The properties of these HM_r–AARS complexes are most consistent with multienzyme complexes of aminoacyl-tRNA synthetases [19,20,43, 46]. The physicochemical properties, composition, and stoichiometry of the more rigorously characterized complexes are shown in table 2.

The mechanism(s) of intermolecular interaction between the aminoacyl-tRNA synthetases is not known, but the putative interactions of aminoacyl-tRNA synthetases with a variety of biomolecules have been suggested to play a role in complex formation as shown in table 3. Our present knowledge of the functional significance of HM_r–AARS is profoundly lacking; however, interactions of the aminoacyl-tRNA synthetases with other components of the protein biosynthetic machinery and other enzymes suggest the intriguing possibility of higher organization of eukaryotic protein biosynthesis. Table 4 is a summary of the possible interactions of the aminoacyl-tRNA synthetases with subcellular components and other enzymes.

This presentation is a brief summary of the properties of the high molecular weight eukaryotic aminoacyl-tRNA synthetase complexes. We hope that this compilation will complement that presented in [41] and will provide useful information for workers in this and other related fields.

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Table 1
Occurrence of high M_r aminoacyl-tRNA synthetases in eukaryotes[a]

Source	Ala	Arg	Asp	Asn	Cys	Gln	Glu	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	References
Mouse liver	+	+	+	+	ND	+	ND	+	+	+	+	+	+	+	+	+	+	ND	+	+	[7–11]
Mouse liver		+	+			+	+			+	+	+	+		+					+	[64]
Mouse embryo		+	+			+	+			+	+	+	+		+					+	[64]
Rat liver	+	+	+	ND	ND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	[5,6,22,24]
Rat liver		+	+		+	ND	+				+	+	+	+	+		+	+		+	[12,28]
Rat liver		+				+	+			+	+	+	+		+						[18–20,42]
Rat liver		+								+	+	+	+								[43]
Rat liver		+	+			+	+	+			+	+	+	+	+	+	+		+		[56]
Rat liver						+				+	+	+	+								[68–71]
Rat liver		+										+									[16,17,29,30]
Rat mammary gland		+			+	+				+	+	+	+							+	[35]
Rat skeletal muscle		+				+	+			+	+	+	+		+					+	[4]
Rabbit reticulocytes		+								+	+	+	+								[61]
Porcine thyroid gland		+	+	+	+	ND	+		+	+	+	+	+	+	+	+	+	ND	+	+	[67]
Sheep liver		+				+	+			+	+	+	+								[13,44–46]
Bovine brain		+	+	+		+	+				+	+			+					+	[65,66]
Calf brain	+	+	+	+	ND	+	+	+	+	+	+	+	+	+	+	+	+	ND	+	+	[15]
Human placenta		+				+	+			+	+	+	+								[21]
Chick embryo		+				+	+			+	+	+	+		+					+	[64]
Friend leukemia cells		+	+			+	+			+	+	+	+		+						[64]
Chinese hamster ovary cells		+	+			+	+			+	+	+	+		+		+				[27,33,52,53]
Ehrlich ascites cells[a]										+	+	+	+	+							[54,55]
Drosophila[a]	+											+		+						+	[58]
Wheat germ[a]		+									+		+	+							[50]
Yeast[a]												+									[25,26]

[a] Only a few synthetase activities were examined; ND = not determined

Table 2
Physicochemical properties and composition of eukaryotic aminoacyl-tRNA synthetase complexes [a,b]

Source	M_r ($\times 10^{-3}$)	$s_{20,w}$	Ala	Arg	Asp	Asn	Cys	Gln	Glu	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	References
Chinese hamster ovary	–	30	–	+	+	–	–	+	+	–	–	+	+	+	+	–	+	–	+	–	–	–	[52]
Rat liver	–	18	–	–	–	–	–	+	–	–	–	+	+	+	+	–	–	–	–	–	–	–	[69,71]
Rat liver[c]	1000	18	–	+	–	–	–	(+)	–	–	–	(1)	(1)	2	1	–	–	–	–	–	–	–	[43]
Rat liver	900	24	–	+	–	–	–	+	+	–	–	+	+	+	+	–	+	–	–	–	–	–	[20]
Rat liver[d]	285	12	–	(2)	–	–	–	–	–	–	–	–	–	(2)	–	–	–	–	–	–	–	–	[17]
Rat mammary gland	–	20–28	–	+	–	–	+	+	–	–	–	+	+	+	+	–	–	–	–	–	–	+	[35]
Rabbit reticulocytes	550	16	–	+	–	–	–	–	–	–	–	+	+	+	+	–	–	–	–	–	–	–	[61]
Sheep liver	1000	–	–	+	–	–	–	+	+	–	–	+	+	+	+	–	–	–	–	–	–	–	[46]
Human placenta	–	17–20	–	+	–	–	–	+	+	–	–	+	+	+	+	–	–	–	–	–	–	–	[21]

[a] Only complexes characterized with published activity profiles are included in table 2
[b] A plus signifies that the synthetase activity for the indicated amino acid is present in the complexes
[c] The numbers indicate the stoichiometry determined by active site titration; parentheses signify tentative assignments (details in [43])
[d] The numbers indicate tentative values of the stoichiometry

Table 3
Biomolecules with putative role in HM_r aminoacyl-tRNA synthetase complex formation[a]

Biomolecule	Method of analysis	Enzyme source	References
Carbohydrate	SDS–polyacrylamide gel staining (periodic acid Schiff reagent)	Thr–RS; rat liver	[24]
	Gas chromatography of enzyme hydrolysate	Lys–, Arg–RS; rat liver	[16,29]
Lipid			
Cholesteryl ester, cholesterol	Extraction of enzyme preparation, paper chromatography	Complex; rat liver	[6]
		Complex; rat mammary gland	[35]
Cholesteryl 14-methylhexadecanoate	Extraction of enzyme preparation	Rat liver	[36,37]
Ergosterol	Extraction of enzyme preparation	Lys–RS; yeast	[25]
Glycolipid	Paper chromatography of enzyme preparation extract	Complex; rat liver	[56]
Ribonucleic acid			
tRNA, 4 S RNA	Extraction of enzyme preparation	Complex; mouse liver	[9]
	amino acid acceptor activity	Complex; rat liver	[5]
		Complex; rat liver	[56]
High M_r RNA	Analysis of binding by gel filtration and sucrose gradient ultracentrifugation	Ehrlich ascites cells	[55]
	Affinity chromatography	Rabbit reticulocytes	[3]

[a] Studies included in table 3 vary in levels of exactness and enzyme purity

Table 4
The interaction of aminoacyl-tRNA synthetases with subcellular components and other enzyme activities[a,b]

Organelle or enzyme	Method of analysis	Source	References
Microsome	Cell fractionation	Chinese hamster ovary	[32]
		Rat skeletal muscle	[4]
		Rat liver	[63]
		Chicken embryo	[49]
		Yeast	[26]
		Wheat germ	[50]
Ribosome	Copurification, reconstitution	Rat liver	[63]
	Copurification	Chinese hamster ovary	[48]
	Copurification or reconstitution	Rabbit reticulocyte	[39,59,62,64]
	Enzyme activity stimulation	Rabbit reticulocyte	[31]
	Protection of enzyme activity	Wheat germ	[14]
		Yellow lupin seed	[40]
	Copurification	Friend leukemic cells, chicken embryo, mouse liver, mouse embryo	[64]
	Copurification	Ehrlich ascites cell	[55]
Elongation Factors	Copurification	Rat liver	[60]
		Rabbit reticulocyte	[38]
Peptidyl acetyltransferase	Copurification	Rat liver	[56]
Initiation Factors	Copurification	Rabbit reticulocyte	[38]
tRNA Methyltransferase	Copurification	Human and mouse leukocytes	[1,2]
tRNA Sulfurtransferase	Copurification	Rat liver	[34]
Ribonuclease	Copurification	Porcine thyroid gland	[67]
DNA Polymerase α	Copurification	Hela cell	[51]

[a] Mitochondrial enzymes are different from the cytosolic enzymes [23] and are not considered; nucleolar aminoacyl-tRNA synthetase activities have been detected in purified nucleoli [47]
[b] Studies included in table 4 vary in levels of enzyme purity