**Table S1.** Differentially expressed proteins by primary AML cells derived from patients without relapse or with a later relapse after intensive therapy: a comparison of REL\_M4/5 and REL\_F\_M4/5 patient proteomes. The information is based on the Gene database (accessed 280823) and selected references from the PubMed database (accessed September 13 2023). The table presents the differentially expressed protein identity (left column), a description of the protein function (middle column) and, keywords with regard to the molecular function and references (right column). These proteins were identified in protein-protein interaction (PPI) analyses of the different REL vs REL\_F subgroup comparisons shown in **Figure 5c** of the main text.

|  |  |  |
| --- | --- | --- |
|  | **MITOCHONDRIAL ATP SYNTHESIS PROTON TRANSPORT** |  |
| **Protein id** | **Biological characterization** | **Keywords/References** |
| ATP5A1  (ATP5F1A)  Chromosome 18 | *ATP synthase F1 subunit alpha.* The encoded protein is a subunit of mitochondrial ATP synthase that catalyzes ATP synthesis by using an electrochemical gradient of protons across the inner membrane during oxidative phosphorylation. ATP synthase is composed of two linked multi-subunit complexes: the soluble catalytic core, F1, and the membrane-spanning component, Fo, comprising the proton channel. The catalytic portion of mitochondrial ATP synthase consists of 5 different subunits (alpha, beta, gamma, delta, and epsilon) assembled with a stoichiometry of three alpha, three beta and a single chain of the other three. The proton channel consists of three main subunits (a, b, c). This gene encodes the alpha subunit of the catalytic core. | Mitochondria;  ATP synthase;  Catalytic core subunit/[1-10] |
| ATP5B  (ATP5F1B)  Chromosome 12 | *ATP synthase F1 subunit beta.* The encoded subunit of mitochondrial ATP synthase that is composed of the soluble catalytic core (F1) and the membrane-spanning (Fo) proton channel. The catalytic portion of mitochondrial ATP synthase consists of 5 different subunits (alpha, beta, gamma, delta, and epsilon) assembled with a stoichiometry of 3 alpha, 3 beta, and a single representative of the other 3. This gene encodes the beta subunit of the catalytic core. | Mitochondria;  ATP synthase;  Catalytic core subunit/[3-11] |
| ATP5C1 (ATP5F1C)Chromosome 10 | *ATP synthase F1 subunit gamma.* This gene encodes the gamma subunit of the catalytic core of the mitochondrial ATP synthase. | Mitochondria;  ATP synthase;  Catalytic core subunit/[3-10] |
| ATP5D  (5F1D)  Chromosome 19 | *ATP synthase F1 subunit delta.* This encoded protein is the delta subunit of the catalytic core of the mitochondrial ATP synthase. | Mitochondria;  ATP synthase;  Catalytic core subunit/[3-10] |
| ATP5F1  (ATP5PB)  Chromosome 1 | *ATP synthase peripheral stalk-membrane subunit b.* The encoded protein is the b subunit of the proton channel of the mitochondrial ATP synthase. | Mitochondria;  ATP synthase;  Proton channel subunit/[3-10] |
| ATP5H  (ATP5PD)  Chromosome 17 | *ATP synthase peripheral stalk subunit d.* This gene encodes the d subunit of the proton channel complex of mitochondrial ATP synthase. | Mitochondria;  ATP synthase;  Proton channel subunit/[3-10] |
| ATP5I  Chromosome 4 | *ATP synthase, H+ transporting, mitochondrial Fo complex subunit E.* This encoded protein is the e subunit of the catalytic core of the mitochondrial ATP synthase. | Mitochondria;  ATP synthase;  Catalytic core subunit/[3-10] |
| ATP5J  (ATP5PE)  Chromosome 21 | *ATP synthase peripheral stalk subunit F6.* This gene encodes the F6 subunit of the proton channel subunit of mitochondrial ATP synthase. The protein is required for F1 and Fo interactions. | Mitochondria;  ATP synthase;  Proton channel subunit/[3-10] |
| ATP5O  (ATP5PO)  Chromosome 21 | *ATP synthase peripheral stalk subunit OSCP.* The encoded protein is a component of the F-type ATPase found in the mitochondrial matrix. F-type ATPases are composed of a catalytic core and a membrane proton channel. The protein appears to be part of the connector linking these two components and may be involved in transmission of conformational changes or proton conductance. | F-type ATPase /[3-10] |
| MT-ATP8  Mitochondrial | *Mitochondrially encoded ATP synthase 8.* The encoded protein *c*ontributes to the mitochondrial proton-transporting ATP synthase activity that is involved in mitochondrial ATP synthesis coupled proton transport. This protein is a part of mitochondrial proton-transporting ATP synthase complex. | Mitochondria;  ATP synthase;  Proton transport/[3-10] |
| USMG5  (ATP5MK)  Chromosome 10 | *ATP synthase membrane subunit k.* The encoded protein is a subunit of the mitochondrial proton-transporting ATP synthase complex. | Mitochondria;  ATP synthase;  Proton transport/[3-10] |
|  | **MITOCHONDRIAL ELECTRON TRANSPORT** |  |
| COX15  Chromosome 10 | *Cytochrome c oxidase assembly homolog COX15.* Cytochrome c oxidase (COX) is the terminal component of the mitochondrial respiratory chain and catalyzes the electron transfer from reduced cytochrome c to oxygen. This component is a heteromeric complex consisting of 3 catalytic subunits encoded by mitochondrial genes and multiple structural subunits encoded by nuclear genes. The mitochondrially-encoded subunits function in electron transfer, and the nuclear-encoded subunits may function in the regulation and assembly of the complex. This nuclear gene encodes a protein which is not a structural subunit, but may be essential for the biogenesis of COX formation. This protein is predicted to contain 5 transmembrane domains localized in the mitochondrial inner membrane. | Mitochondrial respiratory chain;  Cytochrome C oxidase;  Electron transfer;  Nuclear gene;  Transmembrane domains/[12-16] |
| COX5B  Chromosome 2 | *Cytochrome c oxidase subunit 5B.* Cytochrome C oxidase (COX) is the terminal enzyme of the mitochondrial respiratory chain. It is a multi-subunit enzyme complex that couples the transfer of electrons from cytochrome c to molecular oxygen and contributes to a proton electrochemical gradient across the inner mitochondrial membrane. The complex consists of 13 mitochondrial- and nuclear-encoded subunits. The mitochondrially-encoded subunits perform the electron transfer and proton pumping activities. The functions of the nuclear-encoded subunits are unknown but they may play a role in the regulation and assembly of the complex. This gene encodes the nuclear-encoded subunit Vb of this enzyme. | Mitochondrial respiratory chain;  Cytochrome C oxidase;  Electron transfer;  Nuclear gene/[12-16] |
| NDUFB3  Chromosome 2 | *NADH:ubiquinone oxidoreductase subunit B3.* This gene encodes an accessory subunit of the mitochondrial membrane respiratory chain NADH dehydrogenase (Complex I) that is the first enzyme in the electron transport chain. This protein localizes to the inner membrane of the mitochondrion. | Mitochondrial respiratory chain  Complex I/[17-22] |
| NDUFC2  Chromosome 11 | *NADH:ubiquinone oxidoreductase subunit C2.* The encoded mitochondrial protein is involved in mitochondrial respiratory chain complex I assembly. | Mitochondrial respiratory chain  Complex I/[17-22] |
| NDUFS7  Chromosome 19 | *NADH:ubiquinone oxidoreductase core subunit S7.* This gene encodes one of the more than 40 subunits found in complex I of the mitochondrial respiratory chain, the nicotinamide adenine dinucleotide (NADH):ubiquinone oxidoreductase. This complex functions in the transfer of electrons from NADH to the respiratory chain, and ubiquinone is believed to be the immediate electron acceptor for the enzyme. | Mitochondrial respiratory chain  Complex I/[17-22] |
| NDUFV2  Chromosome 18 | *NADH:ubiquinone oxidoreductase core subunit V2.* The NADH-ubiquinone oxidoreductase complex (complex I) of the mitochondrial respiratory chain catalyzes the transfer of electrons from NADH to ubiquinone, and consists of at least 43 subunits. The complex is located in the inner mitochondrial membrane. This gene encodes the 24 kDa subunit and is involved in electron transfer. | Mitochondrial respiratory chain  Complex I;  Electron transfer/[17-22] |
| UQCRC2  Chromosome 16 | *Ubiquinol-cytochrome c reductase core protein 2.* The encoded mitochondrial protein is part of the ubiquinol-cytochrome c reductase complex (also known as complex III) that constitutes a part of the mitochondrial respiratory chain. | Mitochondrial respiratory chain  Complex 3/[17,23,24] |
| UQCRQ  Chromosome 5 | *Ubiquinol-cytochrome c reductase complex III subunit VII.* The encoded ubiquinone-binding protein is a small core-associated protein that is a subunit of ubiquinol-cytochrome c reductase complex III. This complex is part of the mitochondrial respiratory chain. | Mitochondrial respiratory chain  Complex 3/[17,23,24] |
|  | **MITOCHONDRIAL TRANSLATION ELONGATION\*** |  |
| MRPL10  Chromosome 17 | *Mitochondrial ribosomal protein L10*. Mammalian mitochondrial ribosomal proteins are encoded by nuclear genes and help in protein synthesis within the mitochondrion. Mitochondrial ribosomes (mitoribosomes) consist of a small 28S subunit and a large 39S subunit. This gene encodes a 39S subunit protein. Sequence analysis identified three transcript variants that encode two different isoforms. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL11  Chromosome 11 | *Mitochondrial ribosomal protein L11*. This nuclear gene encodes a 39S subunit component of the mitochondrial ribosome. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL22  Chromosome 5 | *Mitochondrial ribosomal protein L22*. This gene encodes a 39S subunit protein that belongs to the L22 ribosomal protein family. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL54  Chromosome 19 | *Mitochondrial ribosomal protein L54*. This gene encodes a 39S subunit protein. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL12  Chromosome 17 | *Mitochondrial ribosomal protein L12*. This gene encodes a 39S subunit protein which forms homodimers. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL16  Chromosome 11 | *Mitochondrial ribosomal protein L16*. This gene encodes a 39S subunit protein. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL20  Chromosome 1 | *Mitochondrial ribosomal protein L20*. This gene encodes a 39S subunit protein. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL24  Chromosome 1 | *Mitochondrial ribosomal protein L24*. This gene encodes a 39S subunit protein. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPS18A  Chromosome 6 | *Mitochondrial ribosomal protein S18A*. This gene encodes a 28S subunit protein that belongs to the ribosomal protein S18P family. The primary sequences of the three human mitochondrial S18 proteins are no more closely related to each other than they are to the prokaryotic S18 proteins. | Mitochondrial ribosome  28S subunit/[25-30] |
| MRPL28  Chromosome 16 | *Mitochondrial ribosomal protein L28*. This gene encodes a 39S subunit protein, a part of which was originally isolated by its ability to recognize tyrosinase in an HLA-A24-restricted fashion. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL38  Chromosome 17 | *Mitochondrial ribosomal protein L38*. This gene encodes a 39S subunit protein. | Mitochondrial ribosome  39S subunit/[25-30] |
| MRPL57  Chromosome 13 | *Mitochondrial ribosomal protein L57*. This gene encodes a protein which belongs to an undetermined ribosomal subunit and which seems to be specific to animal mitoribosomes. | Mitochondrial ribosomal subunit/[25-30] |
| MRPS27  Chromosome 5 | *Mitochondrial ribosomal protein S27*. This gene encodes a 28S subunit protein that may be a functional partner of the death associated protein 3 (DAP3). Alternative splicing results in multiple transcript variants encoding different isoforms. | Mitochondrial ribosome  28S subunit/[25-30] |
|  | **TRANSCRIPTION ELONGATION FROM RNA POLYMERASE II PROMOTER** |  |
| SSRP1  Chromosome 11 | *Structure specific recognition protein 1.* The encoded protein is a subunit of a heterodimer that, along with SUPT16H, forms chromatin transcriptional elongation factor FACT. FACT interacts with histones H2A/H2B to effect nucleosome disassembly and transcription elongation. FACT and cisplatin-damaged DNA may be crucial to the anticancer mechanism of cisplatin. The protein also functions as a co-activator of the transcriptional activator p63. | Transcriptional elongation;  Histone  Chemosensitivity/[31-33] |
| CHD1  Chromosome 5 | *Chromodomain helicase DNA binding protein 1.* The CHD protein family is characterized by the presence of chromo (chromatin organization modifier) domains and SNF2-related helicase/ATPase domains. CHD genes alter gene expression possibly by modification of chromatin structure. | Transcription;  Chromatin modulation/[31-33] |
| CTR9  Chromosome 11 | *CTR9 homolog, Paf1/RNA polymerase II complex component.* The encoded protein is a component of the PAF1 complex, which associates with RNA polymerase II and functions in transcriptional regulation and elongation. This complex also plays a role in histone modification. | Transcriptional elongation;  Histone/[31-33] |
| RTF1  Chromosome 15 | *RTF1 homolog, Paf1/RNA polymerase II complex component.* This locus may represent a gene involved in regulation of transcription elongation and chromatin remodeling, based on studies of similar proteins in other organisms. | Transcription  Chromatin/[31-33] |
| CDC73  Chromosome 1 | *Cell division cycle 73.* This gene encodes a tumor suppressor that is involved in transcriptional and post-transcriptional control pathways. The protein is a component of the the PAF complex, which associates with the RNA polymerase II subunit POLR2A and with a histone methyltransferase complex. This protein appears to facilitate the association of 3' mRNA processing factors with actively-transcribed chromatin. | Transcription;  Histone methyltransferase/[31-33] |
| CCNK  Chromosome 14 | *Cyclin K.* The protein encoded by this gene is a member of the transcription cyclin family. These cyclins may regulate transcription through their association with and activation of cyclin-dependent kinases (CDK) that phosphorylate the C-terminal domain (CTD) of the large subunit of RNA polymerase II. This gene product may play a dual role in regulating CDK and RNA polymerase II activities. | Transcription/[31-33] |
| CDK13  Chromosome 7 | *Cyclin-dependent kinase 13.* The encoded protein is a member of the cyclin-dependent serine/threonine protein kinase family. Members of this family function as master switches in cell cycle control. The exact function of this protein has not yet been determined, but it may play a role in mRNA processing. | Cell cycle regulation;  mRNA processing/[31-33] |

\*There are four mitochondrial translational elongation PPI networks in Figure 5c. Only some of the proteins belonging to these networks are fully described in the table.

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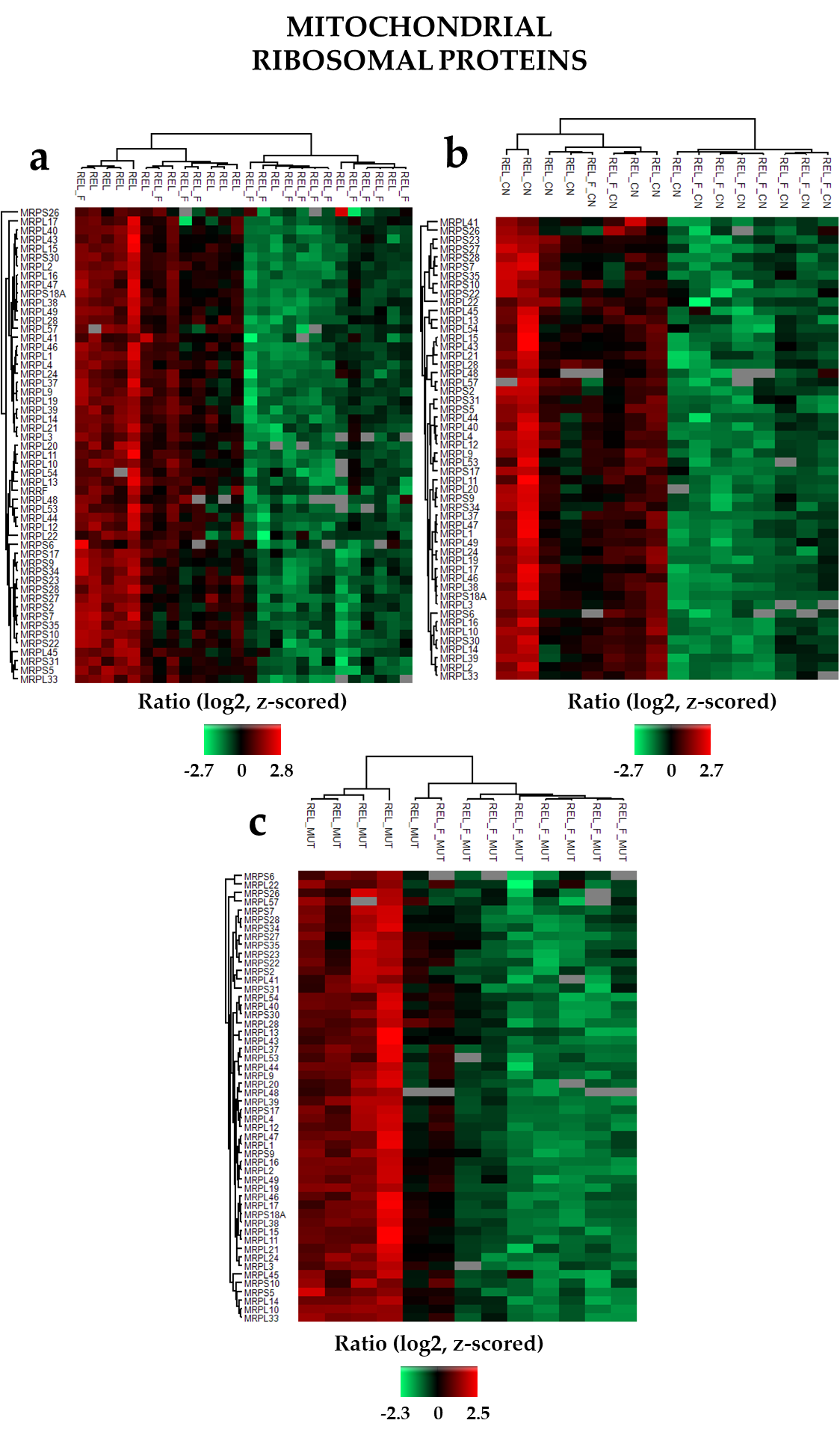
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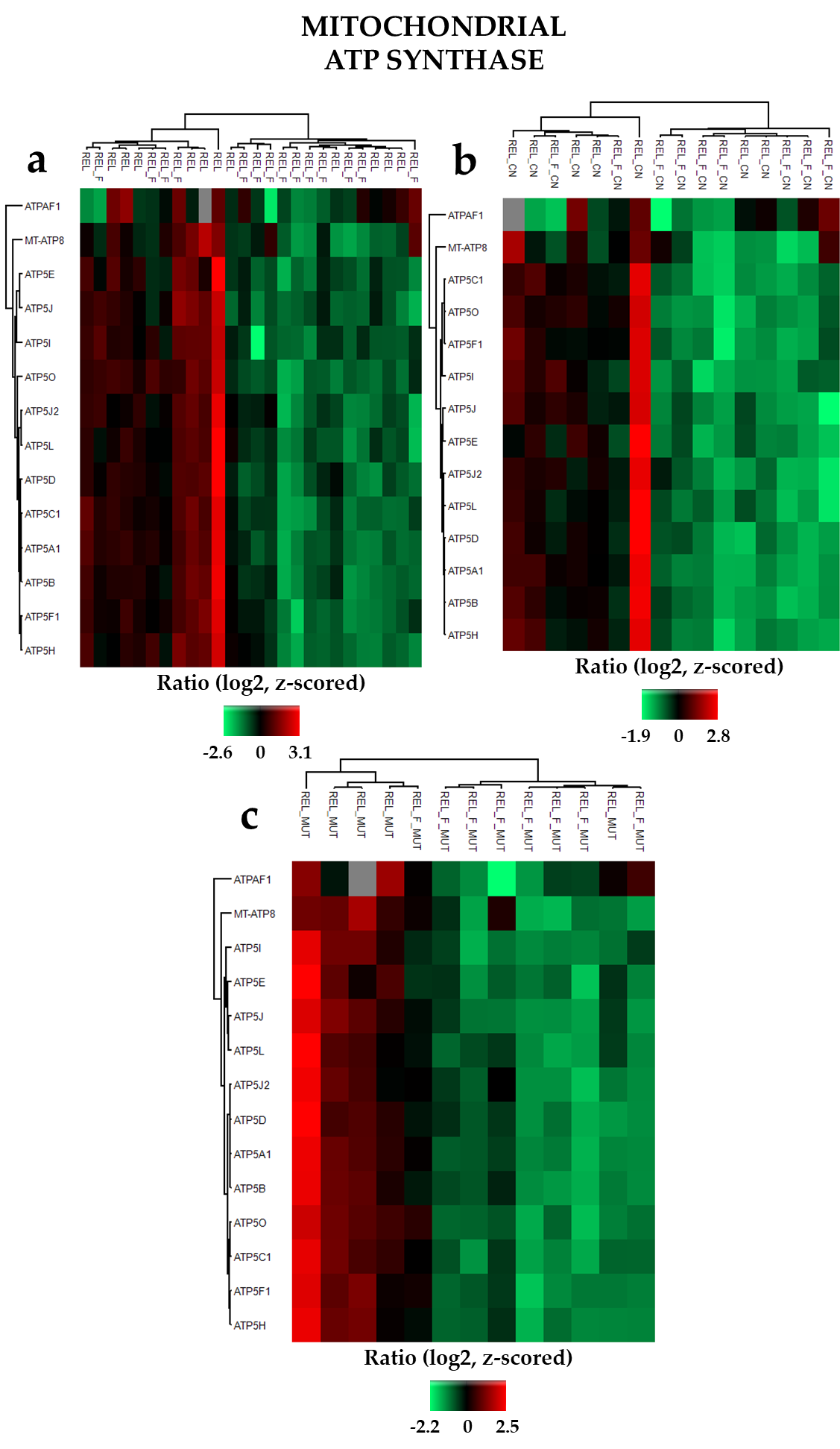
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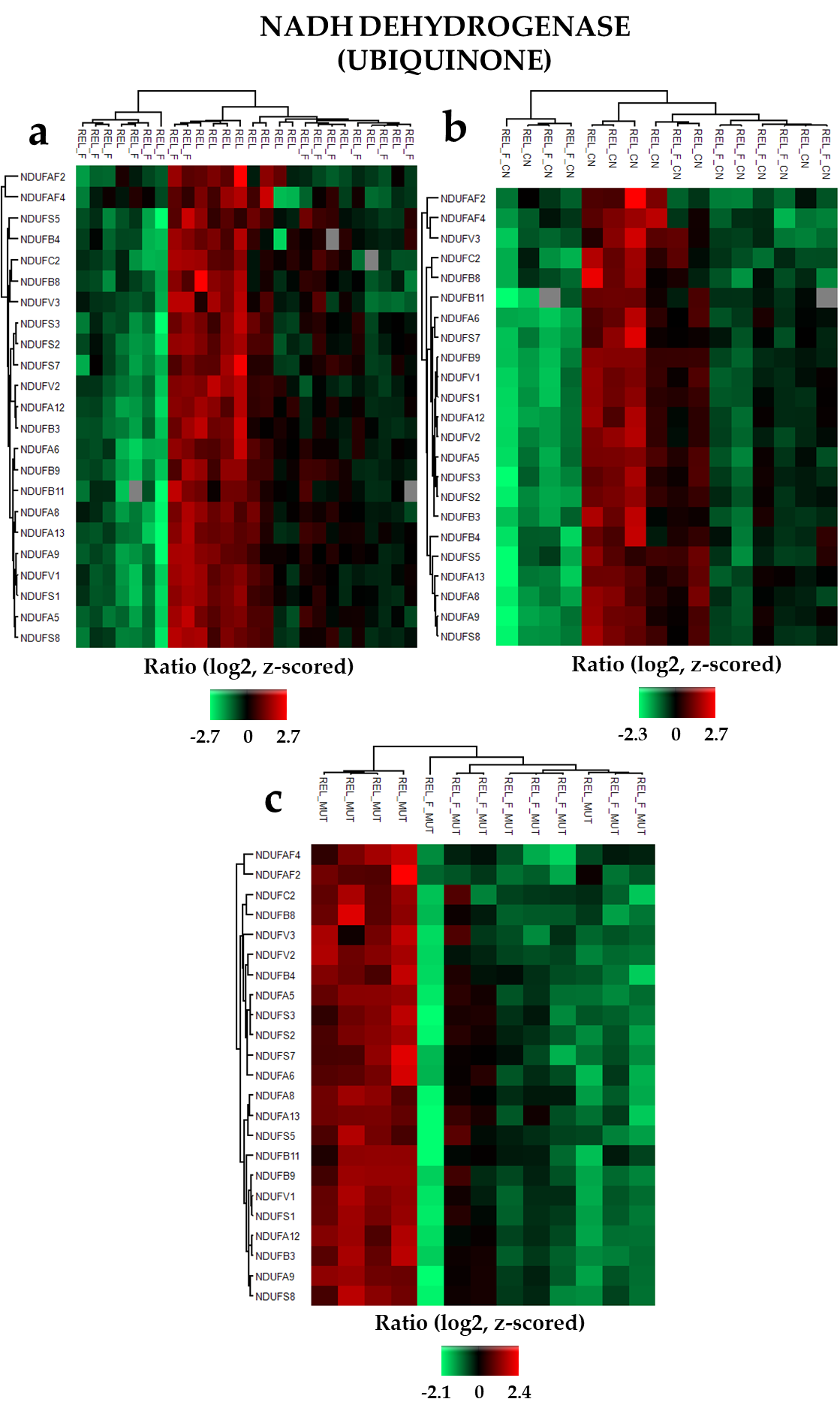
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**Figure S1.** Hierarchical clustering of all M4/M5-FAB classified relapse (REL) and relapse-free (REL\_F) patients (**a**), M4/M5-FAB classified REL and REL\_F patients with normal cytogenetics -CN- (**b**), and M4/M5-FAB classified REL and REL\_F patients with *NPM1* Ins mutation -MUT- **(c**), based on the expression of mitochondrial ribosomal proteins with a significantly different regulation identified by ANOVA.

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**Figure S2.** Hierarchical clustering of all M4/M5-FAB classified relapse (REL) and relapse-free (REL\_F) patients (**a**), M4/M5-FAB classified REL and REL\_F patients with normal cytogenetics -CN- (**b**), and M4/M5-FAB classified REL and REL\_F patients with *NPM1* Ins mutation -MUT- **(c**), based on the expression of mitochondrial ATP synthase proteins with a significantly different regulation identified by ANOVA.



**Figure S3.** Hierarchical clustering of all M4/M5-FAB classified relapse (REL) and relapse-free (REL\_F) patients (**a**), M4/M5-FAB classified REL and REL\_F patients with normal cytogenetics -CN- (**b**), and M4/M5-FAB classified REL and REL\_F patients with *NPM1* Ins mutation -MUT- **(c**), based on the expression of NADH dehydrogenase (ubiquinone) proteins with a significantly different regulation identified by ANOVA.