

Mitochondrial DNA in pediatric leukemia patients

Agata Kodroń¹✉, Magda Ghanim¹, Katarzyna K. Krawczyk¹,
Anna Stelmaszczyk-Emmel², Katarzyna Tońska¹, Urszula Demkow² and Ewa Bartnik^{1,3}✉

¹Institute of Genetics and Biotechnology, Faculty of Biology, University of Warsaw, Warsaw, Poland; ²Department of Laboratory Diagnostics and Clinical Immunology of Developmental Age, Medical University of Warsaw, Warsaw, Poland; ³Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland

Numerous studies of mitochondrial DNA (mtDNA) in cancer have shown differences between mtDNA sequences in tumor and normal tissue and at various stages of cancer treatment in the same patient. However, there is little data on acute lymphoblastic leukemia (ALL), the most common type of leukemia in children. In this study we compared mitochondrial sequence variation in the D-loop region and in 5 genes of mtDNA in bone marrow samples of 6 pediatric patients with ALL at various stages of therapy. We found several common polymorphisms and one variant at position 3688 whose level varied during leukemia treatment. Our results suggest that mitochondrial DNA mutations, whose levels change during patient treatment, could be potential biomarkers for monitoring treatment efficacy and disease progression.

Key words: pediatric ALL, mtDNA, chemotherapy

Received: 20 October, 2016; revised: 11 November, 2016; accepted: 06 December, 2016; available on-line: 09 March, 2017

✉ e-mail: ebartnik@igib.uw.edu.pl (EB), agatakodron@wp.pl (AK)

Abbreviations: mtDNA, mitochondrial DNA; ALL, acute lymphoblastic leukemia; D-loop, displacement loop

Appendix 1.

Table 3. Summary of mtDNA sequence variation in bone marrow cells from pediatric leukemia patients without prior chemotherapy.

Patient	Nucleotide position	Gene/Region	Change	Hetero/homoplasmic	Result	
P1	152	D loop	T>C	Homoplasmic	Polymorphism	
	263	D loop	A>G	Homoplasmic	Polymorphism	
	16519	D loop	T>C	Homoplasmic	Polymorphism	
	8860	ATPase6	A>G	Homoplasmic	Thr>Ala Polymorphism	
	9071	ATPase6	C>T	Homoplasmic	Ser>Leu Polymorphism	
	15326	cytB	A>G	Homoplasmic	Thr>Ala Polymorphism	
P2	73	D loop	A>G	Homoplasmic	Polymorphism	
	150	D loop	C>T	Homoplasmic	Polymorphism	
	195	D loop	T>C	Homoplasmic	Polymorphism	
	215	D loop	A>G	Homoplasmic	Polymorphism	
	263	D loop	A>G	Homoplasmic	Polymorphism	
	295	D loop	C>T	Homoplasmic	Polymorphism	
	319	D loop	T>C	Homoplasmic	Polymorphism	
	489	D loop	T>C	Homoplasmic	Polymorphism	
	514	D loop	CA insertion	Homoplasmic	Polymorphism	
	16069	D loop	C>T	Homoplasmic	Polymorphism	
	16126	D loop	T>C	Homoplasmic	Polymorphism	
	16145	D loop	G>A	Homoplasmic	Polymorphism	
	16231	D loop	T>C	Homoplasmic	Polymorphism	
	16261	D loop	C>T	Homoplasmic	Polymorphism	
		3688	ND1	G>A	Heteroplasmic	Ala>Thr Unknown
		4216	ND1	T>C	Homoplasmic	Tyr>His Polymorphism
		7789	COXII	G>A	Homoplasmic	Polymorphism
		8860	ATPase6	A>G	Homoplasmic	Thr>Ala Polymorphism
	15257	cytB	G>A	Homoplasmic	Asp>Asn Polymorphism	
	15326	cytB	A>G	Homoplasmic	Thr>Ala Polymorphism	
	15452	cytB	C>A	Homoplasmic	Leu-Ile Polymorphism	
P3	263	D loop	A>G	Homoplasmic	Polymorphism	
	3505	ND1	A>G	Homoplasmic	Thr>Ala Polymorphism	
	8860	ATPase6	A>G	Homoplasmic	Thr>Ala Polymorphism	
	15326	cytB	A>G	Homoplasmic	Thr>Ala Polymorphism	
	15758	cytB	A>G	Homoplasmic	Ile>Val Polymorphism	
P4	73	D loop	A>G	Homoplasmic	Polymorphism	
	263	D loop	A>G	Homoplasmic	Polymorphism	
	303	D loop	1C insertion	Homoplasmic	Polymorphism	
	4216	ND1	T>C	Homoplasmic	Tyr>His Polymorphism	
	8697	ATPase8	G>A	Homoplasmic	Met>Met Polymorphism	
	8715	ATPase6	T>C	Homoplasmic	Thr>Thr Polymorphism	

Table 3a. Summary of mtDNA sequence variation in bone marrow cells from pediatric leukemia patients without prior chemotherapy.

Patient	Nucleotide position	Gene/Region	Change	Hetero/homoplasmic	Result
P4	8860	ATPase6	A>G	Homoplasmic	Thr >Ala Polymorphism
	14905	cytB	G>A	Homoplasmic	Met>Met Polymorphism
	15257	cytB	G>A	Heteroplasmic	Asp>Asn Polymorphism
	15326	cytB	A>G	Homoplasmic	Thr>Ala Polymorphism
	15452	cytB	C>A	Homoplasmic	Leu>Ile Polymorphism
	15607	cytB	A>G	Homoplasmic	Lys>Lys Polymorphism
	16126	D loop	T>C	Homoplasmic	Polymorphism
	16294	D loop	C>T	Homoplasmic	Polymorphism
	16296	D loop	C>T	Homoplasmic	Polymorphism
	16519	D loop	T>C	Homoplasmic	Polymorphism
P5	73	D loop	A>G	Homoplasmic	Polymorphism
	152	D loop	T>C	Homoplasmic	Polymorphism
	185	D loop	G>A	Homoplasmic	Polymorphism
	228	D loop	G>A	Homoplasmic	Polymorphism
	263	D loop	A>G	Homoplasmic	Polymorphism
	295	D loop	C>T	Homoplasmic	Polymorphism
	462	D loop	C>T	Homoplasmic	Polymorphism
	489	D loop	T>C	Homoplasmic	Polymorphism
	546	D loop	A>G	Homoplasmic	Polymorphism
	4216	ND1	T>C	Homoplasmic	Tyr>His Polymorphism
	8860	ATPase6	A>G	Homoplasmic	Thr >Ala Polymorphism
	14766	cytB	C>T	Heteroplasmic	Leu>Leu Polymorphism
	14798	cytB	T>C	Homoplasmic	Phe>Leu Polymorphism
	15326	cytB	A>G	Homoplasmic	Thr >Ala Polymorphism
	15452	cytB	C>A	Homoplasmic	Leu>Ile Polymorphism
15706	cytB	A>G	Homoplasmic	Leu>Leu Polymorphism	
16069	D loop	C>T	Homoplasmic	Polymorphism	
16126	D loop	T>C	Homoplasmic	Polymorphism	
16261	D loop	C>T	Homoplasmic	Polymorphism	
P6	73	D loop	A>G	Homoplasmic	Polymorphism
	152	D loop	T>C	Homoplasmic	Polymorphism
	189	D loop	A>G	Homoplasmic	Polymorphism
	194	D loop	C>T	Homoplasmic	Polymorphism
	195	D loop	T>C	Homoplasmic	Polymorphism
	204	D loop	T>C	Homoplasmic	Polymorphism
	207	D loop	G>A	Homoplasmic	Polymorphism
	263	D loop	A>G	Homoplasmic	Polymorphism
	303	D loop	1C insertion	Homoplasmic	Polymorphism
	3505	ND1	A>G	Homoplasmic	Thr>Ala Polymorphism
	8251	ATPase8	G>A	Homoplasmic	Gly>Gly Polymorphism

Table 3b. Summary of mtDNA sequence variation in bone marrow cells from pediatric leukemia patients without prior chemotherapy.

Patient	Nucleotide position	Gene/Region	Change	Hetero/homoplasmic	Result
P6	8860	ATPase6	A>G	Homoplasmic	Thr >Ala Polymorphism
	8994	ATPase6	G>A	Homoplasmic	Leu>Leu Polymorphism
	14766	cytB	C>T	Homoplasmic	Ile>Thr Polymorphism
	15106	cytB	G>A	Homoplasmic	Leu>Leu Polymorphism
	15326	cytB	A>G	Homoplasmic	Thr>Ala Polymorphism
	15784	cytB	T>C	Homoplasmic	Pro>Pro Polymorphism
	15884	cytB	G>C	Homoplasmic	Ala>Thr Polymorphism
	16223	D loop	C>T	Homoplasmic	Polymorphism
	16292	D loop	C>T	Homoplasmic	Polymorphism
	16519	D loop	T>C	Homoplasmic	Polymorphism