ANIMAL MODELS OF MITOCHONDRIAL DISEASES

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Introduction

Mitochondrial diseases are a group of chronic diseases caused by mutations which lead to mitochondrial dysfunction. Mice are the main species used to create models for these diseases.

Objectives

- Set a conceptual basis to understand mitochondrial diseases.
- Describe some of the models used in their study and how they are created.
- Expose some conclusions about the importance of these models and the current situation of these diseases.

	Mouse Model	Genetic modification
mtDNA	Mito-mice (Kearns-Sayre síndrome)	Cytoplasmic hybrid introducing mutant mtDNA into embryo (Deletion in various genes)
	LHON disease	Cytoplasmic hybrid introducing mutant mtDNA into embryo (ND6 gene)
nDNA	Mrps34 (Leigh syndrome)	Point mutation induced by N-ethyl-N-nitrosourea (MRPS34 gene)
	RNAseH1 (CPEO)	Knock-out (RNASEH1 gene)
	TK2 (MDS)	Knock-in (TK2 gene)
	MTO1 (COXPD10)	Knock-down (MTO1 gene)

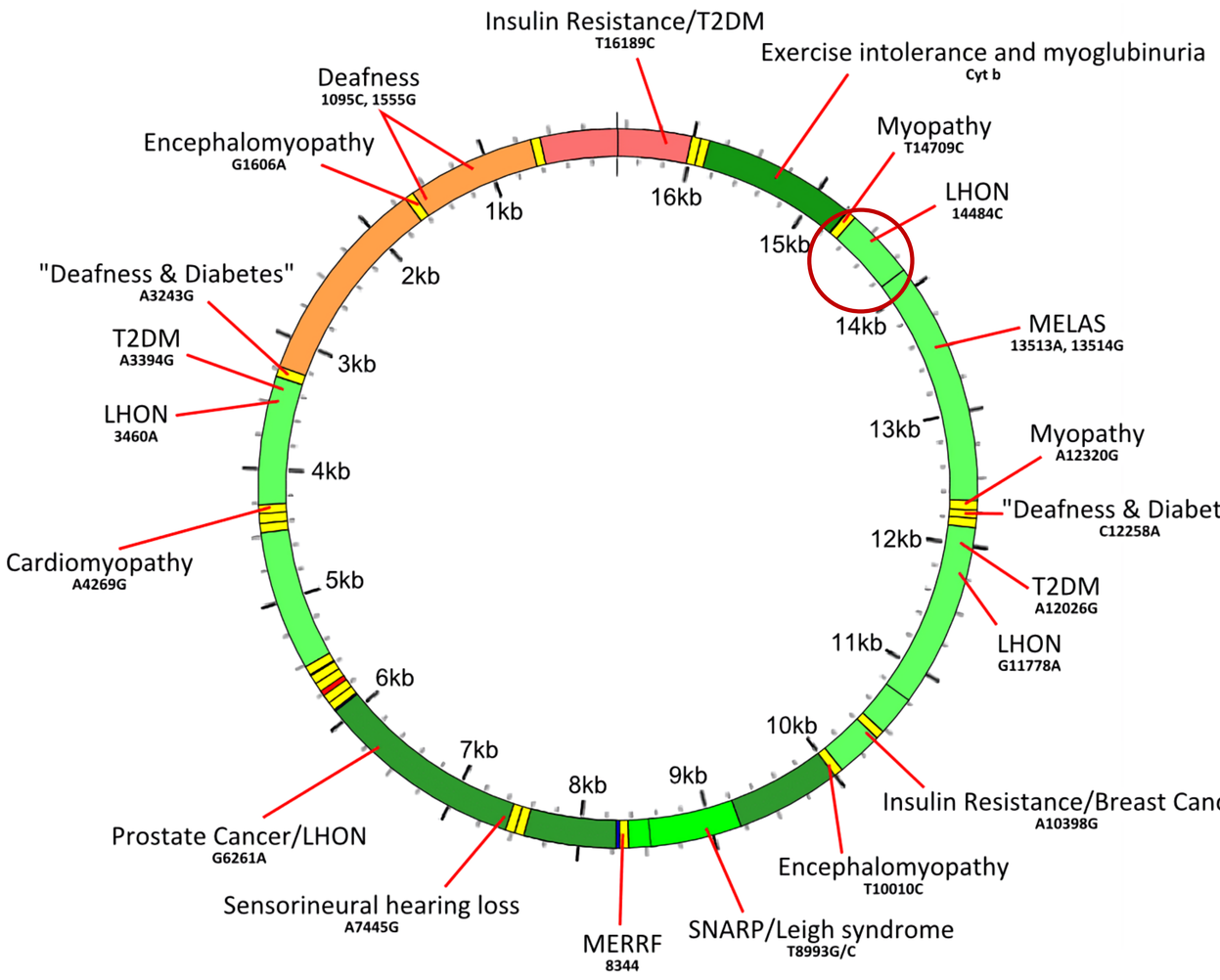

Figure 1. Mitochondrial genome. Adapted from www.wikipedia.com.

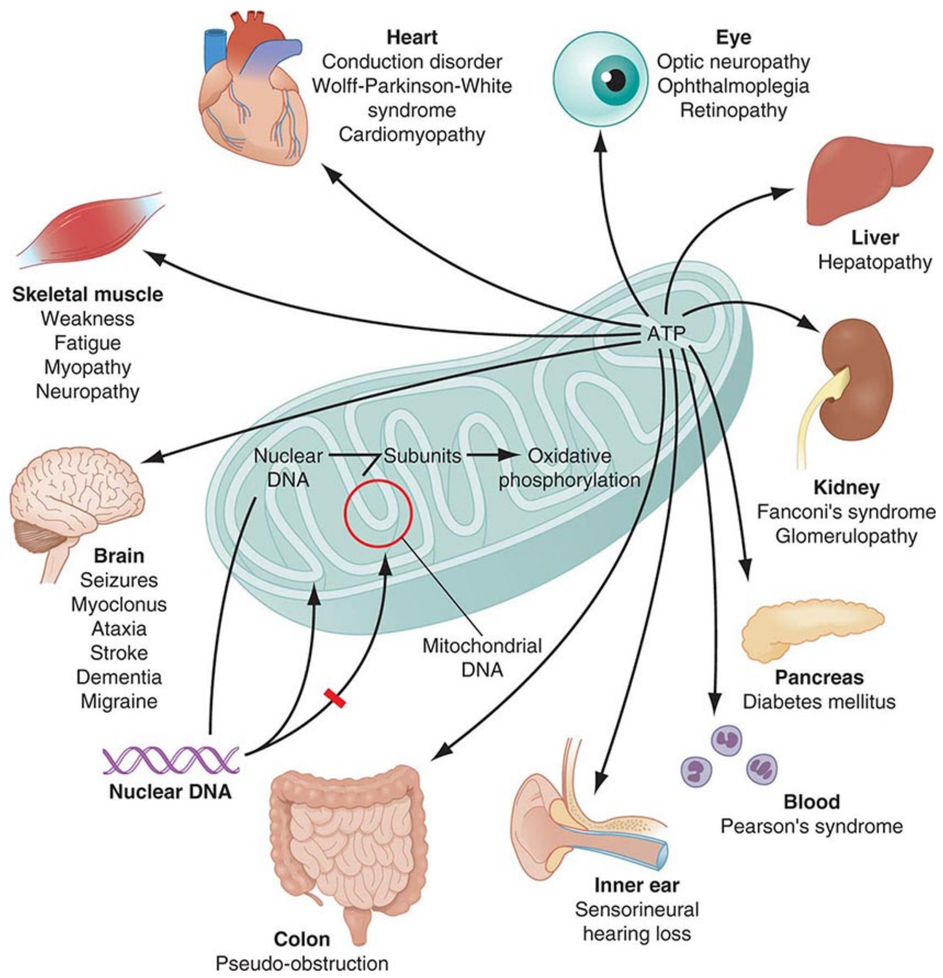

Figure 2. Multiple organ manifestations of mitochondrial disease. Image source: www.clinicalgate.com

Conclusions

- Still many challenges, mainly developing therapies.
- Next-generation sequencing has helped a lot in the diagnosis.
- Animal models are essential to understand the patophysiology of these diseases and to perform clinical trials.
- Still a lot of investigation needed.