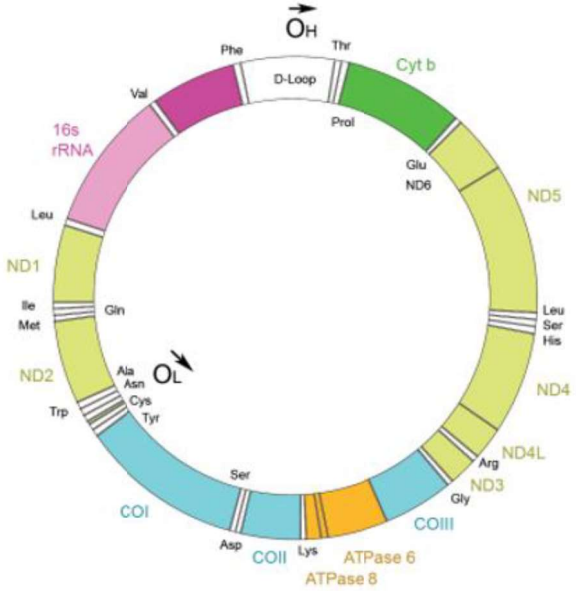
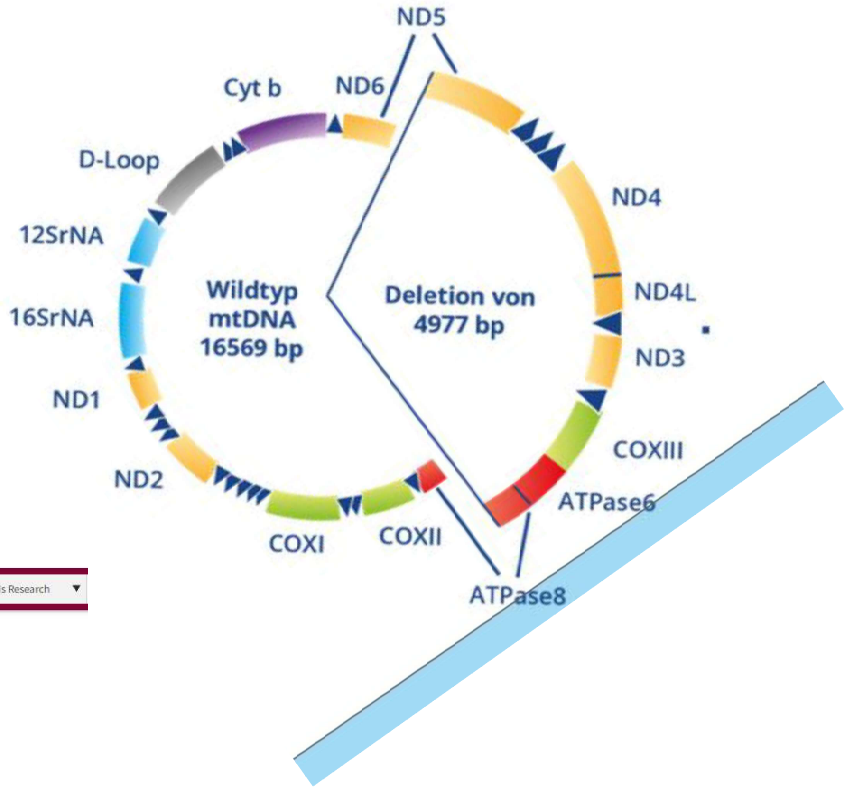
The “common deletion” mDNA^{4977} is caused by oxidative stress

Oxidative stress





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Article Contents

Abstract
INTRODUCTION
MATERIALS AND METHODS
RESULTS
DISCUSSION
FUNDING
ACKNOWLEDGEMENTS
REFERENCES

JOURNAL ARTICLE

Oxidative stress induces degradation of mitochondrial DNA

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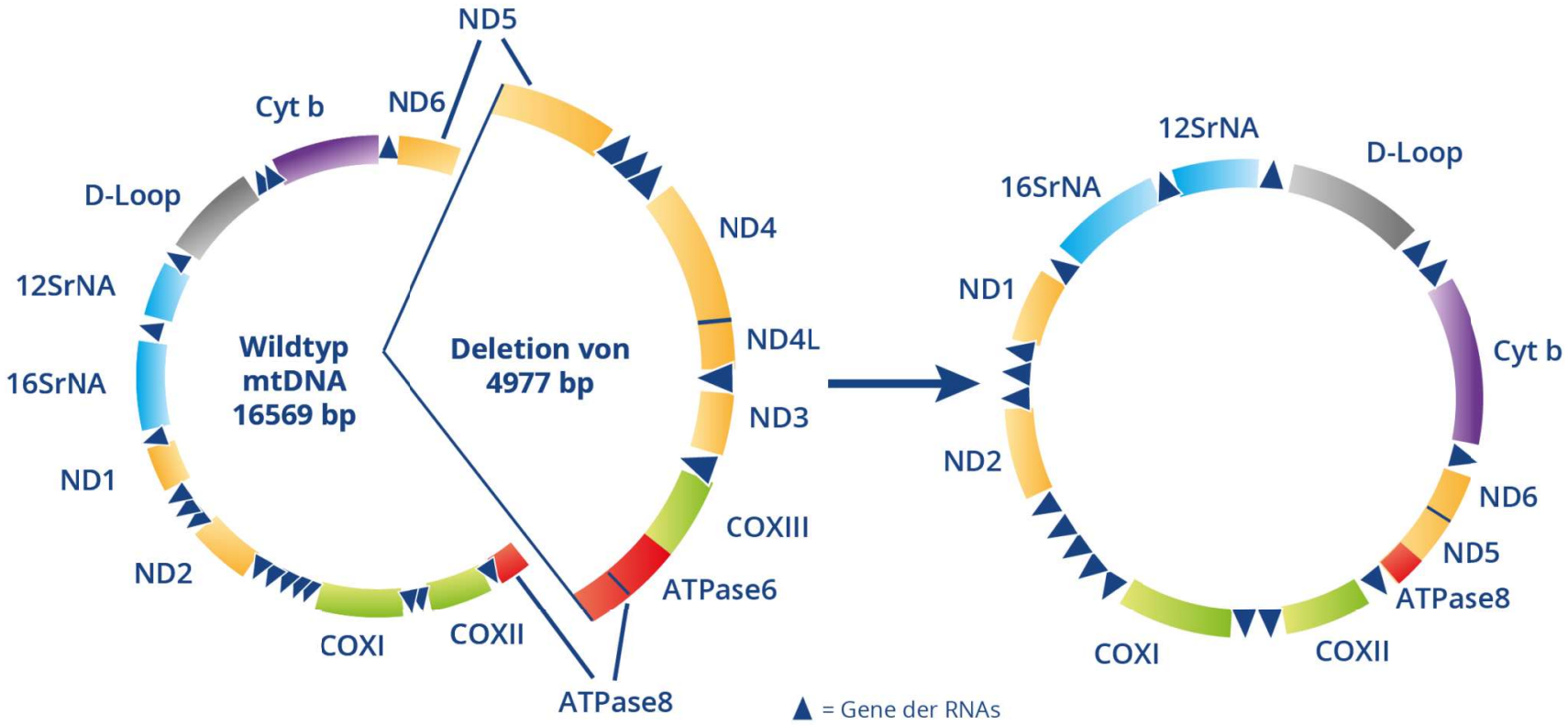
Abstract

Mitochondrial DNA (mtDNA) is located in close proximity of the respiratory chains, which are the main cellular source of reactive oxygen species (ROS). ROS can induce oxidative base lesions in mtDNA and are believed to be an important cause of the mtDNA mutations, which accumulate with aging and in diseased states. However, recent studies indicate that cumulative levels of base substitutions in mtDNA can be very low even in old individuals. Considering the reduced complement of DNA repair pathways available in mitochondria and higher susceptibility of mtDNA to oxidative damage than nDNA, it is presently

Source: MMD GmbH & Co KG Author Prof. Dr. Brigitte König

This can be measured, and shows the degree of oxidative stress the mitochondria are suffering …

Oxidative stress



Before deletion
Wildtype mtDNA = 16569 base pairs

After deletion
mtDNA = 11562 base pairs

Source: MMD GmbH & Co KG Author Prof. Dr. Brigitte König

… as well as any damage to mitochondrial DNA

Deletion mutant 4977

Oxidative stress

Example 1:

Mitochondrial 4977 Deletion mutant (mt4977del) **1.03E+06**



Number of copies of non-mutated mtDNA to 1 copy mt4977del



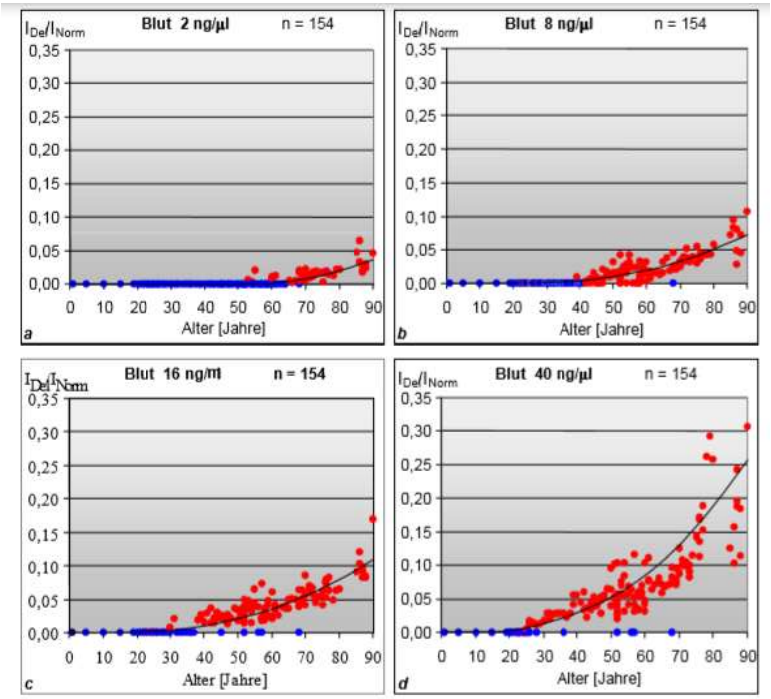
The mitochondrial deletion mutant mt4977bp is noticeably enhanced. This indicates oxidative stress and damage to mitochondrial DNA.

Among mtDNA deletions, one of the most vital that causes huge destruction of almost one third in length of the mitochondrial genome is the 4977-bp mtDNA deletion ($mDNA^{4977}$). This is one of the best-described large-scale mtDNA deletions, and has been found to accumulate in numerous disorders (literature available upon request). It is often known as a “common deletion” due to the frequency with which it has been reported. The deleted region encodes seven polypeptides essential for the OXPHOS pathway: four for Complex I, one for Complex IV, and two for Complex V. **This can cause complete failure of ATP production in the mitochondria affected.**

Action can be taken: it can be reversed …

Oxidative stress

Mitochondrial DNA – common deletion



DNA test	result	reference range
Mitochondrial 4977 Deletion mutant (mt4977del)	6.44E+05	

Number of copies of non-mutated mtDNA to 1 copy mt4977del

Reference range mt4977del			
<1E+06	1E+06 - 1E+07	>1E+07	>1E+08

The mitochondrial deletion mutant mt4977bp **is detectable at a greatly increased level. This indicates mitochondria with a lack of ability to generate ATP and greatly increased oxidative stress.**

Significantly increased **Undetectable**

This is not an inherited polymorphism: it arises due to endogenous and exogenous factors, especially oxidative stress. This is why checking for it can be very useful, as measures can be taken to reduce the levels, and repeat tests document a decline in levels if the initiatives are successful.

Source: MMD GmbH & Co KG Author Prof. Dr. Brigitte König