Association between genetic variants in the Coenzyme Q$_{10}$ metabolism and Coenzyme Q$_{10}$ status in humans

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Abstract

**Background:** Coenzyme Q$_{10}$ (CoQ$_{10}$) is essential for mitochondrial energy production and serves as an antioxidant in extramitochondrial membranes. The genetics of primary CoQ$_{10}$ deficiency has been described in several studies, whereas the influence of common genetic variants on CoQ$_{10}$ status is largely unknown. Here we tested for non-synonymous single-nucleotide polymorphisms (SNP) in genes involved in the biosynthesis (CoQ$_3$G272S, CoQ$_6$M406V, CoQ$_7$M103T), reduction (NQO1P187S, NQO2L47F) and metabolism (apoE3/4) of CoQ$_{10}$ and their association with CoQ$_{10}$ status. For this purpose, CoQ$_{10}$ serum levels of 54 healthy male volunteers were determined before (T$_0$) and after a 14 days supplementation (T$_{14}$) with 150 mg/d of the reduced form of CoQ$_{10}$.

**Findings:** At T$_0$, the CoQ$_{10}$ level of heterozygous NQO1P187S carriers were significantly lower than homozygous S/S carriers (0.93 ± 0.25 μM versus 1.34 ± 0.42 μM, p = 0.044). For this polymorphism a structure homology-based method (PolyPhen) revealed a possibly damaging effect on NQO1 protein activity. Furthermore, CoQ$_{10}$ plasma levels were significantly increased in apoE4/E4 genotype after supplementation in comparison to apoE2/E3 genotype (5.93 ± 0.151 μM versus 4.38 ± 0.792 μM, p = 0.034). Likewise heterozygous CoQ$_3$G272S carriers had higher CoQ$_{10}$ plasma levels at T$_{14}$ compared to G/G carriers but this difference did not reach significance (5.30 ± 0.96 μM versus 4.42 ± 1.67 μM, p = 0.082).

**Conclusions:** In conclusion, our pilot study provides evidence that NQO1P187S and apoE polymorphisms influence CoQ$_{10}$ status in humans.

Background

Coenzyme Q$_{10}$ (CoQ$_{10}$) is the predominant form of endogenous ubiquinone in humans. Synthesized in the mitochondrial inner membrane, CoQ$_{10}$ is comprised of a ubiquinone head group attached to a trial of 10 five-carbon isoprenoid units, that anchors the molecule to the membranes [1]. Intracellular synthesis is the major source of CoQ$_{10}$, however it can also be acquired through the diet and dietary supplements [2]. CoQ$_{10}$ acts in the respiratory chain and is necessary for pyrimidine biosynthesis as well as a cofactor of uncoupling proteins [3]. CoQ$_{10}$ has been also identified as a modulator of gene expression [4-6], inflammatory processes [7-9] and apoptosis [10,11].

The CoQ$_{10}$ biosynthetic pathway comprises 10 steps, including methylations, decarboxylations, hydroxylations and isoprenoid synthesis and transfer [12]. The elucidation of this pathway was mainly due to studies in respiration-deficient mutants of *E. coli* and *S. cerevisiae* [13,14]. In humans, rare genetic variants in genes encoding enzymes of CoQ$_{10}$ synthesis causes mitochondrial dysfunction, as CoQ$_{10}$ carries electrons from complex I and complex II to complex III in the mitochondrial respiratory chain. Several forms of human CoQ$_{10}$ deficiencies were characterized by infantile encephalomyopathy, renal failure, cerebellar ataxia or myopathy [15-17].

The complexity of CoQ$_{10}$ biosynthesis suggests that genetic defects in different biosynthetic enzymes or regulatory proteins may cause different clinical syndromes. Although several studies have been undertaken to look...
into primary CoQ₁₀ deficiency, the influence of common genetic variants on CoQ₁₀ status is largely unknown. Therefore a proof of principle study in humans was performed to associate single nucleotide polymorphisms (SNPs) in genes encoding proteins of CoQ₁₀ biosynthesis, reduction and metabolism with CoQ₁₀ status before and after supplementation.

**Methods**

**Participants and study design**

Sample characteristics of subjects and study design have been recently described [18]. In short: 54 healthy male volunteers received 150 mg of the reduced form of CoQ₁₀ (ubiquinol, KANEKA Corporation, Japan) daily in form of three capsules with each principal meal for 14 days. Fasting blood samples were taken before (T₀) and after (T₁₄) supplementation with ubiquinol from all study participants. The participants, aged 30.1 ± 6.7 years, had an average Body Mass Index (BMI) of 24.1 ± 2.5, no history of gastrointestinal, hepatic, cardiovascular or renal diseases, a habit of non- or occasional smoking (≤ 3 cigarettes/day) and maintenance of usual nutrition habits. The study was approved by the ethics committee of the Medical Faculty of Kiel University, Germany, and was conformed to Helsinki Declaration. All volunteers gave written informed consent.

**Genotyping**

Genomic DNA was isolated from whole blood samples. Genotyping of all SNPs investigated (Table 1) was performed with the TaqMan system. Fluorescence was measured with ABI Prism 7900 HT sequence detection system (ABI, Foster City, USA).

**HPLC analysis**

CoQ₁₀ analysis was based on the method of high-pressure liquid chromatography (HPLC) with electrochemical detection and internal standardisation using ubihydroquinone-9 and ubiquinone-9 as standards and has been described elsewhere [18].

**Statistical analysis**

Data are expressed as means ± SD. Differences in the characteristics of the study population between two genotype groups were examined using the Student t-test and additionally for CoQ₆[^M406V] the χ²-test in a dominant genetic model. To determine statistical significance between all genotypes, test for linear trend in one way analysis of variance (ANOVA) was performed. P-values ≤ 0.05 were considered statistically significant and all statistical analyses were computed using SPSS (Version 13.0). In order to analyze the impact of non-synonymous SNPs on the structure and function of proteins, PolyPhen server [19] was used. For power calculation, the GPower program (Version 3.1) was applied.

**Results and Discussion**

**Selection of genes and single nucleotide polymorphisms**

In order to identify common SNPs which may be associated with the CoQ₁₀ status, we searched in the HapMap data base for non-synonymous variants in genes which are involved in CoQ₁₀ biosynthesis and metabolism. As shown in table 1, we selected SNPs in the CoQ₃ (rs6925344, C>T, Gly272Ser), CoQ₆ (rs8500, A>G, Met406Val) and CoQ₇ (rs11074359, T>C, Met103Thr) gene. These genes code for enzymes of CoQ₁₀ biosynthesis. Functional variants [20,21] in the NQO1 (rs1800566, C>T, Pro187Ser) and NQO2 (rs1143684, T>C, Leu47Phe) gene were also included, as the encoded NAD(P)H:quinone oxidoreductases are involved in the recycling of CoQ₁₀. Furthermore they protect cells from oxidative damage by catalyzing reduction of carcinogenic quinone compounds to their hydroquinone forms [22]. Two SNPs determining the apolipoprotein E (apoE) haplotypes E2, E3 and E4 (rs429358, rs7412) were further included. Both SNPs led to an amino acid change from cysteine to arginine at position 112 (rs429358) and 158 (rs7412), which gives rise to six possible diplotypes: E2/E2, E2/E3, E2/E4, E3/E3, E3/E4 and E4/E4. The apoE diplotypes have been associated with cholesterol metabolism [23,24], atherosclerosis [25], inflammation [26], lipid peroxidation [27] and longevity [28].

**Genotype distributions in the cohort**

The selected SNPs were genotyped in 54 healthy male volunteers. The obtained genotype distribution (Figure 1 and 2) were in accordance to the HapMap data base for non-synonymous variants in genes which are involved in CoQ₁₀ biosynthesis and metabolism.
for G/S (25%) and 1 homozygous for S/S (2%), while 1 sample failed genotyping. Analysis of the CoQ6 M406V genotype showed 19 homozygous for M/M (36%), 24 heterozygous for M/V (44%) and 11 homozygous for V/V (20%). Genotyping of CoQ7 M103T polymorphism revealed 25 M/M (48%), 17 M/T (33%) and 10 T/T (19%) carriers.

Two samples failed genotyping. Concerning the distribution of the NQO1 P187S SNP, 30 persons are carriers of two P/P alleles (56%), 22 persons were heterozygous with one P and one S allele (41%) and two participants were carriers of two S/S alleles (3%). NQO2 L47F genotyping displayed 35 participants were homozygous L/L carriers.

Figure 1 Effect of amino acid exchange polymorphisms on CoQ10 plasma levels. SNPs in genes encoding enzymes of the CoQ10 synthesis pathway (CoQ3 G272S, CoQ6 M406V, CoQ7 M103T) before (T0) and after (T14) ubiquinol supplementation (150 mg/day) in humans are shown. Values are mean ± SD and n numbers (genotype distribution) are given in brackets. Differences between two genotype groups were examined using Student t-test and between all genotypes using "test for linear trend" (ANOVA).
(65%), 15 participants were heterozygous for L/F (28%) and 4 participants were homozygous F/F carriers (7%). The genotype distribution of apoE was as follows: 1 person with E2/E2 genotype (2%), 7 persons with E2/E3 (14%), 29 persons with E3/E3 (58%), 11 persons with E3/E4 (22%) and 2 persons with E4/E4 (4%). For 4 persons, genotyping of one or both SNPs respectively failed. Thus, the Apo E genotype distribution in our cohort of 54 healthy men was comparable with previously published data [29,30].
Table 2 Total CoQ10 distribution in a chi-square crosstabulation as a function of CoQ6<sup>M406V</sup> genotype (rs8500)

| CoQ6 (rs8500) | Pearson $\chi^2$ | $< 0.96$ (μmol/L) | $> 0.96$ (μmol/L) | Total |
|---------------|------------------|--------------------|-------------------|-------|
| M/M           |                  | 7                  | 12                | 19    |
| M/V+V/V       |                  | 21                 | 13                | 34    |
| Total         |                  | 28                 | 25                | 53    |

Person Chi-Square $\chi^2$: $p = 0.081$

Distribution was calculated according to a dominant model. CoQ10 mean value of 0.96 μmol/L was used for group classification.

Association between genotypes and CoQ10 level at baseline T0 and after supplementation T14 with the reduced form of CoQ10

As previously described [18], 54 healthy male volunteers received 150 mg of the reduced form of CoQ10 daily in form of three capsules with each principal meal for 14 days. This supplementation led to a significant 4-fold increase in total CoQ10 plasma levels at T14 (4.60 ± 1.55 μmol/L) compared to T0 (0.96 ± 0.31 μmol/L) [18]. As shown in Figure 1 and 2, SNPs determined in the CoQ7 and NQO2 genes were not associated with total CoQ10 levels. Trend analysis (ANOVA) over all genotype variants of CoQ7<sup>M103T</sup> and NQO2<sup>T47T</sup> revealed $p$ values $>0.05$ and were therefore considered as not significant.

CoQ3<sup>G272S</sup>

The COQ3 gene encodes an O-methyltransferase required for two steps in the biosynthetic pathway of CoQ10 [31]. Analysing CoQ3 rs6925344 SNP in association to plasma CoQ10 levels at T0, no significant differences between genotypes could be revealed. Yet at T14, G/S carriers in CoQ3<sup>G272S</sup> genotype had a higher total CoQ10 content (5.30 ± 0.96 μmol/L) after supplementation compared to G/G carriers (4.42 ± 1.67 μmol/L) with borderline significance ($p = 0.082$, t-test).

CoQ6<sup>M406V</sup>

CoQ6 is mapped to human chromosome 14q24.3 and encodes a monoxygenase, which is required in CoQ10 biosynthesis for incorporation of oxygen to the benzoquinone ring [32]. CoQ10 plasma levels were not significantly changed within genotype distribution of CoQ6 rs8500 SNP before (T0) and after (T14) supplementation. However, considering total CoQ10 distribution at T0 in a chi-square cross tabulation as a function of CoQ6 rs8500 genotype (Table 2) a person chi-square $\chi^2$ value of $p = 0.081$ was evident, which again can be considered as marginal significant. Therefore a power calculation for CoQ6 genotype rs8500 was conducted using GPower program (Version 3.1). This disclosed a total of 898 individuals are required to receive 95% power.

NQO1<sup>P187S</sup>

It has been shown, that NQO1 can generate and maintain the reduced state of ubiquinones in membrane systems and liposomes, thereby promoting their antioxidant function [33,34]. NQO1<sup>P187S</sup> SNP was associated with CoQ10 levels at T0 (P/S versus S/S, $p = 0.044$). Thus, this pilot study indicates that Pro187Ser SNP in NQO1 gene could participate in abnormal CoQ10 metabolism. SNP prediction of functional effects of human nsSNPs with structure homology-based method (PolyPhen) revealed a possibly damaging effect of NQO1<sup>P187S</sup> SNP with a score of 0.215. However, genotype distribution of the S/S genotype was low ($n = 2$), which reflects the ethnic variation of this polymorphism with the highest prevalence of the S allele in East Asian populations (e.g. 22% prevalence in Chinese populations) and the lowest prevalence in Caucasians (4%) [35]. Furthermore Han et al [36] found a significant association of this SNP with carotid artery plaques in type 2 diabetic patients in east Asian populations. As this genetic variation may play a more significant role in an East Asian rather than in a Caucasian population, evaluation of the Pro187Ser SNP in association with CoQ10 metabolism in an East Asian population may be preferable.

apoE

Apolipoprotein E (apoE) is a polymorphic multifunctional protein with three common isoforms in humans (E2, E3 and E4). Presence of the apoE4 allele is associated with a 40-50% higher risk of cardiovascular disease [37]. There is increasing evidence demonstrating that the apoE4 allele may be associated with elevated oxidative stress and chronic inflammation [38]. Thus apoE was considered as a candidate gene explaining variance in CoQ10 status. At T0, total CoQ10 levels were higher in E4/E4 carriers as compared to all other genotype groups, however $p$ values did not reach significance ($p = 0.065$, E2/E3 vs E4/E4, Figure 2). These results confirm the results found by Battino et al [29] in a cohort of 106 healthy blood donors. Interestingly, in our study total CoQ10 levels increased significantly ($p = 0.034$) in E4/E4 carriers after supplementation (T14), which has to the best of our knowledge not been shown so far. Thus, E4/E4 carriers may be more responsive towards a dietary CoQ10 supplementation than non E2/E3 carriers. The underlying physiological and/or molecular mechanisms for this finding still need to be elucidated.

Conclusions

Taken together, our pilot study with 54 volunteers provides evidence that NQO1<sup>P187S</sup> and apoE polymorphisms may influence CoQ10 status in humans. According to our results and power calculation, larger cohorts are needed.
in further studies to determine the association between single nucleotide polymorphisms in genes encoding proteins of CoQ10 biosynthesis, reduction and metabolism and CoQ10 status.

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Authors’ contributions

AF analysed the data and wrote the manuscript. CS participated in the design of the study, acquired and analysed the data. GR participated in the design of the study and critically revised the manuscript. PN and TM carried out the CoQ10 measurements. FD was responsible for the concept and design of the study and the writing of the paper. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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References

1. Turunen M, Olsson J, Dallner G: Metabolism and function of coenzyme Q. Biochim Biophys Acta 2004, 1660:2-171-199.
2. Kwong LK, Karmszul S, Rebrin I, Bayne AC, Jana CK, Morris P, Forster MJ, Sohal RS: Effects of coenzyme Q(10) administration on its tissue concentrations, mitochondrial oxidant generation, and oxidative stress in the rat. Free Radic Biol Med 2002, 33(5):627-638.
3. Bentinger M, Tekle M, Dallner G: Coenzyme Q–biosynthesis and functions. Biochimie Biosphys Res Commun 396(1):74-79.
4. Gronberg DA, Kindermann B, Atthammer M, Klapper M, Vormann J, Littarru GP, Doring F: Coenzyme Q10 affects expression of genes involved in cell signalling, metabolism and transport in human CaCo-2 cells. Int J Biochem Cell Biol 2005, 37(6):1208-1218.
5. Schmelzer C, Doring F: Identification of LPS-inducible genes downregulated by ubiquinone in human THP-1 monocytes. Biofactors 2010, 36(4):222-238.
6. Lee CK, Pugh TD, Kopp RG, Edwards J, Allison DB, Weindruch R, Prolla TA: Effects of Coenzyme Q10 on TNF-alpha secretion in human CaCo-2 cells. Biofactors 2007, 31(4):211-217.
7. Schmelzer C, Lorenz G, Rimbach G, Doring F: In Vitro Effects of the Reduced Form of Coenzyme Q(10) on Secretion Levels of TNF-alpha and Chemokines in Response to LPS in the Human Monocytic Cell Line THP-1. J Clin Biochem Nutr 2009, 44(1):62-66.
8. Schmelzer C, Lorenz G, Lindner I, Rimbach G, Niklowitz P, Menke T, Doring F: Effects of Coenzyme Q10 on TNF-alpha secretion in human and murine monocytic cell lines. Biofactors 2007, 31(1):35-41.
9. Barroso MP, Gomez-Diaz C, Villablanca JM, Buron MI, Lopez-Lluch G, Navas P: Plasma membrane ubiquinone controls ceramide production and prevents cell death induced by serum withdrawal. J Bioenerg Biomembr 1997, 29(3):259-267.
10. Gonzalez R, Ferrin G, Hidalgo AB, Ranchal I, Lopez-Gilloro P, Santos-Gonzalez M, Lopez-Lluch G, Briceno J, Gomez MA, Poyato A, et al: N-acetylcysteine, coenzyme Q10 and superoxide dismutase mimetic prevent mitochondrial cell dysfunction and cell death induced by d-galactosamine in primary culture of human hepatoctyes. Chem Biol Interact 2009, 181(1):95-106.
11. Tzagoloff A, Dieckmann CL: PET genes of Saccharomyces cerevisiae. Microbiol Rev 1990, 54(3):211-225.
12. Makishima E, Cecchin G: The quinone-binding and catalytic site of complex II. Biochim Biophys Acta 1797(12):1877-1882.
13. Miki R, Saiki R, Ozoe Y, Kawamura M: Comparison of a coq7 deletion mutant with other respiration-defective mutants in fission yeast. Fems J 2008, 275(2):5309-5324.
14. Quirini C, Naini A, Salviati L, Trevisson E, Navas P, Dimaruco S, Hirano M: A mutation in para-hydroxybenzoate-polypropenyl transferase (CCQ2) causes primary coenzyme Q10 deficiency. Am J Hum Genet 2006, 78(2):345-349.
15. Lopez LC, Schuekel M, Quirini CM, Kaniki T, Rodenburg RJ, Naini A, Dimaruco S, Hirano M: Leigh syndrome with nephropathy and CoQ10 deficiency due to decarboxyl diphosphate synthase subunit 2 (PDSS2) mutations. Am J Hum Genet 2008, 79(1):115-129.
16. DiMauro S, Quirini CM, Hirano M: Mutations in coenzyme Q10 biosynthetic genes. J Clin Invest 2007, 117(3):587-589.
17. Schmelzer C, Niklowitz P, Okun JG, Haas D, Menke T, Doring F: Ubiquinolinduced expression signature are translated into altered parameters of erythropoiesis and reduced density lipoprotein cholesterol levels in humans. JAMA 2011, 631(1):42-48.
18. PolyPhen, http://genetics.bwh.harvard.edu/pph/.
19. Traver RD, Siegel D, Beall HD, Phillips RM, Gibson NW, Franklin WA, Ross D: Characterization of a polymorphism in NAD(P)H:quinone oxidoreductase (DT-diaphorase). Br J Cancer 1997, 75(1):69-75.
20. Jameson D, Wilson K, Fidgeon S, Margett JS, Edmondson RJ, Leung HY, Knox R, Bovdy AV: NAD(P)H:quinone oxidoreductase 1 and nrfquinone oxidoreductase 2 activity and expression in bladder and ovarian cancer and lower Nrfquinone oxidoreductase 2 activity associated with an NQO2 exon 3 single-nucleotide polymorphism. Clin Cancer Res 2007, 13(5):1584-1590.
21. Vasiloiu V, Ross D, Nebert DW: Update of the NAD(P)H:quinone oxidoreductase (NQO) gene family. Hum Genomics 2006, 2(3):329-335.
22. Pellecchia M, Tekle M, Dallner G: Oxidative stress and ApoE isoforms. Biochimie Biosphys Res Commun 396(1):74-79.
23. Reitz C, Tang MX, Schupf N, Manly JJ, Mayeux R, Luchsinger JA: Association of higher levels of high-density lipoprotein cholesterol in elderly individuals and lower risk of late-onset Alzheimer disease. Arch Neural 67(12):1491-1497.
24. Alvim RO, Freitas SR, Ferreira NE, Santos PC, Cunha RS, Mill JG, Knerje JE, Pereira AC: APOE polymorphism is associated with lipid profile, but not with arterial stiffness in the general population. Lipids Health Dis 9:128.
25. Humphries SE, Talmud PJ, Hawe E, Bolla M, Day IN, Miller GJ: Apolipoprotein E4 and coronary heart disease in middle-aged men who smoke: a prospective study. Lancet 2001, 358(9276):115-119.
26. Johf-Monseny L, Loboda A, Wagner AE, Huebbe P, Boesch-Saadatmandi C, Jaksziewicz A, Minihane AM, Dujuk J, Rimbach G: Effects of apoE genotype on macrophage inflammation and heme oxygenase-1 expression. Biochimica e Biophysica Acta Commun 2007, 357(1):319-324.
27. Dietrich M, Hu Y, Block G, Olano E, Packer L, Morrow JD, Hudes MA, Abdukeyum G, Rimbach G, Minihane AM: Associations between apolipoprotein E genotype and circulating F2-isoprostane levels in humans. Lipids 2005, 40(4):329-334.
28. Flachsbart F, Caliebe A, Nithongiel M, Kleinдорf R, Nikolaus S, Schreiber S, Nebel A: Depletion of potential A2M risk haplotype for Alzheimer’s disease in longived individuals. Eur J Hum Genet 2001, 1(5):59-61.
29. Batico M, Giunta S, Galeazzi R, Minihane AM, Dujuk J, Rimbach G: Haplotypes of higher levels of high-density lipoprotein cholesterol in elderly individuals and lower risk of late-onset Alzheimer disease. Arch Neural 67(12):1491-1497.
30. Flachsbart F, Caliebe A, Nithongiel M, Klein дорф R, Nikolaus S, Schreiber S, Nebel A: Depletion of potential A2M risk haplotype for Alzheimer’s disease in longived individuals. Eur J Hum Genet 2001, 1(5):59-61.
31. Batico M, Giunta S, Galeazzi R, Minihane AM, Dujuk J, Rimbach G: Haplotypes of higher levels of high-density lipoprotein cholesterol in elderly individuals and lower risk of late-onset Alzheimer disease. Arch Neural 67(12):1491-1497.
maintenance of the reduced antioxidant form of coenzyme Q in membrane systems. Proc Natl Acad Sci USA 1996, 93(6):2528-2532.

34. Landi L, Fiorentini D, Galli MC, Segura-Aguilar J, Beyer RE. DT-Diaphorase maintains the reduced state of ubiquinones in lipid vesicles thereby promoting their antioxidant function. Free Radic Biol Med 1997, 22(1-2):329-335.

35. Kelsey KT, Ross D, Traver RD, Christiani DC, Zuo ZF, Spitz MR, Wang M, Xu X, Lee BK, Schwartz BS, et al: Ethnic variation in the prevalence of a common NAD(P)H quinone oxidoreductase polymorphism and its implications for anticancer chemotherapy. Br J Cancer 1997, 76(7):852-854.

36. Han SJ, Kang ES, Kim HJ, Kim SH, Chun SW, Ahn CW, Cha BS, Nam M, Lee HC. The C609T variant of NQO1 is associated with carotid artery plaques in patients with type 2 diabetes. Mol Genet Metab 2009, 97(1):85-90.

37. Rimbach G, Minihane AM. Nutrigenetics and personalised nutrition: how far have we progressed and are we likely to get there? Proc Nutr Soc 2009, 68(2):162-172.

38. Jofre-Monseny L, Minihane AM, Rimbach G. Impact of apoE genotype on oxidative stress, inflammation and disease risk. Mol Nutr Food Res 2008, 52(1):131-145.

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