The mitochondrial DNA content of cumulus granulosa cells is linked to embryo quality

Titre	The mitochondrial DNA content of cumulus granulosa cells is linked to embryo quality
Type de publication	Article de revue
Auteur	Desquiret-Dumas, Valérie [1], Clément, A [2], Seegers, Valérie [3], Boucret, Lisa [4], Ferré-L'Hotellier, Véronique [5], Bouet, Pierre-Emmanuel [6], Descamps, Philippe [7], Procaccio, Vincent [8], Reynier, Pascal [9], May-Panloup, Pascale [10]
Editeur	Oxford University Press (OUP)
Type	Article scientifique dans une revue à comité de lecture
Année	2017
Langue	Anglais
Date	Mars 2017
Numéro	3
Pagination	607-614
Volume	32
Titre de la revue	Human Reproduction
ISSN	1460-2350
Mots-clés	Adult [11], Cumulus cells [12], DNA, Mitochondrial [13], Embryo implantation [14], Embryo Transfer [15], Female [16], Fertilization in Vitro [17], Humans [18], Oocytes [19]

Résumé en anglais	STUDY QUESTION: Could the mitochondrial DNA (mtDNA) content of cumulus granulosa cells (CGCs) be related to oocyte competence? SUMMARY ANSWER: The quality of embryos obtained during IVF procedures appears to be linked to mtDNA copy numbers in the CGCs. WHAT IS KNOWN ALREADY: Oocyte quality is linked to oocyte mtDNA content in the human and other species, and the mtDNA copy number of the oocyte is related to that of the corresponding CGCs. Moreover, the quantification of CGC mtDNA has recently been proposed as a biomarker of embryo viability. STUDY DESIGN SIZE, DURATION: An observational study was performed on 452 oocyte-cumulus complexes retrieved from 62 patients undergoing ICSI at the ART Center of the University Hospital of Angers, France, from January to May 2015. PARTICIPANTS/MATERIALS, SETTING, METHODS: The average mtDNA content of CGCs was assessed by using a quantitative real-time PCR technique. The relationship between CGC mtDNA content and oocyte maturity and fertilizability, on one hand, and embryo quality, on the other, was investigated using univariate and multivariate generalized models with fixed and mixed effects. MAIN RESULTS AND THE ROLE OF CHANCE: No relationship was found between CGC mtDNA content and oocyte maturity or fertilizability. In contrast, there was a significant link between the content of mtDNA in CGCs surrounding an oocyte and the embryo quality, with significantly higher mtDNA copy numbers being associated with good quality embryos compared with fair or poor quality embryos [interquartile range, respectively, 738 (250-1228) and 342 (159-818); P = 0.006]. However, the indication provided by the quantification of CGC mtDNA concerning the eventuality of good embryo quality was seriously subject to patient effect (AUC = 0.806, 95%CI = 0.719-0.869). The quantity of CGC mtDNA was influenced by BMI and smoking. LARGE SCALE DATA: N/A. LIMITATIONS REASONS FOR CAUTION: The quantification of CGC mtDNA may indicate embryo quality. However, since it is affected by patient specificity, it should be used with caution. It remains to be seen whether this marker could directly predict the implantation capacity of the embryo, which is the main objective in IVF practice. WIDER IMPLICATIONS OF THE FINDINGS: Our study suggests that the quantification of CGC mtDNA may be a novel biomarker of embryo viability. However, patient specificity makes it impossible to establish a general threshold value, valid for all patients. Nevertheless, further studies are needed to determine whether the quantification of CGC mtDNA may, in combination with the morpho-kinetic method, offer an additional criterion for selecting the best embryo for transfer from a given cohort. STUDY FUNDING/COMPETING INTEREST(S): This work was supported by the University Hospital of Angers, the University of Angers, France, and the French national research centres INSERM and the CNRS. There were no competing interests.
URL de la notice	http://okina.univ-angers.fr/publications/ua18932 [20]
DOI	10.1093/humrep/dew341 [21]
Lien vers le document	https://academic.oup.com/humrep/article/32/3/607/2859462 [22]
Autre titre	Hum. Reprod.
Identifiant (ID) PubMed	28077604 [23]

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