

Influence of food sources on the energy centers of cells – mitochondria in the ovary

Vanya Dimitrova*, Desislava Abadjieva

Institute of Biology and Immunology of Reproduction "Acad. Kiril Bratanov",

Bulgarian Academy of Sciences

1113 Sofia, bul. "Tsarigradsko shose" 73,

v.dimitrova@ibir.bas.bg*

Summary

Animal fertility depends on several environmental factors, including nutrition and the food sources consumed, to obtain essential vitamins, minerals, and other elements. Changes in nutrient intake directly affect the functioning of the reproductive system. The mitochondria are some of the most important organelles in any mammalian organ, including the ovary. These unique structures are responsible for meeting the energy needs of cells by being involved in metabolic processes, and they also possess mitochondrial DNA (mtDNA). The number and function of mtDNA decline with age in various tissues, including the ovaries. It is known that certain nutrients can influence mitochondrial function. Nutrient deficiencies reflect metabolic processes that take place in mitochondria. However, the mitochondrial mechanisms that contribute to ovarian aging and infertility are not fully understood. This article aims to summarize key evidence and current knowledge regarding the impact of dietary sources on mitochondrial function in the ovary, as well as to identify potential strategies for extending reproductive longevity and improving fertility.

Key words: nutrients, mitochondria, ovary;

Introduction

Nutrition is a major source of energy for the body and a means of obtaining vital substances, such as vitamins and minerals. Changes in nutritional resources affect reproductive processes (Bindari et al., 2013). For example, reduced nutrient intake leads to declining ovarian function in ovarian cancer (Crane et al., 2014). One important component of all cells that is directly related to an individual's diet is the mitochondria, also known as the nuclear headquarters of cells. This unique double-membrane organelle is involved in metabolic processes such as oxidative phosphorylation and metabolic regulation (McBride et al., 2006). Mitochondria are essential for producing adenosine triphosphate (ATP) and meeting the energy

needs of cells. The number of mitochondria in a cell can vary greatly depending on its activity level and energy needs. ATP is produced in mitochondria by oxidative phosphorylation using five complexes of the electron transport chain (St John, 2007; Singh and Costello, 2009). Mitochondria play an important role in follicle development and growth as they have a large energy requirement. Another very important feature of mitochondria is that they are inherited from the mother (Podolak et al., 2022). Another very important feature of mitochondria possesses their own DNA (mtDNA) that encodes certain proteins in the respiratory chains, enzymes and control the electron transport apparatus. In mtDNA, 37 genes have been found that encode certain 13 proteins that are directly involved in oxidative phosphorylation, the remaining proteins are encoded by nuclear DNA (Chiang et al., 2020). These proteins that are encoded by mtDNA are of great importance for the development of oocytes and future embryos, as DNA changes such as deletions and point mutations can directly poison mtDNA and disrupt fertility and early embryogenesis (Wei & Kao, 2000; Chiang et al., 2020; Podolak et al., 2022). In the process of oocyte development and growth, the number of mitochondria and mtDNA copy number increases and reaches very high values (May-Panloup et al., 2007). As the mother ages-or more specifically as the ovaries age-the quality of oocytes deteriorates, which is an indication that the quality and quantity of mitochondria also deteriorates (Müller-Höcker et al., 1996; Ju et al., 2024). As we age, the changes that occur in the ovary have a direct impact on mtDNA, since the ovary has a high energy consumption (Wei & Kao, 2000; Alberts et al., 2007; May-Panloup et al., 2016).

Another very important point in reproductive biology is pregnancy and early embryo development. In these two important events, energy consumption increases due to the dynamics of early embryo development (Rodríguez-Cano et al., 2020). Mitochondria play a major role in metabolic processes at many levels and there are multiple physiological changes in pregnancies that depend on nutrient intake (Rodríguez-Cano et al., 2020; Hsu & Tain, 2019; Langley-Evans, 2015). The importance of mitochondria in energy production and their presence in tissues with high energy requirements is based on a certain balance that is largely dependent on nutrient intake before and during pregnancy (Rodríguez-Cano et al., 2020).

The aim of this review is to provide a brief overview of nutrients that reflect over mitochondrial functions as a key site of energy transformation in the ovarian structure.

Nutrients and mitochondria

Nutrition is an important source of vitamins and minerals that are of particular importance to any individual. Nutritional resources appear as a direct factor that influences the

reproductive system. Fertility can be improved through short-term changes in the quality and quantity of food consumed. In reproductive biology, these changes in dietary intake are referred to as "focused feeding." This approach aims to optimize energy balance, which is essential for the development and growth of eggs. Research shows that dietary patterns, especially those high in fat, affect not only maternal health, but also egg quality and mitochondrial integrity in female offspring. This study synthesizes these findings by focusing on the mechanistic pathways involved in mitochondrial adaptations due to dietary influences. With reduced nutrient intake, ovarian functions decline and wait for better conditions (Georgiev & Petrov, 1994; Martin & Kadokawa, 2006; Ahmadi et al., 2025).

The ovary is a dynamic structure that, under the influence of sex hormones, undergoes cyclical changes. As a result, eggs are released for subsequent fertilization. Female gonads are characterized by high energy consumption caused by the development and growth of oocytes. To satisfy its energy needs during egg growth and development, the number of mitochondria increases.

Mitochondria are double-membrane organelles localized in nearly all cells that are involved in many processes. Their primary role is to produce energy and participate in processes that require high energy. They play an important role in metabolic processes by producing adenosine triphosphate (ATP), which is associated with cell signalling, differentiation, and death (Wesselink et al., 2019; Borcharding & Brestoff, 2023). However, many factors can affect mitochondrial function, such as free radicals and oxidative stress. Under normal conditions, the production of reactive oxygen species (ROS) is balanced, and there is no risk of mitochondrial damage. However, in conditions of oxidative stress in ovary, it's found that mitochondrial dysfunction disrupts the bi-directional interaction between oocytes and GCs, hindering cell growth and development (Wang et al., 2024). Excessive ROS production can damage not only the mitochondrial membrane, and mitochondrial DNA (mtDNA), resulting in cell damage and subsequent cell death. Damage to mtDNA can result in ROS-induced release of ROS, which lead to damage to the electron transport chain. This process is known as "mitochondrial catastrophe" (Indo et al., 2007; Galley, 2011). Mitochondrial catastrophe occurs because mtDNA encodes proteins that play an important role in the electron transport system of mitochondrial membranes (DiMauro & Schon, 2006). Mitochondria almost always perform a metabolic function directly related to the input of nutrients. However, their function depends on the input of nutrients and their conversion into cellular energy.

Nutrients are a diverse array of vitamins and minerals that affect cells and mitochondria in specific ways. Numerous studies have demonstrated that certain elements have beneficial effects on mitochondria (Fig. 1).

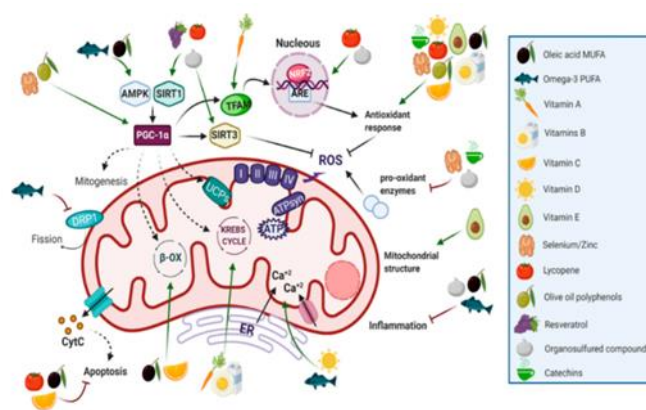


Figure 1. Major nutrients with beneficial effects on mitochondrial function (García-García et al., 2020)

Studies have shown that high-fat dietary patterns increase lipid peroxidation and oxidative stress, disrupting normal mitochondrial function and cellular homeostasis (Wen et al., 2024). These stressors can lead to mitochondrial dysfunction, which is characterized by impaired ATP production. ATP is critical for oocyte maturation and follicular development (Gonnella et al., 2022). The accumulation of reactive oxygen species (ROS) under these conditions can exacerbate mitochondrial dysfunction further and contribute to poor oocyte quality (Cox et al., 2021). Some additives, for example, carnitine, a non-proteinogenic amino acid, play a crucial role in many energy metabolism pathways as a regulator of lipid metabolism, β -oxidation and antioxidant capabilities of oocytes. L-carnitine functions as a cofactor for the translocation of long-chain fatty acids from the cytosol to the mitochondria and can suppress ROS action (Placidi et al., 2022). L-carnitine improved nuclear maturation, augmented the quantity of active mitochondria in pig oocytes, diminished intracellular lipids, and facilitated preimplantation development of bovine blastocysts (Paczkowski et al., 2013).

Foods that favourably affect mitochondrial function are rich in B-complex vitamins, vitamin E, vitamin C, melatonin, and other nutrients (Wesselink et al., 2019; Yan et al., 2022). In a study of rat diets, Bishop and Evans discovered "factor X," which was later named vitamin E and was found to have a beneficial effect on reproduction (Evans & Bishop, 1922). Numerous subsequent studies have examined vitamin E, proving it to be an antioxidant that strongly

influences oxidative factors (Kagan & Tyurina, 1998). Vitamin E is a general term for eight naturally occurring homologs: four tocopherols and four tocotrienols. Vitamin E is fat-soluble and known for its strong antioxidant properties (Zingg, 2007). One of the most basic isomers of vitamin E is α -tocopherol, which is primarily isolated from sunflower and olive oils. Tocopherols from the four isomeric forms are mainly isolated from oils of various origins used in the food industry. Vitamin E has been found to have a beneficial effect on fertility in female mice. In a study conducted at the IBIR-BAS, 45 female BALB/C mice were given vitamin E supplementation. An increase in the concentration of vitamin E, in the form of α -tocopherol acetate, was recorded while the level of tocopherol decreased. Based on these results, it can be concluded that the mice absorbed the vitamin and that it positively affects fertility. Of all the vitamin E homologues, α -tocopherol is the most active. When vitamin absorption was monitored, the presence of vitamin E in the blood serum was detected by gas chromatography (Fig. 2).

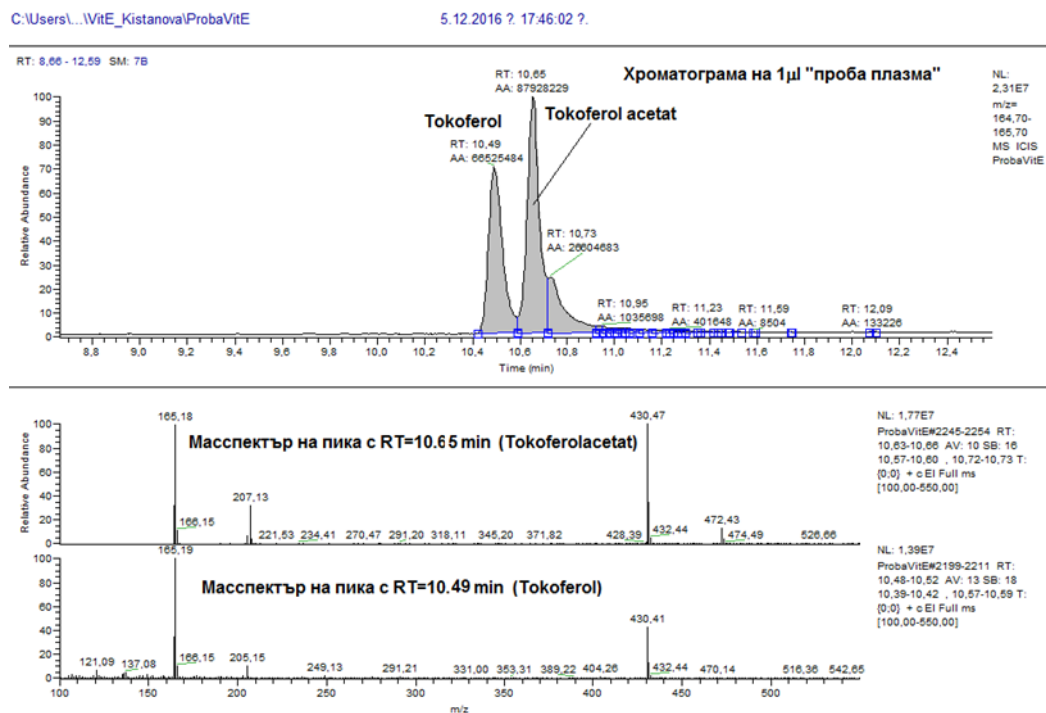


Figure 2. Chromatogram and mass spectrogram of blood serum from pooled samples of animals receiving vitamin E supplementation (Mladenova et al., 2017).

Vitamin C (ascorbic acid) is a water-soluble, low-molecular-weight compound belonging to the simple carbohydrates. It is directly distributed and interacts synchronously with vitamin E. Ascorbate reduces and regenerates one of the main homologues of vitamin E

(α -tocopherol) from its oxidative form (α -tocopheroxyl radical). This results in the inhibition of lipid peroxidation. Vitamin C is essential for cell growth, collagen production, and immune system function. It is also known for its antioxidant properties and ability to fight free radicals. Scientific literature shows that ascorbic acid protects against oxidative cell damage (Lykkesfeldt et al., 2010; Lykkesfeldt et al., 2014). Mitochondria play a major role in metabolic processes, actively participating in the metabolism and processing of important metabolic intermediates. The relationship between vitamin C and mitochondria is such that, due to its antioxidant properties, the vitamin inhibits ROS levels, which are crucial for mitochondrial function (González et al., 2010; Carew & Huang, 2002). The B-complex vitamins are a heterogeneous group of vitamins based on their water solubility and binding to coenzymes. All vitamins of the group originate from plant sources. The exception is B-12, which is of animal origin; it is produced by bacteria and isolated from foods of animal origin (Kennedy, 2016; Ali et al., 2022). One crucial time of B vitamin intake is during pregnancy and lactation, a period during which the requirements are increased. Foods rich in B-complex vitamins include meat, eggs, fish, nuts, avocados, and a range of plant foods (Hanna et al., 2022).

A number of studies have shown that dietary patterns, especially high-fat diets, affect not only maternal health, but also egg quality and mitochondrial integrity in female offspring. This response is based on the mechanistic pathways involved in mitochondrial adaptations due to dietary influences. Maternal consumption of an obesogenic diet has been shown to adversely affect ovarian function in offspring, particularly with respect to mitochondrial development and function. Aiken et al. (2015) reported that high-fat maternal diets can lead to reduced ovarian reserve and mitochondrial biogenesis dysregulation in young females. Offspring exposed to such diets often have altered mitochondrial morphology and function, which can have long-term consequences throughout their reproductive lives (Xhonneux et al., 2024; Di Berardino et al., 2024). These scientific findings suggest that dietary modulation may mitigate the adverse effects of poor nutritional status on mitochondrial health.

Conclusion

Nutrients play a key role in the life of organisms and their cells. The body can function adequately by acquiring and absorbing nutrients. Fertility is an important aspect of an organism's function and the preservation of offspring. The relationship between diet, mitochondrial function, and ovarian health is multifaceted and underscores the significance of maternal nutrition in reproductive outcomes. Researching the molecular mechanisms that link

nutrient intake to mitochondrial dynamics and oxidative stress is essential for developing effective strategies to improve reproductive health amid increasing hormonal issues associated with declining fertility.

Reproductive medicine must be aware of the role of mitochondria on female fertility and reproductive technology to ensure a better clinical practice. But food improvement and understand them, can be part of future alternatives and also will have a place evoke a for infertility treatment.

References

1. Ahmadi, P., Bayat, N. and Abbasi, B., 2025. Diet diversity score might be associated with reproductive health in women and infant outcomes: a systematic review. *Journal of Nutritional Science*, 13, p. e98. <https://doi.org/10.1017/jns.2024.81>.
2. Aiken, C.E., Tarry-Adkins, J.L., Penfold, N.C., Dearden, L. and Ozanne, S.E., 2015. Decreased ovarian reserve, dysregulation of mitochondrial biogenesis, and increased lipid peroxidation in female mouse offspring exposed to an obesogenic maternal diet. *The FASEB Journal*, 30(4), p.1548. doi: 10.1096/fj.15-280800.
3. Alberts, Bruce; Alexander Johnson; Julian Lewis; Martin Raff; Keith Roberts; Peter Walter, 2007. *Molecular Biology of the Cell*. New York: Garland Publishing Inc. ISBN 10: 0815341059.
4. Ali, M.A., Hafez H.A., Kamel M.A., Ghamry H.I., Shukry M. and Farag M.A., 2022. Dietary vitamin B complex: orchestration in human nutrition throughout life with sex differences. *Nutrients*, 14(19), p.3940. <https://doi.org/10.3390/nu14193940>.
5. Antico Arciuch, V. G., Elguero, M. E., Poderoso, J. J., & Carreras, M. C. (2012). Mitochondrial regulation of cell cycle and proliferation. *Antioxidants & redox signaling*, 16(10), 1150-1180.
6. Bindari, Y. R., Shrestha, S., Shrestha, N., & Gaire, T. N., 2013. Effects of nutrition on reproduction-A review. *Advances in Applied Science Research*, 4(1), 421-429.
7. Borchering, N. & Brestoff, J.R., 2023. The power and potential of mitochondria transfer. *Nature*, 623, p.283-291. <https://doi.org/10.1038/s41586-023-06537-z>.
8. Carew JS, Huang P. 2002. Mitochondrial defects in cancer. *Mol Cancer*; 1:9. DOI: 10.1186/1476-4598-1-9.
9. Chiang JL, Shukla P, Pagidas K, Ahmed NS, Karri S, Gunn DD, Hurd WW, Singh KK. Mitochondria in Ovarian Aging and Reproductive Longevity. *Ageing Res Rev*. 2020 Nov;63:101168. doi: 10.1016/j.arr.2020.101168. Epub 2020 Sep 4. PMID: 32896666; PMCID: PMC9375691.
10. Cox, R.T., Poulton, J. and Williams, S.A., 2021. The role of mitophagy during oocyte aging in human, mouse, and Drosophila: implications for oocyte quality and mitochondrial disease. *Reproduction and Fertility*, 2 (4), pp. R113-R129. <https://doi.org/10.1530/RAF-21-0060>.
11. Crane, T. E., Khulpateea, B. R., Alberts, D. S., Basen-Engquist, K., & Thomson, C. A., 2014. Dietary intake and ovarian cancer risk: a systematic review. *Cancer epidemiology, biomarkers & prevention*, 23(2), 255-273.
12. Di Berardino C., Barceviute U., Camerano Spelta Rapini C., Peserico A., Capacchietti G., Bernabò N., Russo V., Gatta V., Konstantinidou, F., Donato, M. and Barboni

B., 2024. High-fat diet-negative impact on female fertility: from mechanisms to protective actions of antioxidant matrices. *Frontiers in Nutrition*, 11, p. 1415455. <https://doi.org/10.3389/fnut.2024.1415455>.

13. DiMauro, S., Schon, E.A., 2006. The mitochondrial respiratory chain and its disorders. In: DiMauro, S., Hirano, M., Schon, E.A. (Eds.), *Mitochondrial Medicine*. Informa Healthcare, Oxon, pp. 7–26.

14. Galley, H.F., 2011. Oxidative stress and mitochondrial dysfunction in sepsis. *Br J Anaesth*; 107:57e64. <https://doi.org/10.1093/bja/aer093>.

15. García-García, F.J., Monistrol-Mula, A., Cardellach, F. and Garrabou, G., 2020. Nutrition, bioenergetics, and metabolic syndrome. *Nutrients*, 12(9), p. 2785. <https://doi.org/10.3390/nu12092785>.

16. Georgiev, G. and Petrov, M., 1994, In the Beginning of Life Biology and Function of Sex Cells, *Science and Art*, Sofia, p.51, ISBN 954-02-0157-8.

17. Gonnella, F., Konstantinidou, F., Di Berardino, C., Capacchietti, G., Peserico, A., Russo, V., Barboni, B., Stuppia, L. and Gatta, V., 2022. A systematic review of the effects of high-fat diet exposure on oocyte and follicular quality: a molecular point of view. *International journal of molecular sciences*, 23(16), p.8890. <https://doi.org/10.3390/ijms23168890>.

18. González MJ, Rosario-Pérez G, Guzmán AM, Miranda-Massari JR, Duconge J, Lavergne J, Fernandez N, Ortiz N, Quintero A, Mikirova N, Riordan NH, Ricart CM. Mitochondria, Energy and Cancer: The Relationship with Ascorbic Acid. *J Orthomol Med*. 2010;25(1):29-38. PMID: 23565030; PMCID: PMC3615720.

19. Evans, H.M.; Bishop, K.S. On the existence of a hitherto unrecognized dietary factor essential for reproduction. *Science*. 1922, 56, 650–665.

20. Hanna, M., Jaqua, E., Nguyen, V. and Clay, J.B., 2022. Vitamins: functions and uses in medicine. *Perm. J*, 26(2), pp.89-97. <https://doi.org/10.7812/TPP/21.204>.

21. Horn, M., Gunn, P., Van Emon, M., Lemenager, R., Burgess, J., Pyatt, N.A. and Lake, S.L., 2010. Effects of natural (RRR α -tocopherol acetate) or synthetic (all-rac α -tocopherol acetate) vitamin E supplementation on reproductive efficiency in beef cows. *Journal of animal science*, 88(9), pp.3121-3127.

22. Hsu, C. N., & Tain, Y. L. (2019). The good, the bad, and the ugly of pregnancy nutrients and developmental programming of adult disease. *Nutrients*, 11(4), 894.

23. Indo HP, Davidson M, Yen H-C, Suenaga S, Tomita K, Nishii T, et al., 2007. Evidence of ROS generation by mitochondria in cells with impaired electron transport chain and mitochondrial DNA damage. *Mitochondrion*; 7: 106e18. <https://doi.org/10.1016/j.mito.2006.11.026>.

24. Ju, W., Zhao, Y., Yu, Y., Zhao, S., Xiang, S., & Lien, F., 2024. Mechanisms of mitochondrial dysfunction in ovarian aging and potential interventions. *Frontiers in Endocrinology*, 15, 1361289. Zingg, Jean-Marc, 2007. Vitamin E: An overview of major research directions, *Molecular Aspects of Medicine*, 28, 400–422.

25. Kagan, V.E. and Tyurina, Y.Y., 1998. Recycling and redox cycling of phenolic antioxidants. *Annals of the New York Academy of Sciences*, 854(1), pp.425-434.

26. Kennedy, D.O., 2016. B vitamins and the brain: mechanisms, dose and efficacy—a review. *Nutrients*, 8(2), p.68. <https://doi.org/10.3390/nu8020068>.

27. Langley-Evans, S. C. (2015). Nutrition in early life and the programming of adult disease: a review. *Journal of Human Nutrition and Dietetics*, 28, 1-14.

28. Lykkesfeldt J, Michels AJ, Frei B. 2014 Vitamin C. *Adv Nutr.* Jan 1;5(1):16-8. doi: 10.3945/an.113.005157.
29. Lykkesfeldt, J. and Poulsen, H.E., 2010. Is vitamin C supplementation beneficial? Lessons learned from randomised controlled trials. *British journal of nutrition*, 103(9), pp.1251-1259. <https://doi.org/10.1017/S0007114509993229>.
30. Martin, G.B. and Kadokawa, H., 2006. "Clean, green and ethical" animal production. Case study: Reproductive efficiency in small ruminants. *Journal of Reproduction and Development*, 52(1), pp.145-152. <https://doi.org/10.1262/jrd.17086-2>.
31. May-Panloup P, Chretien MF, Malthiery Y, Reynier P. Mitochondrial DNA in the oocyte and the developing embryo. *Curr Top Dev Biol.* 2007; 77:51-83. doi: 10.1016/S0070-2153(06)77003-X. PMID: 17222700.
32. May-Panloup P, Boucret L, Chao de la Barca JM, Desquiere-Dumas V, Ferré-L'Hotellier V, Morinière C, Descamps P, Procaccio V, Reynier P. Ovarian ageing: the role of mitochondria in oocytes and follicles. *Hum Reprod Update.* 2016 Nov;22(6):725-743. doi: 10.1093/humupd/dmw028. Epub 2016 Aug 25. PMID: 27562289.
33. McBride, H. M., Neuspiel, M., & Wasiak, S., 2006. Mitochondria: more than just a powerhouse. *Current biology*, 16(14), R551-R560.
34. Mladenova V., Abadjieva D., Kistanova E., 2017. Effect of the vitamin E enriched feed additive and superovulation on the parameters of the reproductive tract in mice. *Journal of Mountain Agriculture on the Balkans*, 20 (2), 89-99.
35. Müller-Höcker J, Schäfer S, Weis S, Münscher C, Strowitzki T. Morphological-cytochemical and molecular genetic analyses of mitochondria in isolated human oocytes in the reproductive age. *Mol Hum Reprod.* 1996 Dec;2(12):951-8. doi: 10.1093/molehr/2.12.951. PMID: 9237239.
36. Paczkowski, M., Silva, E., Schoolcraft, W.B., Krisher, R.L., 2013. Comparative importance of fatty acid beta-oxidation to nuclear maturation, gene expression, and glucose metabolism in mouse, bovine, and porcine cumulus oocyte complexes. *Biology of reproduction*, 88 (111), 111-111.
37. Placidi, M., Di Emidio, G., Virmani, A., D'Alfonso, A. Artini, P.G., D'Alessandro, A.M., Tatone, C., 2022. Carnitines as mitochondrial modulators of oocyte and embryo bioenergetics. *Antioxidants*, 11, 745.
38. Podolak, A., Woclawek-Potocka, I., & Lukaszuk, K., 2022. The role of mitochondria in human fertility and early embryo development: what can we learn for clinical application of assessing and improving mitochondrial DNA? *Cells*, 11(5), 797
39. Rodríguez-Cano, A. M., Calzada-Mendoza, C. C., Estrada-Gutierrez, G., Mendoza-Ortega, J. A., & Perichart-Perera, O. (2020). Nutrients, mitochondrial function, and perinatal health. *Nutrients*, 12(7), 2166.
40. Singh, K., & Costello, L. (Eds.), 2009. *Mitochondria and cancer*. Springer Science & Business Media. p 1-23.
41. St John, J. C., 2007. The mitochondrion in the germline and early development. *Curr Top Dev Biol*, 77, 1-328. p 23-25.
42. Wang, Z.H., Wang, Z.J., Liu, H.C., Wang, C.Y., Wang, Y.Q., Yue, Y., Zhao, C., Wang, G., Wan, J.P., 2024. Targeting mitochondria for ovarian aging: new insights into mechanisms and therapeutic potential. *Front Endocrinol (Lausanne)*, 17 (15):1417007. doi: 10.3389/fendo.

43. Wei, Y. H., & Kao, S. H., 2000. Mitochondrial DNA mutation and depletion are associated with decline of fertility and motility of human sperm. *Zoological Studies-Taipei*, 39(1), 1-12.
44. Wen, J., Feng, Y., Xue, L., Yuan, S., Chen, Q., Luo, A., Wang, S. and Zhang, J., 2024. High-fat diet-induced L-saccharopine accumulation inhibits estradiol synthesis and damages oocyte quality by disturbing mitochondrial homeostasis. *Gut Microbes*, 16(1), p. 2412381. <https://doi.org/10.1080/19490976.2024.2412381>
45. Wesselink, E., Koekkoek, W.A.C., Grefte, S., Witkamp, R.F. and Van Zanten, A.R.H., 2019. Feeding mitochondria: Potential role of nutritional components to improve critical illness convalescence. *Clinical Nutrition*, 38(3), pp. 982-995. <https://doi.org/10.1016/j.clnu.2018.08.032>.
46. Xhonneux, I., Marei, W.F., Meulders, B., Sloomans, J., Pintelon, I. and Leroy, J.L., 2024. The impact of offspring and maternal obesogenic diets on adult offspring oocyte mitochondrial morphology in primordial and prenatal follicles. *Plos one*, 19(6), p. e0305912. <https://doi.org/10.1371/journal.pone.0305912>.
47. Yan, F., Zhao, Q., Li, Y., Zheng, Z., Kong, X., Shu, C., Liu, Y. and Shi, Y., 2022. The role of oxidative stress in ovarian aging: a review. *Journal of ovarian research*, 15(1), p.100. <https://doi.org/10.1186/s13048-022-01032-x>.
48. Zingg, J.M., 2007. Vitamin E: an overview of major research directions. *Molecular aspects of medicine*, 28(5-6), pp.400-422. <https://doi.org/10.1016/j.mam.2007.05.004>.