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Oocyte SOS: Can NMN Save the Egg?
Systematic Review and Human Oocyte Transcriptomic Analysis

Hyunseo Noh[1*], Sioban Sen Gupta[1], Srividya Seshadri[1], Xavier Viñals Gonzalez[1,2]
[1]Preimplantation Genetics Group, Institute for Women's Health, University College London, 84-86 Chenies Mews, London, UK
[2]Aria Fertility, 8 Welbeck Way, London, UK
*Correspondence: hyunseo.noh.22@ucl.ac.uk

Study Question: How does nicotinamide adenine dinucleotide (NAD^+) metabolism influence oocyte quality under various reproductive conditions, particularly in relation to nicotinamide mononucleotide (NMN) supplementation?

Summary Answer: NAD^+ metabolism plays a critical role in maintaining oocyte quality by supporting mitochondrial function, reducing oxidative stress, and regulating meiotic progression. NMN supplementation enhances these processes in preclinical models and shows promise for mitigating age- and stress-related reproductive decline.

Introduction: Oocyte quality declines with age and under metabolic or environmental stress, primarily due to mitochondrial dysfunction and oxidative damage[1]. NAD^+ is a key coenzyme in mitochondrial metabolism and redox homeostasis. NMN, a biosynthetic precursor of NAD^+, restores intracellular NAD^+ levels and has been proposed as a metabolic intervention to improve oocyte function[2]. This study combined a systematic review of preclinical models and a transcriptomic analysis of human oocytes to evaluate the role of NAD^+ metabolism and NMN supplementation in supporting oocyte quality.

References
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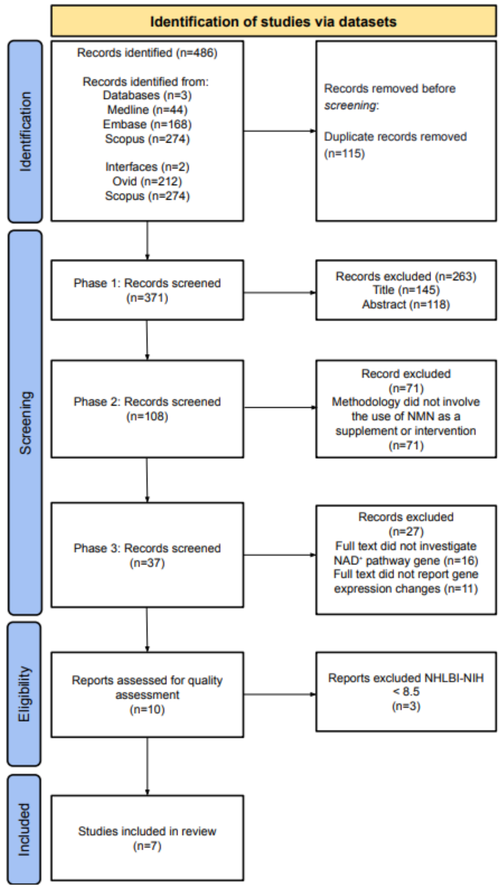


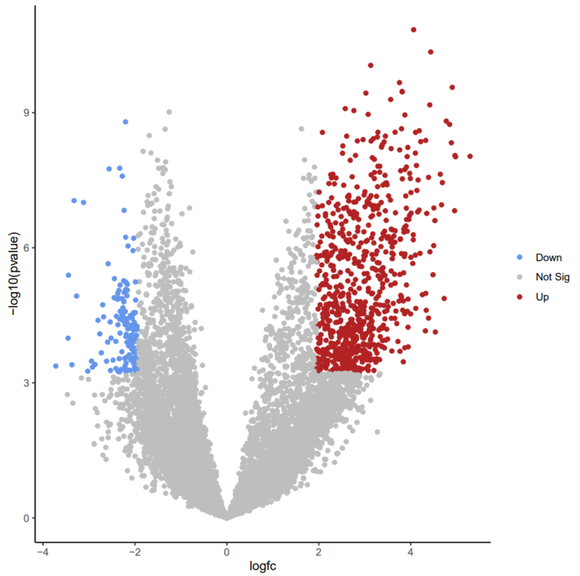
Methodology: A systematic review was conducted in accordance with PRISMA guidelines[3]. Searches were carried out across MEDLINE, Embase, and Scopus. Peer-reviewed original studies published between 2015 and 2024 were screened for inclusion. Study quality was assessed using the NHLBI–NIH tool, with all included studies scoring ≥8.5. In parallel, transcriptomic data from 46 human oocytes—collected from patients aged 27 to 43 years—were analysed across germinal vesicle (GV), metaphase I (MI), and metaphase II (MII) stages to evaluate differential expression of NAD^+-related genes.

Main Results: Across preclinical models (n = 7), NMN improved oocyte quality by:

- Upregulating genes related to mitochondrial biogenesis (*Pgc1α*, *Nrf1*),
- Enhancing redox balance (*Sod1*, *Cat*),
- Modulating apoptotic and inflammatory signalling (*Bax*, *Bcl2*, *Nfkb1*).

Distinct effects were observed across models of metabolic dysregulation, exogenous stress, and reproductive ageing. Transcriptomic analysis revealed stage-specific differential expression of genes—including *SIRT3*, *DNM1L*, and *SOD1*—particularly between GV and MII stages, as shown in the volcano plot. No significant age-related expression differences were found.

Limitations and Reasons for Caution: Findings are based on animal studies, which may not fully reflect human oocyte biology. Variability in NMN dose, delivery, and model design limits comparability. Species-specific metabolic differences and possible off-target effects also warrant caution and further study.



Wider Implications of the Findings: This study highlights the potential of targeting NAD^+ metabolism to improve oocyte quality under age-related and stress-induced conditions. NMN supplementation may serve as a promising adjunct in assisted reproductive technologies by enhancing mitochondrial function, redox balance, and meiotic competence. Establishing standardised protocols and confirming translational relevance in human studies will be essential for clinical application.

The authors declare no competing interests.

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