

Role of AMPK and PKA pathways in chicken spermatozoa functions

Spermatozoa functions include delicate and high energy consuming processes like motility and the ability to perform acrosome reaction, i.e. the fusion of the spermatozoa head cytoplasmic membrane and the underlying outer acrosomal membrane, so that the acrosome content can be released. The 5'-AMP-activated protein kinase (AMPK) is an evolutionarily conserved serine/threonine kinase that acts as a cell energy sensor and subsequently regulates metabolism. It activates energy-producing pathways and deactivates energy-consuming pathways depending on the situation. Recently, the discovery of the key role of AMPK in the control of cell energy homeostasis has placed it in the position of an important kinase regarding the regulation of spermatozoa functions. AMPK might act by phosphorylating downstream protein substrates involved in the axoneme central apparatus or in other related structures that are essential for spermatozoa flagellar motility.

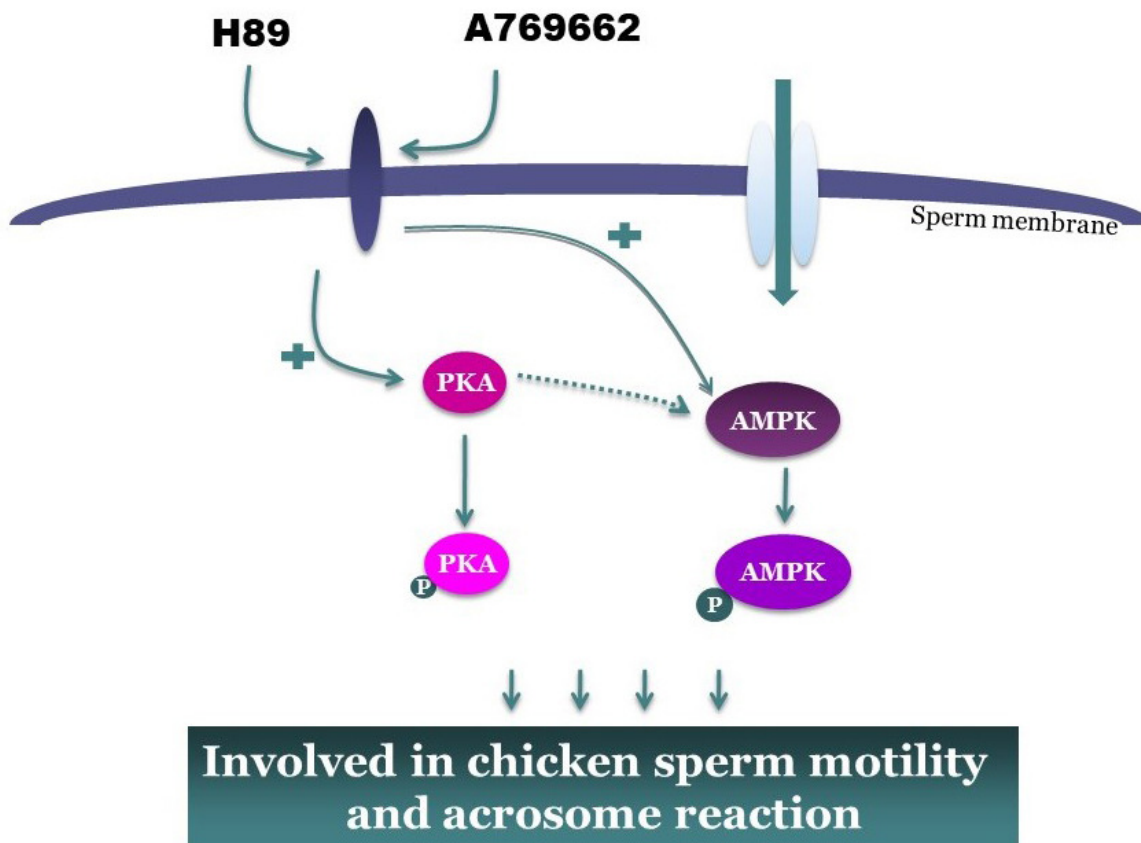


Fig. 1. A769662 and H89 compounds reveal the joint involvement of AMPK and PKA signaling pathways in chicken spermatozoa functions.

Tartarin *et al.*, 2012 showed that the transgenic mice lacking the catalytic subunit $\alpha 1$ gene ($\alpha 1$ AMPK knockout) present a great reduction in spermatozoa motility. We have also shown that the treatment with the non-specific AMPK activators AICAR or metformin increases chicken spermatozoa quality (motility, viability and acrosome reaction). By contrast, pharmacological inhibition of AMPK in chicken spermatozoa,

for example with Compound C, leads to a reduction in motility parameters such as the percentage of motile or of rapid spermatozoa, their curvilinear velocity, or their average path velocity. We also showed the implication of calcium signaling pathways through CaMK and CaMKK in the chicken spermatozoa AMPK activation. Other important signaling pathways are also involved in spermatozoa regulations. Among them, protein kinase A (PKA) signaling is needed for motility and acrosome reaction.

The aim of our study was to understand better the biochemical mechanisms underlying the regulation of spermatozoa functions. We were to determine precisely the role of AMPK activation, and the interaction between AMPK and PKA, another signaling pathway in bird spermatozoa. Our results show that a low dose of the direct AMPK activator A769662 was enough to measure an increase in the 3 main parameters: spermatozoa motility, viability, and acrosome reaction. Furthermore, it seems that A769662 slowed down the decrease of viability induced by in vitro incubation that gradually happens over time. We also learnt that AMPK acts differently in human and bird spermatozoa since it has been shown before that A769662 significantly reduced the percentages of motile, progressive, and rapid human spermatozoa. In addition, AMPK phosphorylation levels were greatly decreased by the PKA inhibitor H89 that also decreased chicken spermatozoa motility and acrosome reaction. The inhibitory action of H89 even significantly decreased AMPK activation when it was stimulated by A769662 at the same time. We thus hypothesized that PKA and AMPK were simultaneously inhibited by low H89 concentration, with consequent impairments in spermatozoa functions. This suggests a strong connection between the two pathways in order to regulate spermatozoa motility and acrosome reaction.

In conclusion: AMPK is rapidly activated by a low concentration of A769662 and is regulated upstream by PKA signaling pathway in bird spermatozoa. The use of the AMPK activator A769662 clearly causes a significant and quick improvement in chicken spermatozoa motility and acrosome reaction, which are essential to the fertilization process (Fig. 1). Our findings provide more evidences about the involvement of AMPK activity in the regulation of chicken spermatozoa functions and its relationship with the PKA signaling pathway.

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