

Summary of Research work

Chemotaxis is a highly conserved physiological process essential for directed sperm movement during fertilization. Recent studies in our laboratory have identified N-formyl-L-aspartate (NFA) as a potential sperm chemoattractant. NFA, known to activate the beta-2-adrenergic receptor (β -2-AR), modulates cAMP production and Ca^{2+} mobilization in somatic cells. Given the role of these signaling molecules in sperm chemotaxis, we explored the mechanisms by which NFA may influence sperm movement. To investigate this, we assessed the expression and localization of β -2-AR in sperm through Western blotting and indirect immunofluorescence. We utilized a microfluidics-based chemotaxis assay to evaluate sperm responses to varying concentrations of NFA and ICI-118,551, a specific β -2-AR antagonist. The impact of NFA on intracellular Ca^{2+} levels was measured using a FURA-2 AM-based fluorometric assay. Additionally, we examined the effects of NFA on sperm capacitation and acrosome reaction using Western blotting and immunofluorescence techniques. Our results revealed a bell-shaped dose-response curve for NFA, with the peak response at 0.01 μM , beyond which NFA exhibited an inhibitory effect. β -2-AR was localized to the sperm head and mid-piece region of the flagellum. The use of ICI-118,551 demonstrated that sperm chemotaxis in response to NFA is mediated via β -2-AR. Notably, while NFA increased intracellular Ca^{2+} levels, it reduced cAMP in capacitating sperm. However, NFA did not induce capacitation, as evidenced by unchanged tyrosine phosphorylation and membrane potential in uncapacitated sperm. Furthermore, PSA-FITC staining showed no significant impact of NFA on acrosome structure. In conclusion, our data demonstrate that NFA stimulates sperm chemotaxis through the β -2-AR, via non-canonical signaling pathways in directing sperm movement via β -2-AR. This study, also ignites the possibility of using NFA as a chemoattractant to select good quality sperm for enhancing the “take home baby” rate of IVF procedures.



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