The insect repellent N,N-diethyl-m-toluamide (DEET) induces angiogenesis via allosteric modulation of the M3 muscarinic receptor in endothelial cells

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Résumé en anglais	The insect repellent N,N-diethyl-m-toluamide (DEET) has been reported to inhibit AChE (acetylcholinesterase) and to possess potential carcinogenic properties with excessive vascularization. In the present paper, we demonstrate that DEET specifically stimulates endothelial cells that promote angiogenesis which increases tumor growth. DEET activates cellular processes that lead to angiogenesis including proliferation, migration and adhesion. This is associated with an enhancement of NO production and VEGF expression in endothelial cells. M3 silencing or the use of a pharmacological M3 inhibitor abrogates all of these effects which reveals that DEET-induced angiogenesis is M3 sensitive. The experiments involving calcium signals in both endothelial and HEK cells overexpressing M3 receptors, as well as binding and docking studies demonstrate that DEET acts as an allosteric modulator of the M3 receptor. In addition, DEET inhibited AChE which increased acetylcholine bioavailability and binding to M3 receptors and also strengthened proangiogenic effects by an allosteric modulation.
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