

Abstract ▾

Send to: ▾

[J Invest Dermatol.](#) 2015 Feb 10. doi: 10.1038/jid.2015.45. [Epub ahead of print]

Exploiting Cannabinoid-Induced Cytotoxic Autophagy to Drive Melanoma Cell Death.

[Armstrong JL](#)¹, [Hill DS](#)², [McKee CS](#)², [Hernandez-Tiedra S](#)³, [Lorente M](#)³, [Lopez-Valero I](#)⁴, [Eleni Anagnostou M](#)², [Babatunde F](#)², [Corazzari M](#)⁵, [Redfern CP](#)⁶, [Velasco G](#)⁴, [Lovat PE](#)².

Author information

¹1] Dermatological Sciences, Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK [2] Faculty of Applied Sciences, University of Sunderland, Sunderland, UK.

²Dermatological Sciences, Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK.

³Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, Spain.

⁴1] Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, Spain [2] Instituto de Investigaciones Sanitarias San Carlos (IdISSC), Madrid, Spain.

⁵Department of Biology, University of Rome 'Tor Vergata', Rome, Italy.

⁶Northern Institute for Cancer Research, Newcastle University, Newcastle-upon-Tyne, UK.

Abstract

While the global incidence of cutaneous melanoma is increasing, survival rates for patients with metastatic disease remain less than 10%. Novel treatment strategies are therefore urgently required, particularly for patients bearing BRAF/NRAS wildtype tumours. Targeting autophagy is a novel means to promote cancer cell death in chemotherapy-resistant tumours and the aim of the present study was to test the hypothesis that cannabinoids promote autophagy-dependent apoptosis in melanoma. Treatment with Δ^9 -Tetrahydrocannabinol (THC) resulted in the activation of autophagy, loss of cell viability and activation of apoptosis, while co-treatment with chloroquine or knockdown of Atg7, but not Beclin-1 or Ambra1, prevented THC-induced autophagy and cell death in vitro. Administration of Sativex-like (a laboratory preparation comprising equal amounts of THC and cannabidiol (CBD)) to mice bearing BRAF wildtype melanoma xenografts substantially inhibited melanoma viability, proliferation and tumour growth paralleled by an increase in autophagy and apoptosis compared to standard single agent temozolomide. Collectively our findings suggest THC activates non-canonical autophagy-mediated apoptosis of melanoma cells, suggesting cytotoxic autophagy induction with Sativex warrants clinical evaluation for metastatic disease. *Journal of Investigative Dermatology* accepted article preview online, 10 February 2015. doi:10.1038/jid.2015.45.

PMID: 25674907 [PubMed - as supplied by publisher]

LinkOut - more resources 

PubMed Commons

[PubMed Commons home](#) 0 comments[How to join PubMed Commons](#)

Full text links



Save items

 Add to Favorites ▾

Related citations in PubMed

[A combined preclinical therapy of cann: \[Mol Cancer Ther. 2011\]](#)

[Combination treatment with ABT-737 and \[Mol Cancer. 2013\]](#)

[Local delivery of cannabinoid-loaded microp \[PLoS One. 2013\]](#)

[Review Targeting autophagy as a pote \[Semin Cancer Biol. 2013\]](#)

[Review The diverse CB1 and CB2 rece \[Br J Pharmacol. 2008\]](#)

[See reviews...](#)[See all...](#)

Related information

Related Citations

Articles frequently viewed together

MedGen

Recent Activity

[Turn Off](#) [Clear](#)

 [Exploiting Cannabinoid-Induced Cytotoxic](#) PubMed

 [cannabidiol \(1319\)](#) PubMed

 [Cannabidiol \(CBD\) and its analogs: a review of](#) PubMed

 [P414. Cannabidiol for symptomatic treatmer](#) PubMed

[See more...](#)