

Letters

The Inhibitory Effects of Cannabidiol on Systemic Malignant Tumors

To the Editor:

The recent article by Johnson et al.¹ provided for highly stimulating reading. Cannabidiol may attenuate tumor growth in a number of other systemic malignancies. Decreased tumor growth in pulmonary malignancies is seen after administration of cannabidiol. Cannabidiol increases the expression of cyclooxygenase-2 within the cancerous cells.² Cannabidiol also induces tissue inhibitor of metalloproteinase-1 synthesis and activity. Peroxisome proliferator-activated receptor-gamma expression is augmented at the same time. Intercellular adhesion molecule-1 induction also is seen typically.³ As a result, intratumoral apoptosis is markedly accentuated. Cannabidiol also downregulates the expression of plasminogen activator inhibitor-1.⁴ Increased nuclear translocation of peroxisome proliferator-activated receptor-gamma accompanies the above changes. Tumor metastasis also is markedly attenuated.

Similar attenuation of tumor growth is seen in breast malignancies. It mediates this anti-neoplastic effect by attenuating mammalian target of rapamycin signaling.⁵ Endoplasmic reticulum stress is typically accentuated and the cytoplasmic release of cytochrome C is markedly enhanced. *ID1* expression also is inhibited at the same time.⁶ On the other hand, *ID2* expression is markedly upregulated. AKT inhibition accompanies the above changes. As a consequence, there is both increased apoptosis and intratumoral autophagy. Interestingly, beclin-1 plays a major role in these changes.

The above examples clearly illustrate the significant antineoplastic effects of cannabidiol. Hopefully, the next few years will see increased studies to fully and further evaluate these anti-neoplastic effects.

Shailendra Kapoor, MD
Chicago, Illinois, USA

<http://dx.doi.org/10.1016/j.jpainsymman.2013.02.002>

References

1. Johnson JR, Lossignol D, Burnell-Nugent M, Fallon MT. An open-label extension study to investigate the long-term safety and tolerability of THC/CBD oromucosal spray and oromucosal THC spray in patients with terminal cancer-related pain refractory to strong opioid analgesics. *J Pain Symptom Manage* 2012. [Epub ahead of print].
2. Ramer R, Heinemann K, Merkord J, et al. COX-2 and PPAR-gamma confer cannabidiol-induced apoptosis of human lung cancer cells. *Mol Cancer Ther* 2013;12:69–82.
3. Ramer R, Bublitz K, Freimuth N, et al. Cannabidiol inhibits lung cancer cell invasion and metastasis via intercellular adhesion molecule-1. *FASEB J* 2012; 26:1535–1548.
4. Ramer R, Rohde A, Merkord J, Rohde H, Hinz B. Decrease of plasminogen activator inhibitor-1 may contribute to the anti-invasive action of cannabidiol on human lung cancer cells. *Pharm Res* 2010;27: 2162–2174.
5. Shrivastava A, Kuzontkoski PM, Groopman JE, Prasad A. Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk between apoptosis and autophagy. *Mol Cancer Ther* 2011;10:1161–1172.
6. McAllister SD, Murase R, Christian RT, et al. Pathways mediating the effects of cannabidiol on the reduction of breast cancer cell proliferation, invasion, and metastasis. *Breast Cancer Res Treat* 2011;129:37–47.