The synthetic cannabinoid URB447 exerts antitumor effect in colon carcinoma and reduces liver metastasis in mice

1 Cell Biology and Histology Department, Faculty of Medicine and Nursing, University of the Basque Country.
2 Department of Biomolecular Sciences, University of Urbino Carlo Bo, Urbino, Italy.

Background
The endocannabinoid system represents a ubiquitous receptor family in the body, with a wide spectrum of different functions. We aim to find out the involvement of CB1 and CB2 receptors in the malignant phenotype of colon carcinoma cells and subsequent liver metastasis using the URB447 synthetic cannabinoid, which plays a dual role as CB1 antagonist and CB2 agonist.

Methods
Murine colon carcinoma MCA38 cells were treated with different concentrations of URB447, ranging from 10 µM up to 50 µM. Tumor cell viability, apoptosis, cell cycle and cell migration were analyzed in vitro. An in vivo orthotropic liver metastasis model was carried out to uncover the role of CB1-antagonism/ CB2-agonism in the metastatic growth in this organ.

Results
UBR447 reduced cancer cell viability in a dose-dependent trend, with around 70% decrease in cells treated with 50 µM, 40% with 25 µM and 10% when stimulated with 10 µM after 48 hours. 50 and 25 µM URB447 boosted cancer cell apoptosis as detected through flow cytometry. URB447 slightly interfered with cell cycle, leading to increased cell counts in G0/G1 phase when treated with 10 µM. Interestingly, cell migration was reduced in 10 µM-stimulated colorectal cancer cells. Finally, URB447 reduced liver metastasis after 14 days of cancer cell inoculation.

Conclusion
The modulation of CB1 and CB2 receptors arises as a potential therapeutic target for the treatment of colon carcinoma liver metastasis.