

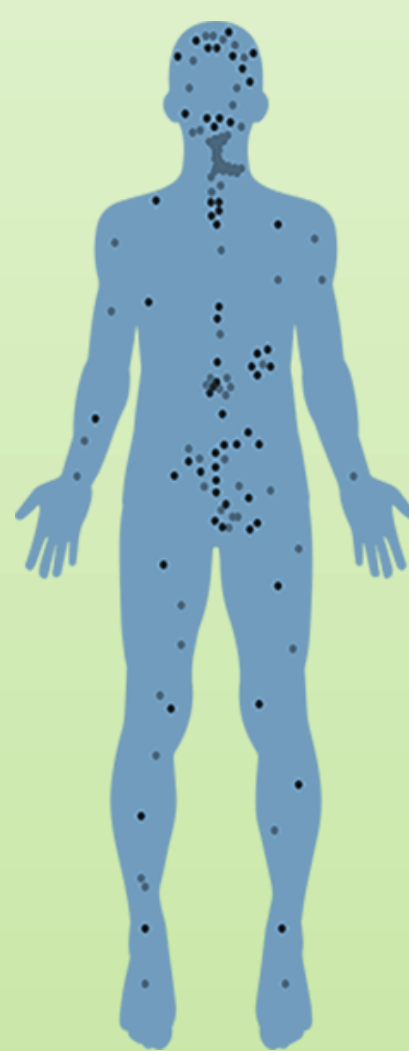
Exploring the multifaceted role of Endocannabinoid System *in vivo* and *in vitro*

Fiorenza Sella – Tutor Prof.ssa Oliana Carnevali

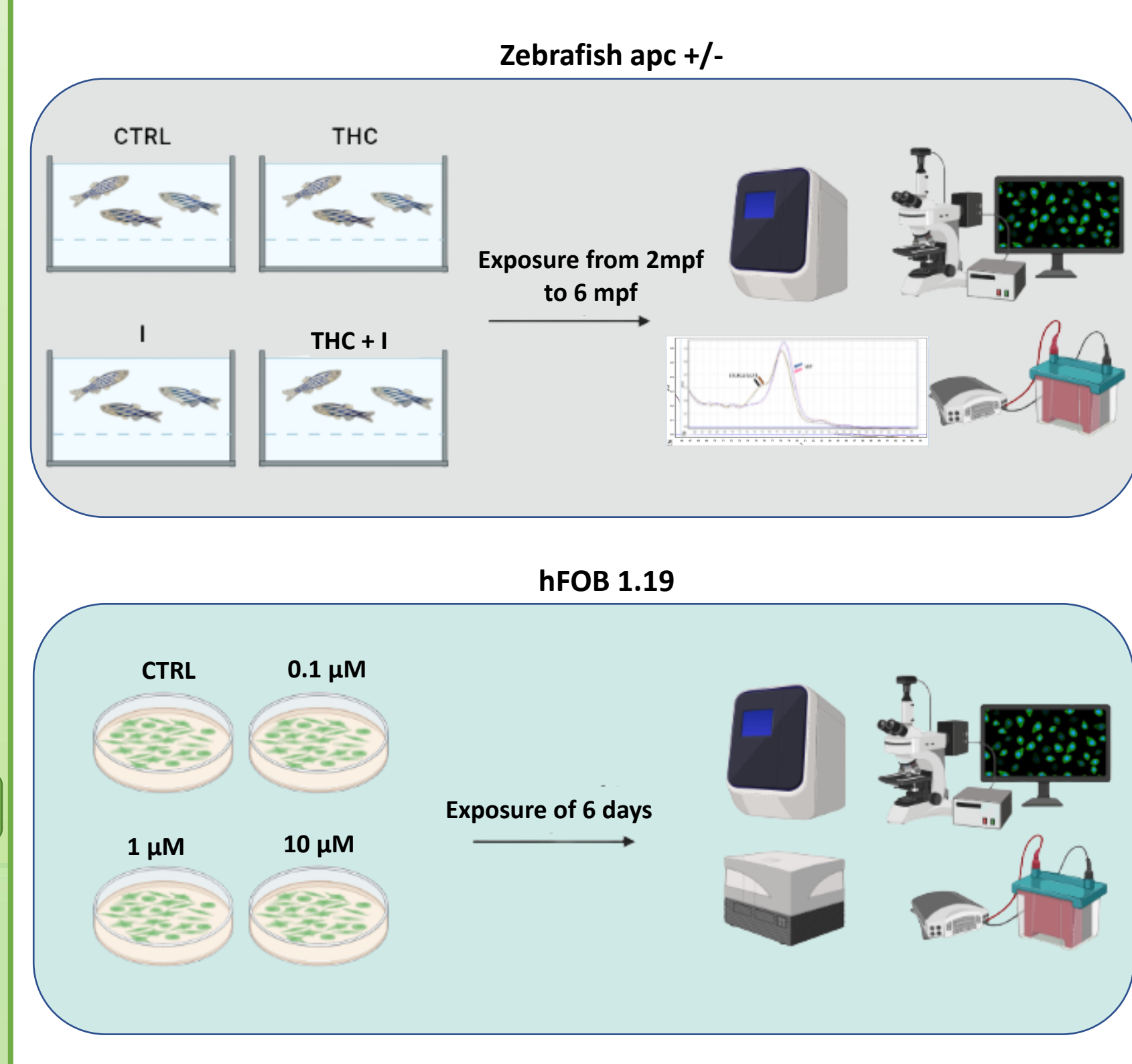
Laboratorio di Biologia dello Sviluppo e della Riproduzione, DiSVA

INTRODUCTION

The Endocannabinoid System (ECS) is composed by endocannabinoids, cannabinoid receptors and the enzymes responsible for their biosynthesis and degradation¹ and is present in several organs and tissues². A lot of studies have investigated the biological role of ECS in health and disease "conditions" and among others, it plays a proven role in the management of several Inflammatory and immunological conditions³. In recent years, several studies focused on the role of Endocannabinoid System (ECS) in tumorigenesis and tumor suppression⁴ by controlling inflammation and immunomodulation⁵. In addition, it was reported that endocannabinoids (eCBs) and cannabinoid receptors (CBRs) play important role in bone homeostasis and metabolism. Epithelial inflammation has been recently deemed as one of the hallmarks of Colorectal cancer (CRC), the third most common tumor form in the world population⁶. The inflammation impacts all stages of carcinogenesis, including initiation, proliferation, and progression⁷. Within coexistent inflammations, chronic inflammatory disorders could affect bone homeostasis and are frequently associated with the presence of osteoporosis⁸. In this context, pre-clinical studies showed that ECB prevents osteoporosis (OP) and favours fracture healing by targeting bone pathological process leading to inflammation⁹.



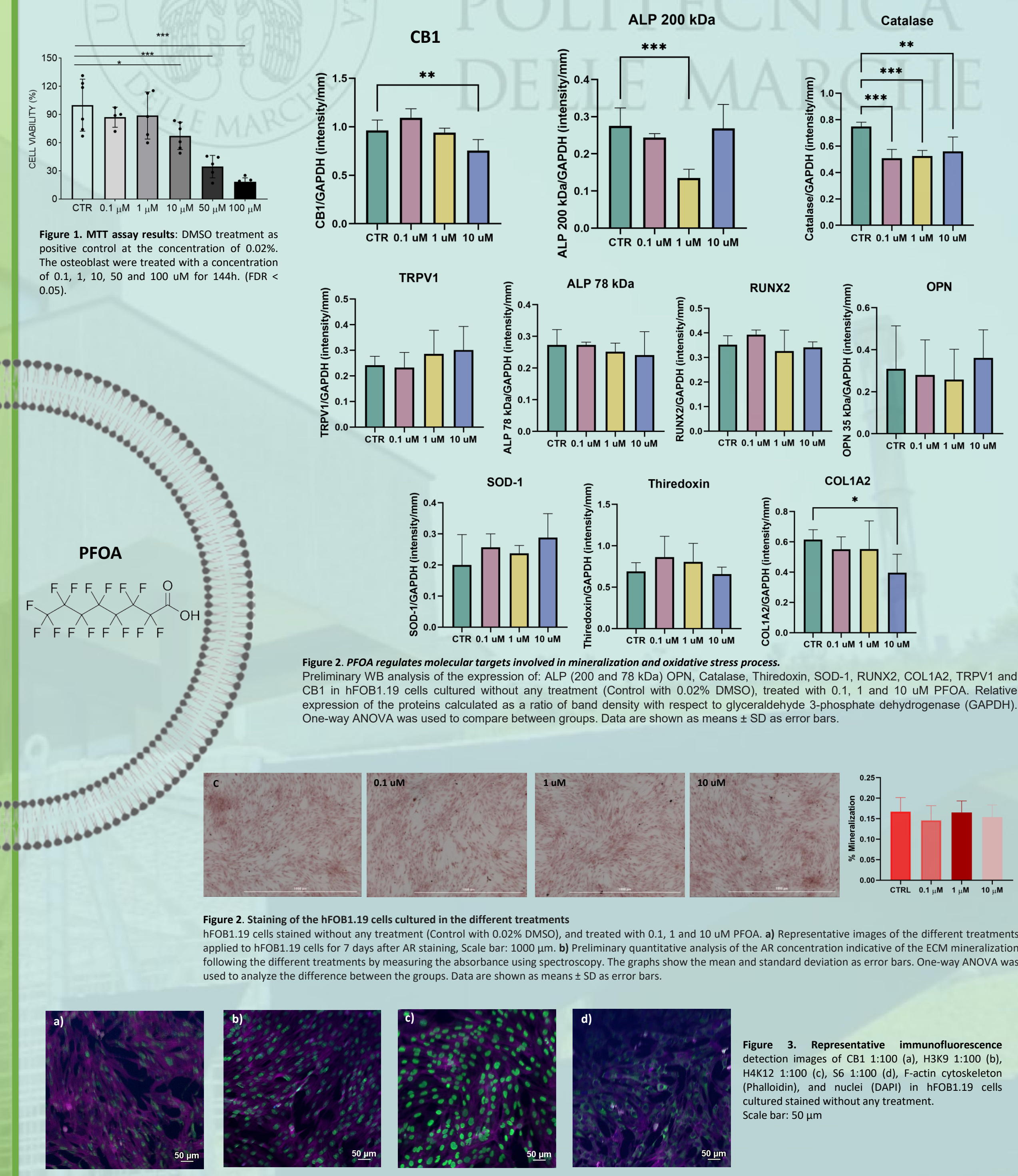
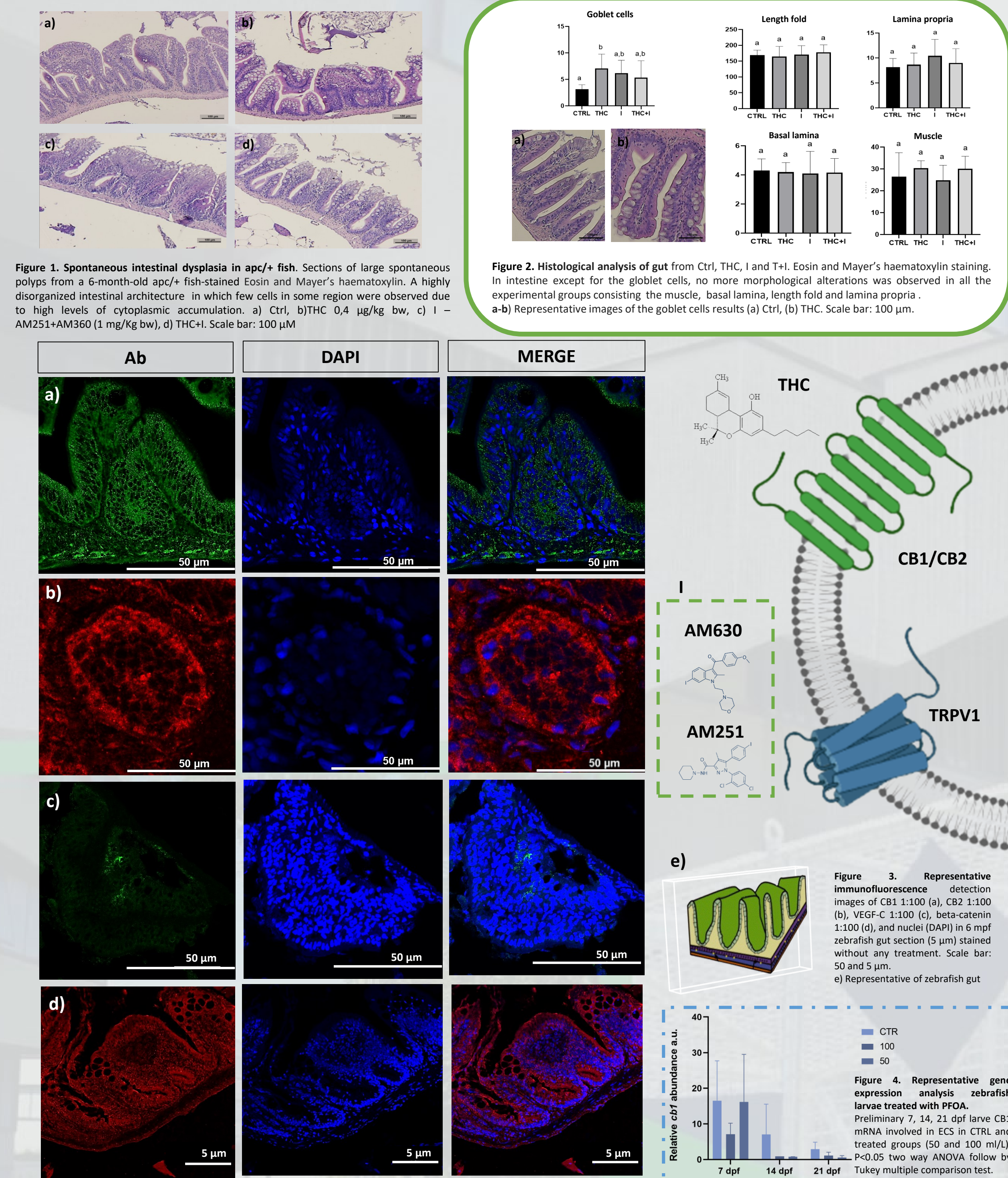
METHODS



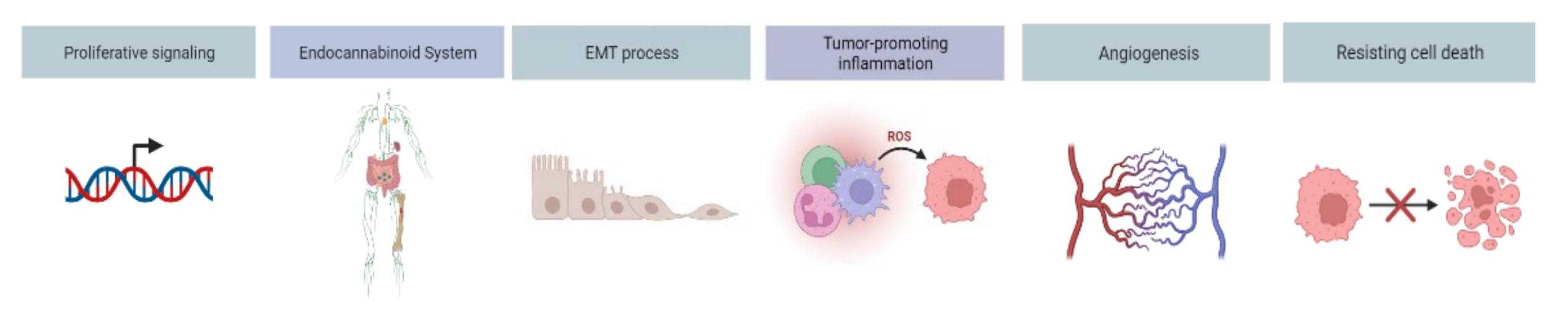
AIM

The aim of this study is to investigate the role of ECS in the pathogenesis of CRC and OP in different biological models. Regarding *in vivo* studies, the effect of THC exposure have been investigated in the development of CRC and inflammatory response in *apc^{mcr}* zebrafish mutants. Concerning *in vitro* models, this proposal will evaluate the role of ECS in human fetal osteoblast (hFOB 1.19) under inflammatory conditions, caused by Perfluorooctanoic acid (PFOA) exposure.

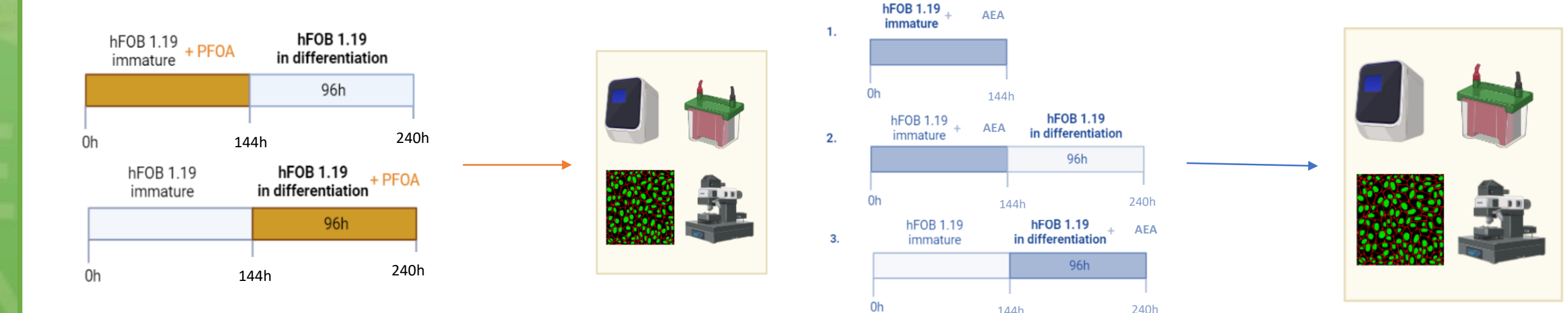
PRELIMINARY RESULTS



FUTURE PROSPECTIVES



FUTURE PROSPECTIVES



1. Lu HC, Mackie K. Review of the Endocannabinoid System. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2021 Jun;6(6):607-615. doi:10.1016/j.bpsc.2020.07.016
 2. Tibrija E. The multiple functions of the endocannabinoid system: a focus on the regulation of food intake. *Diabetol Metab Syndr*. 2010 Jan 21;2(5). doi:10.1186/1758-5996-2-5
 3. Behl T, Makkar R, Sehgal A, Singh S, Makeen HA, Albratty M, Alhazmi HA, Meraya AM, Bungau S. Exploration of Multiverse Activities of Endocannabinoids in Biological Systems. *Int J. Mol. Sci*. 2022; 23, 5734. <https://doi.org/10.3390/ijms23105734>
 4. Moreno E, Cavic M, Krivokucic A, Casado V, Canela E. 2019. The endocannabinoid system as a target in cancer diseases: Are we there yet? *Front. Pharmacol*. 2019; 10:3389. <https://doi.org/10.3389/fphar.2019.00339>
 5. Xin Y, Tang A, Pan S, Zhang J. Components of the Endocannabinoid System and Effects of Cannabinoids Against Bone Diseases: A Mini-Review. *Front. Pharmacol*. 2022 Jan 15;12:793750. doi:10.3389/fphar.2021.793750
 6. Shamseddine A, Saleh A, Charafeddine M, et al. Cancer trends in Lebanon: a review of incidence rates for the period of 2003–2008 and projections until 2018. *Popul Health Metrics* 12, 4 (2014). <https://doi.org/10.1186/1478-7954-12-4>
 7. Heavay PM, McKenna D, Rowland IR. Colorectal cancer and the relationship between genes and the environment. *Nutr Cancer*. 2004;48(2):124-41. doi:10.1207/s15327914nc4802_2
 8. Ke K, Arra M, Abu-Amer Y. Mechanisms Underlying Bone Loss Associated with Gut Inflammation. *Int J. Mol. Sci*. 2019; 20, 6323. <https://doi.org/10.3390/ijms20246323>
 9. Ahmed I, Rehman S, U, Shahmohamadnejad S, Zia M, Ahmad M, Saeed M, Akram Z, Iqbal H, M, N, Liu Q. 2021. Therapeutic Attributes of Endocannabinoid System against Neuro-Inflammatory Autoimmune Disorders. *Molecules* 26, 3389. <https://doi.org/10.3390/MOLECULES26113389>