Cannabidiol inhibits Endothelial-to-mesenchymal transition and also promotes

the reverse process in vitro

Muthu Kumar Krishnamoorthi, PhD, Keith A. Youker, PhD, Arvind Bhimaraj, MD, MPH, FACC, FHFSA Houston Methodist DeBakey Heart & Vascular Center, 6565 Fannin St, Houston, Texas 77030, USA

INTRODUCTION

- · Cannabidiol (CBD) has been investigated in cardiovascular ailments.
- Endothelial-to-Mesenchymal transition (EndoMT) could contribute to cardiac fibrosis and eventually heart failure (HF).
- CBD also exhibited anti-fibrotic effect in our nonischemic mouse model of HF.
- We show that CBD inhibits EndoMT and also promotes the reverse process Mesenchymal-toendothelial (MEndoT) transition in vitro. **Hypothesis:** CBD administration will improve cardiac function by targeting anti-fibrotic mechanisms.

METHODS

HUVECs were used as an endothelial cell model. A combination of L-NAME and Ang-II was used as EndoMT inducing agents. **EndoMT** characterized through was immunofluorescence (IF) studies for endothelial (CD31) mesenchymal and (Vimentin) markers (Krishnamoorthi MK et al., Front Pharmacol. 2022) . To evaluate the impact of CBD on EndoMT, CBD was added during the EndoMT induction process and IF studies were performed. Independently, CBD was added to EndoMT transitioned cells (after day 4 of EndoMT) and IF studies were performed at day 8.

RESULTS

Fig 1a: Inhibition of EndoMT

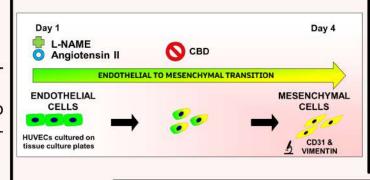


Fig. 1b: Endothelial cells on Day 4 from the experiment shown in Fig 1a. shows reduced Vimentin expression (Red color IF level) indicating that CBD inhibited in vitro EndoMT in a dose dependent manner.

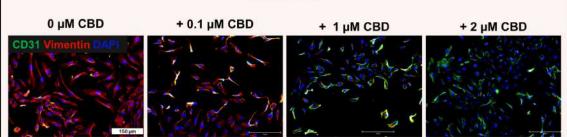


Fig 2a: Reversal of EndoMT

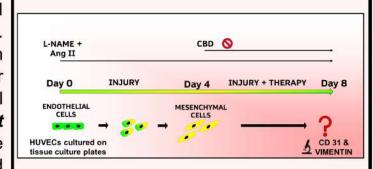
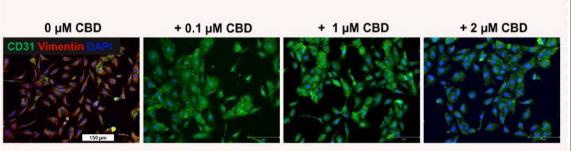


Fig. 2b: Endothelial cells on Day 8 from the experiment shown in Fig. 2a. shows reduced Vimentin expression (Red color in IF). This suggests that CBD promoted reversal of in vitro EndoMT (compared to

persistence of high Vimentin expresssion in controls- not shown here)



CONCLUSION

In conclusion, CBD not only inhibits EndoMT but also promotes MKK was supported by the Kaplar the reverse process of MEndoT transition in an in vitro model. Foundation Postdoctoral award. Part of this KAYouker@ Further, CBD protects cardiac function and exhibits an anti-work was supported by a research gran fibrotic effect, possibly mediated by EndoMT inhibition.

ACKNOWLEDGEMENT

from Cardiol Therapeutics Inc.

CONTACT

ABhimaraj@ HoustonMethodist.org HoustonMethodist.org MKrishnamoorthi@ HoustonMethodist.org