# Cannabidiol

Cannabidiol (CBD) has the potential to address metabolic imbalances and improve cognitive functions in neurodegenerative diseases, but its specific effect on TBI remains unclear. Using a fluid percussion injury model, we adopted a comprehensive approach that included behavioral testing, various imaging techniques, and deep cervical lymph node (dCLN) ligation to evaluate CBD's effects on neurological outcomes and lymphatic clearance in a TBI mouse model. Our results demonstrated that CBD markedly enhanced motor, memory, and cognitive functions, correlating with reduced levels of detrimental neural proteins. CBD also expedited the removal of intracranial tracers, increased cerebral blood flow, and improved tracer migration from lymphatic vessels to dCLNs. Intriguingly, CBD treatment modified aquaporin-4 polarization and diminished neuroinflammatory indicators. A key observation was that disrupting efferent lymphatic channels nullified CBD's positive effects on waste removal and cognitive enhancements, whereas its anti-inflammatory benefits continued. This finding suggests that CBD's ability to improve waste clearance may operate via the lymphatic system, thereby improving neurological outcomes in TBI patients. Therefore, our study underscores CBD's potential therapeutic role in TBI management [1)]

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The transcription factor NFκB drives neoplastic progression of many cancers including primary brain tumors (glioblastoma; Glioblastoma). Precise therapeutic modulation of NFκB activity can suppress central oncogenic signaling pathways in Glioblastoma, but clinically applicable compounds to achieve this goal have remained elusive.

In a pharmacogenomics study with a panel of transgenic glioma cells we observed that NFκB can be converted into a tumor suppressor by the non-psychotropic cannabinoid cannabidiol (CBD). Subsequently, we investigated the anti-tumor effects of CBD, which is used as an anticonvulsive drug (Epidiolex) in pediatric neurology, in a larger set of human primary Glioblastoma stem-like cells (hGSC). For this study, we performed pharmacological assays, gene expression profiling, biochemical and cell-biological experiments. We validated our findings using orthotopic in vivo models and bioinformatics analysis of human Glioblastoma-datasets.

Results: We found that CBD promotes DNA binding of the NFκB subunit RELA and simultaneously prevents RELA-phosphorylation on serine-311, a key residue that permits genetic transactivation. Strikingly, sustained DNA binding by RELA lacking phospho-serine 311 was found to mediate hGSC cytotoxicity. Widespread sensitivity to CBD was observed in a cohort of hGSC defined by low levels of reactive oxygen species (ROS), while high ROS content in other tumors blocked CBD-induced hGSC death. Consequently, ROS levels served as a predictive biomarker for CBD-sensitive tumors.

This evidence demonstrates how a clinically approved drug can convert NFκB into a tumor suppressor and suggests a promising repurposing option for Glioblastoma-therapy [2)].

1)
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2)
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