Evaluating novel compounds for neuroprotective effects in animal models of traumatic brain injury (TBI) is a protracted, labor-intensive, and costly effort. However, the present lack of effective options for traumatic brain injury treatment, despite decades of traumatic brain injury research, shows the critical need for alternative methods for screening new drug candidates with neuroprotective properties. Because natural products have been a leading source of new therapeutic agents for human diseases, Weisz et al. used an in vitro model of stretch injury to rapidly assess the pro-survival effects of three bioactive compounds, two isolated from natural products (clovanemagnolol [CM], vinaxanthone [VX]) and the third, a dietary compound (pterostilbene [PT]) found in blueberry. The stretch injury experiments were not used to validate drug efficacy in a comprehensive manner but used primarily, as proof-of-principle, to demonstrate that the neuroprotective potential of each bioactive agent can be quickly assessed in an immortalized hippocampal cell line in lieu of comprehensive testing in animal models of TBI. To gain mechanistic insights into potential molecular mechanisms of neuroprotective effects, they performed a pathway-specific PCR array analysis of the effects of CM on the rat hippocampus and microRNA sequencing analysis of the effects of VX and PT on cultured hippocampal neural progenitor cells. They showed that the neuroprotective properties of these natural compounds are associated with the altered expression of several genes or microRNAs that have functional roles in neurodegeneration or cell survival. The approach could help in quickly assessing multiple natural products for neuroprotective properties and expedite the process of new drug discovery for traumatic brain injury treatment [1)].

1)

Weisz HA, Boone DR, Coggins WS, Edwards GA, Willey HE, Widen SG, Siegel D, Nelson AT, Prough DS, Hellmich HL. Mechanistic insights gained from cell and molecular analysis of the neuroprotective potential of bioactive natural compounds in an immortalized hippocampal cell line. PLoS One. 2022 Jun 3;17(6):e0267682. doi: 10.1371/journal.pone.0267682. PMID: 35657963.