

# Kynurenic acid

Kynurenic acid (KYNA) is the end stage metabolite of tryptophan produced mainly by [astrocytes](#) in the central nervous system (CNS). It has neuroprotective activities but can be elevated in the neuropsychiatric disorders.

Subdural infusion of high dose of KYNA can be used as an experimental tool for the study of mechanisms of [myelin](#) damage and regeneration. On the other hand, the administration of low, physiologically relevant doses of KYNA may help to discover the role of KYNA in control of physiological myelination process <sup>1)</sup>.

Results provide further evidence for the involvement of the kynurenine pathway (KP) in [glioma](#) pathophysiology and highlight a potential role of KP products as novel and highly attractive therapeutic targets to evaluate for the treatment of brain tumors, aimed at restoring anti-tumor immunity and reducing the capacity for malignant cells to produce NAD(+), which is necessary for energy production and DNA repair <sup>2)</sup>.

KYNA was detected in all tested Glioblastoma tumor samples ( $100.3 \pm 17.6$  pmol/g wet weight). In a series of experiments the antiproliferative activity of KYNA against T98G cells was revealed (IC(50) = 1.3 mM). Moreover, KYNA reversed the stimulatory effect of glutamate on glioma cell proliferation and enhanced antiproliferative effect of glutamate receptor antagonists MK801 and GYKI 52466. Next, KYNA at concentrations much lower than those needed to reduce cell proliferation elicited a prominent inhibitory effect on glioma cell motility. Moreover, co-incubation of temozolomide, a drug commonly used in antiglioblastoma therapy, with KYNA gave a superior effect than each of the substances applied alone <sup>3)</sup>.

<sup>1)</sup>

Dabrowski W, Kwiecien JM, Rola R, Klapiec M, Stanisz GJ, Kotlinska-Hasiec E, Oakden W, Janik R, Coote M, Frey BN, Turski WA. Prolonged Subdural Infusion of Kynurenic Acid Is Associated with Dose-Dependent Myelin Damage in the Rat Spinal Cord. PLoS One. 2015 Nov 12;10(11):e0142598. doi: 10.1371/journal.pone.0142598. eCollection 2015. PubMed PMID: 26562835.

<sup>2)</sup>

Adams S, Teo C, McDonald KL, Zinger A, Bustamante S, Lim CK, Sundaram G, Braidy N, Brew BJ, Guillemin GJ. Involvement of the kynurenine pathway in human glioma pathophysiology. PLoS One. 2014 Nov 21;9(11):e112945. doi: 10.1371/journal.pone.0112945. eCollection 2014. PubMed PMID: 25415278; PubMed Central PMCID: PMC4240539.

<sup>3)</sup>

Walczak K, Deneka-Hannemann S, Jarosz B, Zgrajka W, Stoma F, Trojanowski T, Turski WA, Rzeski W. Kynurenic acid inhibits proliferation and migration of human glioblastoma T98G cells. Pharmacol Rep. 2014 Feb;66(1):130-6. doi: 10.1016/j.pharep.2013.06.007. Epub 2014 Feb 1. PubMed PMID: 24905318.

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