Arginase

Arginase (EC 3.5.3.1, arginine amidinase, canavanase, L-arginase, arginine transamidinase) is a manganese-containing enzyme. The reaction catalyzed by this enzyme is: arginine + H2O → ornithine + urea. It is the final enzyme of the urea cycle. It is ubiquitous to all domains of life.

Arginase competes with nitric oxide synthase for substrate arginine to produce ornithine and urea.

There is contradictory evidence in the literature on the role of nitric oxide in the pathophysiology of traumatic brain injury (TBI). These contradictory perspectives are likely due to different NOS isoforms - endothelial (eNOS), inducible (iNOS) and neuronal (nNOS) which are expressed in the central nervous system. Of these, the role of nNOS in acute injury remains less clear.

A study of Madan et al., from the Baylor College of Medicine, Houston, aimed to employ a genetic approach by overexpressing arginase isoforms specifically in neurons using a Thy-1 promoter to manipulate cell autonomous NO production in the context of TBI. The hypothesis was that increased arginase would divert arginine from pathological NO production.

They generated 2 mouse lines that overexpress arginase I (a cytoplasmic enzyme) or arginase II (a mitochondrial enzyme) in neurons of FVB mice.

They found that two-weeks after induction of controlled cortical injury, overexpressing arginase I but not arginase II in neurons significantly reduced contusion size and contusion index compared to wild-type (WT) mice. This study establishes enhanced neuronal arginase levels as a strategy to affect the course of TBI and provides support for the potential role of neuronal NO production in this condition [1].

1)
Madan S, Kron B, Jin Z, Al Shamy G, Campeau PM, Sun Q, Chen S, Cherian L, Chen Y, Munivez E, Jiang MM, Robertson C, Goodman C, Ratan RR, Lee B. Arginase overexpression in neurons and its effect on traumatic brain injury. Mol Genet Metab. 2018 Jul 25. pii: S1096-7192(18)30279-8. doi: 10.1016/j.ymgme.2018.07.007. [Epub ahead of print] PubMed PMID: 30055993.