Necrostatin-1s is a compound that belongs to a class of small molecules known as necrostatins. Necrostatin-1, the parent compound, was originally developed as a specific inhibitor of necroptosis, a form of programmed necrotic cell death. Necroptosis is a regulated cell death mechanism that is distinct from apoptosis and is associated with inflammation.

Necrostatin-1s is a more water-soluble and improved version of Necrostatin-1. It was developed to enhance its bioavailability and pharmacological properties for research and potential therapeutic applications. Necrostatin-1s, like its predecessor, primarily targets the activity of the kinase receptor-interacting protein 1 (RIPK1).

Key points about Necrostatin-1s:

Inhibition of RIPK1: Necrostatin-1s inhibits the activity of RIPK1, a key kinase involved in necroptosis signaling. By inhibiting RIPK1, Necrostatin-1s can block the initiation of necroptosis and promote cell survival.

Role in Research: Necrostatin-1s is commonly used in laboratory research to study necroptosis and its role in various biological processes. It has been instrumental in elucidating the mechanisms of necroptosis and its potential contributions to diseases.

Therapeutic Potential: Because necroptosis has been implicated in several diseases, including inflammatory disorders, neurodegenerative diseases, and tissue injury, Necrostatin-1s and similar compounds are being explored for their therapeutic potential. By inhibiting necroptosis, they may help protect cells and tissues from damage and inflammation.

Caution: It's important to note that while Necrostatin-1s and related compounds show promise in research and preclinical studies, their clinical applications are still in the experimental phase, and their safety and efficacy in humans are not yet fully established. Researchers are actively working to develop more specific and potent necroptosis inhibitors for potential clinical use.

Necrostatin-1s and related compounds are valuable tools in understanding cell death mechanisms and exploring potential interventions in diseases where necroptosis plays a role. However, their development and use as therapeutics require further research and clinical testing to ensure their safety and effectiveness.

Sun et al. found that the expression level of RIPK1 was drastically increased in the brain of Periventricular Leukomalacia neonatal mice models, and treatment of PVL neonatal mice with Necrostatin-1s (Nec-1s), an inhibitor of RIPK1, greatly ameliorated cerebral ischemic injury, exhibiting an increase of body weights, reduction of cerebral infarct size, neuronal loss, and occurrence of necrosis-like cells, and significantly improved the long-term abnormal neurobehaviors of PVL. In addition, Nec-1s significantly suppressed hypomyelination and promoted the differentiation of oligodendrocyte precursor cells (OPCs), as demonstrated by the increased expression levels of MBP and Olig2, the decreased expression level of GPR17, a significant increase in the number of CC-1-positive cells, and suppression of myelin ultrastructure impairment. Moreover, the mechanism of neuroprotective effects of Nec-1s against PVL is closely associated with its suppression of the RIPK1-mediated necrosis signaling molecules, RIPK1, PIPK3, and MLKL. More importantly, inhibition of RIPK1 could reduce microglial inflammatory injury by triggering the M1 to M2 microglial phenotype, appreciably decreasing the levels of M1 marker CD86 and increasing the levels of M2 markers Arg1 or CD206 in PVL mice. Taken together, inhibition of RIPK1 markedly ameliorates the brain injury and long-term neurobehavioral abnormalities of PVL mice through the reduction of neural cell necroptosis

and reversing neuroinflammation [1)]

1)

Sun J, Wang W, Ma Q, Pan X, Zhai H, Wang J, Han Y, Li Y, Wang Y. Necrostatin-1s Suppresses RIPK1-driven Necroptosis and Inflammation in Periventricular Leukomalacia Neonatal Mice. Neurochem Res. 2023 Aug 29. doi: 10.1007/s11064-023-04013-8. Epub ahead of print. Erratum in: Neurochem Res. 2023 Sep 13;: PMID: 37642893.