Chitinase 3-like protein 1

- Cross-Sectional and Longitudinal Associations of Neighborhood Disadvantage With Fluid Biomarkers of Neuroinflammation and Neurodegeneration
- Sleep disorders and Alzheimer's disease: relationship and mechanisms involving neuroinflammation, orexin and Aβ
- Transcriptomic profiling of granuloma in patients with cardiac sarcoidosis
- Identification of protein biomarker candidates associated with organ-specific immune-related toxicity and response to management by plasma proteomics
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- Fh15 Reduces Colonic Inflammation and Leukocyte Infiltration in a Dextran Sulfate Sodium-Induced Ulcerative Colitis Mouse Model
- Clinical utility of YKL-40 for understanding pathophysiology of obstructive airway disorders
- Decoding disease burden in multiple sclerosis: The role of IL-10 as biomarker of neuroinflammation and neurodegeneration

Chitinase 3-like protein 1 (CHI3L1), also known as YKL-40, is a secreted glycoprotein that is approximately 40kDa in size that in humans is encoded by the CHI3L1 gene.

The name YKL-40 is derived from the three N-terminal amino acids present on the secreted form and its molecular mass. YKL-40 is expressed and secreted by various cell-types including macrophages, chondrocytes, fibroblast-like synovial cells, vascular smooth muscle cells, and hepatic stellate cells. The biological function of YKL-40 is unclear. It is not known to have a specific receptor. Its pattern of expression is associated with pathogenic processes related to inflammation, extracellular tissue remodeling, fibrosis and solid carcinomas and asthma.

Chitinase 3-like protein 1 (CHI3L1) is emerging as a promising biomarker for assessing intracranial lesion burden and traumatic brain injury prognosis prediction. Following experimental TBI, Chi3l1 transcripts were detected in reactive astrocytes located within the pericontusional cortex. However, the cellular sources of CHI3L1 in response to hemorrhagic contusions in human brain remain unidentified. Hence, Carabias et al. examined a comprehensive collection of histologically defined acute and subacute human cerebral contusions with various surgical intervals using immunohistochemistry, validated through double immunofluorescence for markers such as GFAP, NeuN, MBP, and Iba-1, along with Fluoro-Jade C histofluorescence staining. CHI3L1 was found at meningeal interfaces, showing significant thickening of subpial glial plate. Paradoxically, CHI3L1-positive astrocytes were identified in neuroanatomical locations distant from hemorrhagic foci, where numerous eosinophilic ischemic neurons also exhibited CHI3L1 immunoreactivity. CHI3L1 immunostaining extended into white matter tracts and highlighted various phagocytic or activated microglia forms after delayed surgical decompressions. Given these findings, we advise against using CHI3L1 as a reactive astrogliosis marker due to its expression in multiple cell types, including astrocytes, neurons, oligodendrocytes, ependymocytes, leptomeningeal cells, microglia, and blood vessels. This non-selective response underscores the potential for CHI3L1 elevation patterns in biofluids to reflect the overall lesion burden extent [1)]

This study provides valuable insights into CHI3L1 expression following TBI, cautioning against its use

as a marker for reactive astrogliosis due to its broad cellular distribution. While promising as a biomarker reflecting overall lesion burden, significant challenges remain in translating these findings into clinical practice. Addressing the functional and temporal aspects of CHI3L1 and correlating its expression with patient outcomes will be crucial for advancing its application in TBI management.

Reviews

Mwale et al. explores the role of CHI3L1 in neurodegenerative disease pathogenesis, with a focus on its contributions to neuroinflammation, immune cell infiltration, and neuronal degeneration. As a key regulator of neuroinflammation, CHI3L1 modulates microglia and astrocyte activity, driving the release of proinflammatory cytokines that exacerbate disease progression. In addition to its role in disease pathology, CHI3L1 has emerged as a promising biomarker for the diagnosis and monitoring of brain disorders. Elevated cerebrospinal fluid (CSF) levels of CHI3L1 have been linked to disease severity and cognitive decline, particularly in AD and MS, highlighting its potential for clinical diagnostics. Furthermore, therapeutic strategies targeting CHI3L1, such as small-molecule inhibitors and neutralizing antibodies, have shown promise in preclinical studies, demonstrating reduced neuroinflammation, amyloid plaque accumulation, and improved neuronal survival. Despite its therapeutic potential, challenges remain in developing selective and safe CHI3L1-targeted therapies, particularly in ensuring effective delivery across the blood-brain barrier and mitigating off-target effects. This review addresses the complexities of targeting CHI3L1, highlights its potential in precision medicine, and outlines future research directions aimed at unlocking its full therapeutic potential in neurodegenerative disease treatments and brain pathologies [2)].

Mwale et al. provide a valuable contribution to the understanding of CHI3L1's role in neurodegenerative diseases, offering a foundation for future research. However, addressing the review's limitations, particularly in therapeutic translation and biomarker validation, is critical for advancing CHI3L1's clinical application. A more balanced exploration of its dual roles and translational challenges would strengthen the review's impact and relevance in the field of neurodegenerative disease research.

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Carabias CS, Alves VC, Hernández Laín A, Lagares A. Characterization of Chitinase 3-like protein 1 spatiotemporal distribution in human post-traumatic brain contusions and other neuropathological scenarios. J Neuropathol Exp Neurol. 2025 Jan 20:nlaf002. doi: 10.1093/jnen/nlaf002. Epub ahead of print. PMID: 39832298.

2)
Mwale PF, Hsieh CT, Yen TL, Jan JS, Taliyan R, Yang CH, Yang WB. Chitinase-3-like-1: a multifaceted player in neuroinflammation and degenerative pathologies with therapeutic implications. Mol Neurodegener. 2025 Jan 18;20(1):7. doi: 10.1186/s13024-025-00801-8. PMID: 39827337; PMCID: PMC11742494.