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CELL FREE DNA (CFDNA) AS BIOMARKER IN STROKE

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ABSTRACT

It highlights the presence of cfDNA across various bodily fluids and its role in inflammation, particularly in the context of stroke-induced tissue injury. The abstract emphasizes recent advancements in quantifying cfDNA and its specificity in distinguishing stroke from its mimics, as well as differentiating between ischemic and hemorrhagic stroke. Kinetic studies reveal the temporal pattern of cfDNA release post-stroke, with notable associations between elevated cfDNA levels and early hospital admission, stroke severity, and response to therapy. Furthermore, correlations with other biomarkers such as neuron-specific enolase, S100 protein, and C-reactive protein underscore the multifaceted utility of cfDNA in stroke diagnosis, subtype classification, and prognostic evaluation. The abstract concludes by advocating for further exploration of cfDNA as a promising tool in clinical stroke management.

KEYWORDS: Cell-free DNA, Tissue injury, Stroke, Inflammation.

Cell Free DNA

All organs continuously release cell free DNA, or cfDNA. 1948 saw the discovery and characterization of cfDNA in the blood plasma of both healthy and ill people.[1] Plasma,[1] as well as other bodily fluids such urine,[2] cerebral spinal fluid,[3] pleural fluid,[4] and sputum,[5] contain cfDNA. Affected tissues may release more cfDNA into the bloodstream under a variety of situations involving altered tissue composition, such as pregnancy, organ transplantation, or cancer.[6]

An ischemic stroke is a sterile tissue injury brought on by an artery supplying the brain becoming blocked. Loss of necrotic cells and damage to tissue integrity result from a shortage of oxygen and glucose. One of the main components of the pathobiology of stroke is inflammation, and the immune system actively contributes to the tissue damage brought on by the initial ischemia.[7]

Damage-associated molecular patterns (DAMPs) are essential mediators of this systemic inflammatory response to stroke. DAMPs are a heterogeneous group of immunogenic molecules including ATP, various proteins, but also DNA and RNA.[8] DAMPs are generally secreted by dying cells.[9] In stroke, it is supposed that DAMPs are mainly released from post-ischemic necrotic and apoptotic brain tissue.[10]

Blood biomarkers for stroke should ideally enable to distinguish not only between stroke and stroke mimics but also between different stroke subtypes.

It is unexpected that blood cfDNA is a fairly specific and precise biomarker in stroke, given that blood cfDNA levels are elevated in a range of physiological and pathological processes.[11] Using cfDNA-based biomarker analysis, several studies were able to discriminate stroke from stroke mimics,[13] as well as ischemic from hemorrhagic stroke.[14,15] They were also able to enhance the approach for consistently quantifying cfDNA.[12]

Information about the dynamics of cfDNA concentration following stroke is scarce in the literature. In one investigation, blood cfDNA levels peaked 48 hours following the onset of symptoms, with repeated tests taken throughout the first 72 hours.[15] A week following a stroke, Geiger et al. monitored higher cfDNA levels.[16]

Blood concentrations of cfDNA were higher in patients admitted to the hospital within 4.5 hours of the stroke's onset than in healthy controls. Additionally, they noticed a trend of decreased cfDNA levels in individuals following tPA therapy who had better neurological state. Other possible biomarkers for stroke, such as C-reactive protein, neuron-specific enolase (NSE), and S100 protein in individuals with ischemic stroke. Blood concentrations of cfDNA, NSE, and S100 at three and six days following a stroke were observed to correlate with the severity of the stroke at the time of hospital admission.

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