DKK1

Dickkopf-related protein 1 is a protein that in humans is encoded by the DKK1 gene.

This gene encodes a protein that is a member of the dickkopf family. It is a secreted protein with two cysteine rich regions and is involved in embryonic development through its inhibition of the WNT signaling pathway.

Dickkopf-1 (DKK-1), an inhibitor of the canonical/-catenin cascade of the Wnt pathway, was upregulated in brain tissues of hemorrhagic stroke rats, and its rising circulating levels were associated with poor prognosis of acute ischemic stroke patients. We attempted to ascertain the relationship between serum DKK-1 levels and 30-day death after severe traumatic brain injury (sTBI).

MATERIALS AND METHODS: Serum DKK-1 levels were gauged in a total of 94 sTBI patients and 94 healthy controls. Trauma severity was assessed using Glasgow Coma Scale (GCS) and Rotterdam classification based on head computerized tomography scan. Prognostic variable was 30-day death.

RESULTS: Compared with controls, serum DKK-1 levels were substantially elevated in patients (median value, 3.7 versus 1.0 ng/ml). Area under receiver operating characteristic curve was 0.802 (95% confidence interval (CI), 0.708-0.877) for predicting 30-day death. Adjusted logistic regression showed that serum DKK-1 levels above 3.7 ng/ml remained as an independent marker of 30-day death (odds ratio, 8.573; 95% CI, 1.386-53.020) and overall survival (hazard ratio, 7.322; 95% CI, 1.320-40.622). An intimate correlation existed between DKK-1 levels and GCS scores (r = -.649) in addition to Rotterdam classification (r = .664).

CONCLUSIONS: High serum levels of DKK-1 are closely associated with increasing severity and rising short-term mortality of sTBI [1)].

Minocycline treatment decreased DKK1 expression but increased Wnt1, β-catenin and Occludin, a phenomenon mimicked by DKK1 silencing. These data suggest that minocycline improves the consequences of intracerebral hemorrhage (ICH) by preserving blood brain barrier (BBB) integrity and attenuating neurologic deficits in a DKK1-related manner that involves enhancement of the Wnt1-β-catenin activity [2)].

Elevated levels of DKK1 in bone marrow, plasma and peripheral blood is associated with the presence of osteolytic bone lesions in patients with multiple myeloma.

Expression of DKK1 was hypoxia dependent in human malignant glioma cell lines. The induction of DKK1 by intracellular crosstalk or hypoxia stimuli sheds light on the intense adaption of glial tumour cells to environmental alterations [3)].

1)
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