

# CHUK (IKK $\alpha$ )

**Full name:** Conserved Helix-Loop-Helix Ubiquitous Kinase **Alias:** IKK $\alpha$  (I $\kappa$ B kinase alpha)

**Biological role:** CHUK encodes a serine/threonine kinase that forms part of the I $\kappa$ B kinase (IKK) complex. It regulates the **NF- $\kappa$ B signaling pathway**, a master controller of inflammation, apoptosis, and cellular stress responses. Upon activation, CHUK phosphorylates I $\kappa$ B proteins, leading to their degradation and subsequent nuclear translocation of NF- $\kappa$ B transcription factors.

## Mendelian Randomization studies

In a [Mendelian Randomization](#) study + in silico gene functional analysis Quanming Zhou et al. from the Department of Neurosurgery, Affiliated Hospital of Putian University, Putian, Fujian, China published in the [International Journal of Neuroscience](#) to determine whether [neuroinflammation-related genes](#) causally influence [intracerebral hemorrhage](#) (ICH) risk using two-sample Mendelian randomization (MR), and to explore underlying mechanisms via protein-protein interaction (PPI), [Gene Ontology](#) (GO), and [Gene Set Enrichment Analysis](#) (GSEA). Increased expression of **CHUK** and **CTLA4** genes is causally associated with higher ICH risk in both EBI-ICH and Finn-ICH datasets (e.g., CHUK OR = 1.17–1.25; CTLA4 OR  $\approx$  1.23–1.29). These associations implicate NF- $\kappa$ B signaling and immune regulation pathways. CHUK and CTLA4 may represent novel therapeutic targets for ICH intervention <sup>1)</sup>

## Critical appraisal

### Strengths

- **Robust MR design:** Use of two independent GWAS datasets (Ebi, Finn) enhances result validity. - **Consistent findings:** Both datasets showed similar effect sizes for CHUK and CTLA4. - **Functional follow-up:** PPI, GO, and GSEA reinforce biological plausibility, particularly NF- $\kappa$ B and immune pathways.

### Limitations

- **SNP significance threshold loosened:** Instrument selection used  $p < 5 \times 10^{-6}$  — more permissive than standard genome-wide ( $p < 5 \times 10^{-8}$ ), potentially increasing weak instrument bias. - **Population limitation:** Both GWAS datasets are European-only; findings may not generalize to other ancestries. - **Gene expression inference:** MR infers expression effects indirectly—no direct transcriptomic or proteomic validation in brain tissues. - **No experimental validation:** While gene-level associations imply causality, functional studies (e.g. knockdown, inhibition) are necessary to prove therapeutic relevance.

### Intellectual rigor

Authors presented sensitivity analyses (MR-Egger, weighted median) and adjusted for pleiotropy. However, quantitative details on IV strength (e.g. F-statistics) and pleiotropy metrics (e.g. MR-PRESSO outputs) are missing in the abstract — these should be transparently reported.

## Final verdict: 6.5 / 10

Good MR methodology and replication, biologically plausible pathways, but limited by relaxed instrument selection, lack of diverse populations, and no direct validation in clinical or experimental settings.

## Takeaway for practicing neurosurgeons

Genetic upregulation of [CHUK](#) and [CTLA4](#) may predispose individuals to ICH via enhanced NF-κB-mediated [neuroinflammation](#). Clinicians should watch for emerging therapies targeting these pathways—as they may offer future risk stratification tools or therapeutic targets.

## Bottom line

This MR study identifies CHUK and CTLA4 as potential causal genetic contributors to ICH risk, supporting the role of NF-κB-driven neuroinflammation in hemorrhagic stroke. Confirmatory functional and clinical studies are required before translation.

Publication date: July 2, 2025

1)

Zhou Q, Wu S, Kang Y. Causal Associations Between [Neuroinflammation-Related Genes](#) and [Intracerebral Hemorrhage](#): An Integrated Study of [Mendelian Randomization](#) and [Gene Functional Analysis](#). *Int J Neurosci*. 2025 Jul 2;1-14. doi: 10.1080/00207454.2025.2529232. Epub ahead of print. PMID: 40601346.

From:  
<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:  
<https://neurosurgerywiki.com/wiki/doku.php?id=chuk&rev=1751483407>

Last update: **2025/07/02 19:10**

