

NEAT1-31

Li et al. identify a novel micropeptide, NEAT1-31, encoded by the long non-coding RNA LincNEAT1, significantly enhancing human macrophages' phagocytic capacity. Using in vitro phagocytosis assays, ribosome profiling, and phosphoproteomic analysis, the authors show that NEAT1-31 directly activates the Aurora-A kinase, leading to stimulation of the PI3K-AKT signaling pathway, which is known to regulate cytoskeletal rearrangement and phagocytosis. NEAT1-31 also synergizes with anti-CD47 therapy to enhance tumor cell clearance, highlighting its potential as an immunotherapeutic adjuvant¹⁾.

□ Critical Analysis

□ Strengths

Novel Mechanism: Demonstrates that a presumed lncRNA can encode a functional peptide with direct immunomodulatory effects.

Mechanistic Clarity: Solid molecular pathway is proposed (NEAT1-31 → Aurora-A → PI3K-AKT → phagocytosis).

Translational Relevance: Enhances effect of anti-CD47, indicating possible clinical synergy in immunotherapy.

Robust methodology: Uses primary macrophages, ribosome profiling, phosphoproteomics, and in vivo validation.

□ Limitations

Preclinical only: No pharmacokinetic or toxicity data; no human trials.

Delivery method unclear: It's not specified how NEAT1-31 would be delivered efficiently in clinical settings.

Limited cancer types tested: Although claimed to act broadly, evidence is strongest for breast cancer models.

□ Implications

Redefines the dogma of non-coding RNAs by revealing a peptide with therapeutic potential.

Provides a blueprint for discovering other hidden immunoregulatory peptides within annotated lncRNAs.

May serve as a next-generation “eat-me” signal enhancer in the context of checkpoint blockade immunotherapy.

¹⁾
Li J, Zhang J, Li X, Liu X, Zeng B, Luo J, Wang H, Zhang H, Gao X. LincNEAT1 Encoded-NEAT1-31

Promotes Phagocytosis by Directly Activating the Aurora-A-PI3K-AKT Pathway. Adv Sci (Weinh). 2025 May 8:e2413473. doi: 10.1002/advs.202413473. Epub ahead of print. PMID: 40344649.

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