Transcriptome Dynamics and ADAR-Mediated RNA Editing In Fluoroquinolone Treated Astrocytes Exposed to Cadmium

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Fluoroquinolones (FQs) are widely prescribed antibiotics with many beneficial pharmacological effects however; they carry FDA black box warnings for neurological side effects. This disconnect represents a critical gap in knowledge. Given the role of ADAR (Adenosine Deaminase Acting on dsRNA) in immune regulation and brain development, I performed computational analysis of RNA-seq data from human astrocytes exposed to cadmium, a neuroinflammatory stressor, treated with moxifloxacin or levofloxacin. KEGG pathway enrichment analysis of TNF signaling, NF-kB, MAPK, and cytokine-cytokine receptor interaction pathways revealed downregulation of anti-apoptotic factors and transcriptional regulators following FQ treatment. Cadmium suppressed ADAR expression by 24.9 percent (69.2 to 52.0 TPM, p less than 0.001), and fluoroquinolone treatment did not restore this suppression. The Alu Editing Index revealed suppressed A to I editing independent of ADAR expression levels, most significantly in intronic regions, where the index dropped from 0.90 to 0.52 with levofloxacin (p equal 9.02e-6). Gene Ontology identified antigen processing and presentation of peptide and endogenous peptide antigens via MHC class I as the top enriched biological processes. Molecular docking of the ADAR2 deaminase domain revealed chelating groups proximal to the catalytic zinc ion, suggesting inhibition through zinc chelation. These findings suggest a novel feedback mechanism in which cadmium suppresses ADAR, FQs further inhibit its activity through zinc chelation, the resulting editing drop disrupts MHC class I immune signaling, and neuroinflammation persists consistent with the documented clinical side effects of FQs.

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