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Transcriptomic gene-network analysis for neurotoxicity and drug repurposing

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Our study established a research scheme of integrative transcriptomic analysis for investigating the neurodegenerative toxicity of silver nanoparticles (AgNPs) and applying to explore drug repurposing of spinal muscular atrophy (SMA). The transcriptomic analysis of mouse brain neural cells after AgNPs exposure found that the gene expressions of C-X-C motif chemokine 13 (CXCL13), macrophage receptor with collagenous structure (MARCO) and glutathione synthetase (GSS) were induced for inflammatory response and oxidative stress, and additionally amyloid precursor protein (APP) was induced and neprilysin (NEP) and low-density lipoprotein receptor (LDLR) were reduced for Aβ plaque production and aggregation. It suggested AgNPs could alter gene expressions of Aβ deposition potentially to cause neurodegenerative disorder (Alzheimer's disease) progression underlying Aβ deposition. On the other hand, the 39 human microarray datasets across different types of SMA tissues were used for the integrative transcriptomic analysis, which identified TNFα-BMP4-SERPINE1-GATA6 pathway associated with disease severity. Down-regulation of bone morphogenetic protein 4 (BMP4) may be one of the key points in SMA pathogenesis. BMP4 expression can be induced by cholesterol lowering drug Atorvastatin. SMA mice receiving Atorvastatin treatment prolonged the lifespan, increased body weight, improved motor coordination and exhibited reduced motor neuron degeneration and muscle and cardiac atrophy. In conclusion, the integrative transcriptomic analysis is a useful tool for toxicological effect evaluation and drug repurposing.

Biography

Chun-Yu Chuang focuses her research on biological effects of environmental factors on gene expression relevant to diseases.

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