

## Identifying Metabolic Pathways Associated with Neuroprotection Mediated by Tibolone in Human Astrocytes under an Induced Inflammatory Model

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**Abstract :** In this work, proteins and metabolic pathways associated with the neuroprotective response mediated by the synthetic neurosteroid tibolone under a palmitate-induced inflammatory model were identified by flux balance analysis (FBA). Three different metabolic scenarios ('healthy', 'inflamed' and 'medicated') were modeled over a gene expression data-driven constructed tissue-specific metabolic reconstruction of mature astrocytes. Astrocyte reconstruction was built, validated and constrained using three open source software packages ('minval', 'g2f' and 'exp2flux') released through the Comprehensive R Archive Network repositories during the development of this work. From our analysis, we predict that tibolone executes their neuroprotective effects through a reduction of neurotoxicity mediated by L-glutamate in astrocytes, inducing the activation several metabolic pathways with neuroprotective actions associated such as taurine metabolism, gluconeogenesis, calcium and the Peroxisome Proliferator Activated Receptor signaling pathways. Also, we found a tibolone associated increase in growth rate probably in concordance with previously reported side effects of steroid compounds in other human cell types.

**Keywords :** astrocytes, flux balance analysis, genome scale metabolic reconstruction, inflammation, neuroprotection, tibolone

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