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Exploring the neuroprotective effects of Tibolone during astrocytic metabolic inflammation: A flux balance analysis approach**Janneth Gonzalez, Daniel Osorio and Andres Pinzon**
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Inflammation is a complex biological response to injuries, metabolic disorders or infections and its dysregulation induce many complex diseases through astrocytic dysfunction. The increase of free saturated fatty acid produce a metabolic inflammation response generally associated with the induction of diverse intracellular stresses, such as mitochondrial oxidative stress, endoplasmic reticulum stress, and autophagy defects. Astrocytes respond to inflammation through a complex reaction called astrogliosis. During astrogliosis, glial cells generally associated to several beneficial activities in the CNS, also act as a source of inflammatory mediators and as generators of ROS that have the potential to damage neurons. In search of compounds with neuroprotective effects that imitate the neuroprotective actions of steroids without their harmful side effects. The synthetic neurosteroid Tibolone was identified. Tibolone acts as an Estrogen Receptor Modulator, a Selective Tissue Estrogenic Activity Regulator (STEAR) and has been shown neuroprotective effects in cultured and under ischemia injury rat neurons. Nevertheless, actually is not well known, the effects of tibolone over glial cells that allows its neuroprotective action. In this work, we model and simulate the metabolic inflammation response in mature astrocytes through Flux Balance Analysis (FBA) and explore the neuroprotective effects of tibolone under the inflamed state. We focused on identification of changes in metabolic pathways activation, functional products, gliotransmitter release and the neuroprotective effects mediated by tibolone over inflamed scenario. The generated network, consisted of 1262 genes encoding for enzymes performing 2,747 reactions distributed across eight compartments, which was studied using constrained-based modeling approach to recreate three different scenarios in mature astrocytes (healthy, inflamed and medicated) and validated with available experimental.

Biography

Janneth Gonzalez is a Professor of Computational and Molecular Biology at the Pontificia Universidad Javeriana, Bogota, Colombia. She has received her Bachelor's, Master's degree in Computational Biochemistry and Doctorate in Biological Sciences from the Pontificia Universidad Javeriana. Her research involves application of computational techniques to problems in biomedicine and in the associated basic sciences.

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