

# Identifying proteins and metabolic pathways associated with the neuroprotective response mediated by tibolone in astrocytes under an induced inflammatory model

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Instituto de Genética, Universidad Nacional de Colombia

**Universidad Nacional de Colombia, November 2016**



# Objectives:

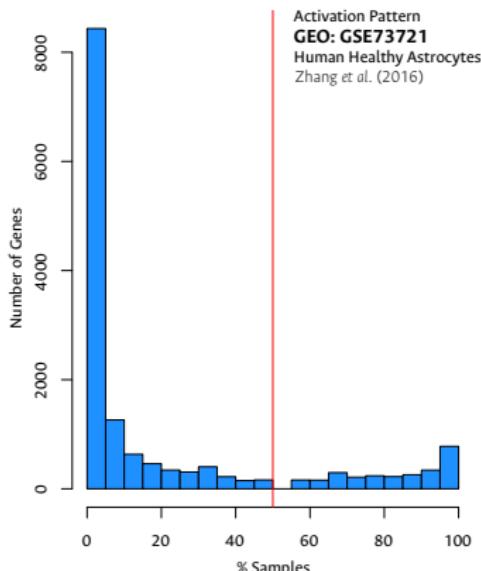
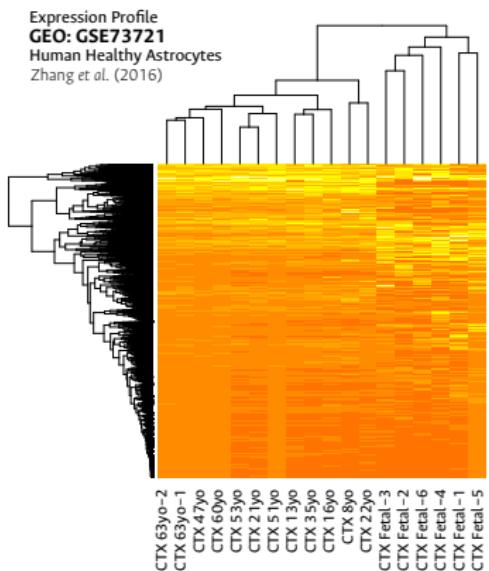
To identify proteins and metabolic pathways involved in the neuroprotective effects of tibolone in human astrocytes based in metabolic scenarios comparation we set:

- ▶ Build a tissue specific computational model of astrocytes metabolism using gene expression data integration.
- ▶ Evaluate the effects caused by the increase of free fatty acids and tibolone presence in astrocytes metabolism.
- ▶ Determine metabolic pathways and relevant functional products in response to steroid tibolone through systems biology approximations.
- ▶ Evaluate the importance of proteins and metabolic pathways previously identified on the dynamics of the metabolic model.

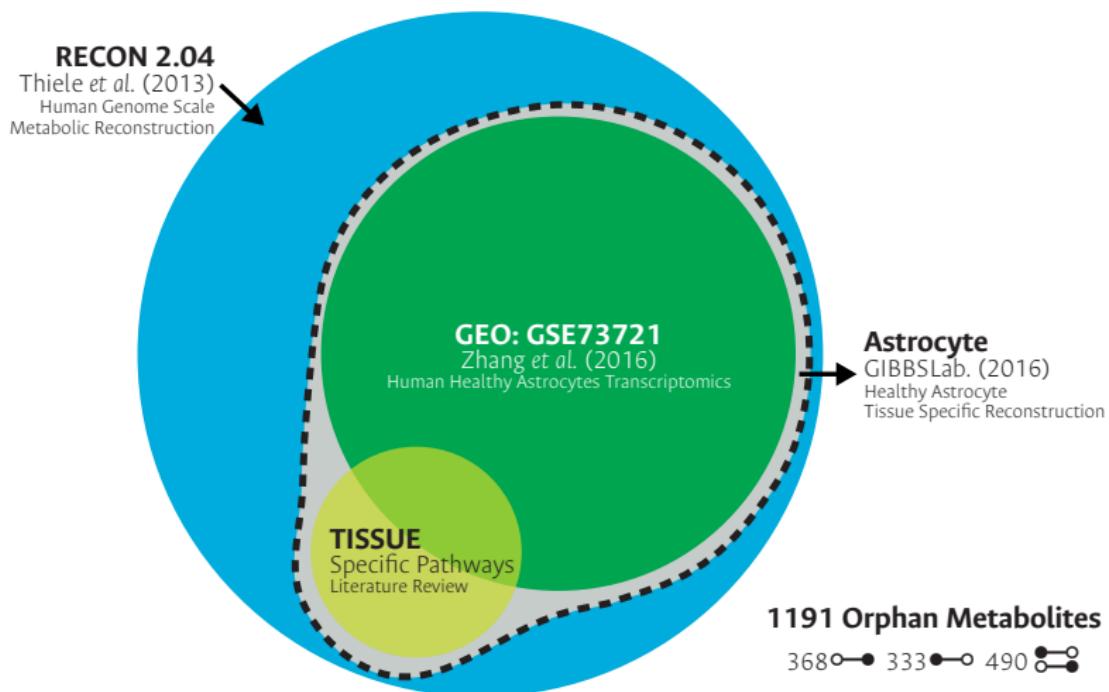
## OBJECTIVE 1:

Build a tissue specific computational model of astrocytes metabolism using gene expression data integration.

# Human Astrocytes Gene Expression Data



# Mapping Reactions



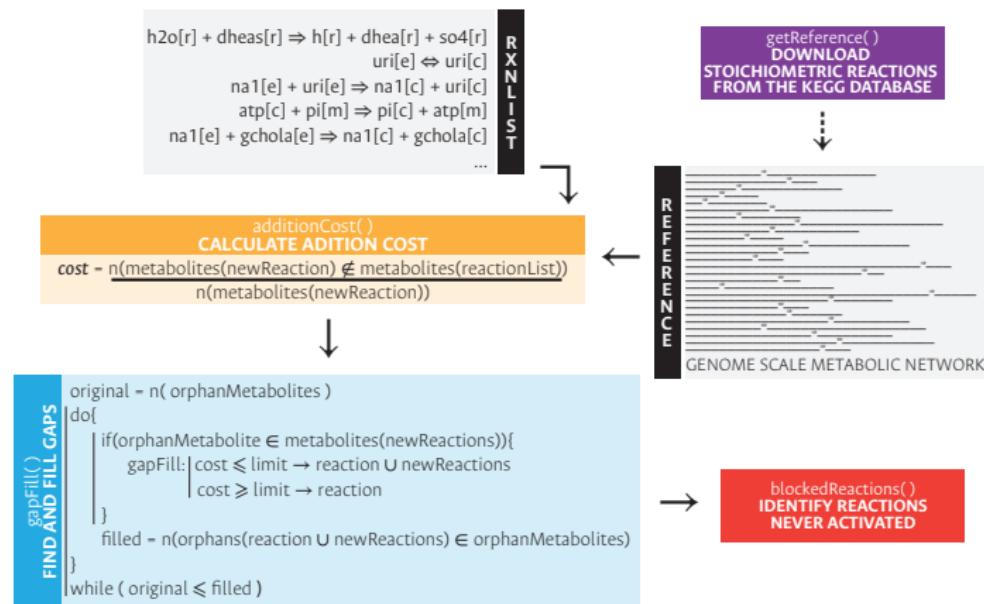
# Software Development



## 'g2f' Package

An R Package to Find and Fill Gaps for genome-scale metabolic networks  
 Kelly Botero, Daniel Osorio, Janneth Gonzalez and Andres Pinzón-Velasco.

Language: R  
 Stable: CRAN  
 Development: gibbslab/g2f  
 License: GPL-2  
 Binaries: Windows - Linux - Mac



## Software Development

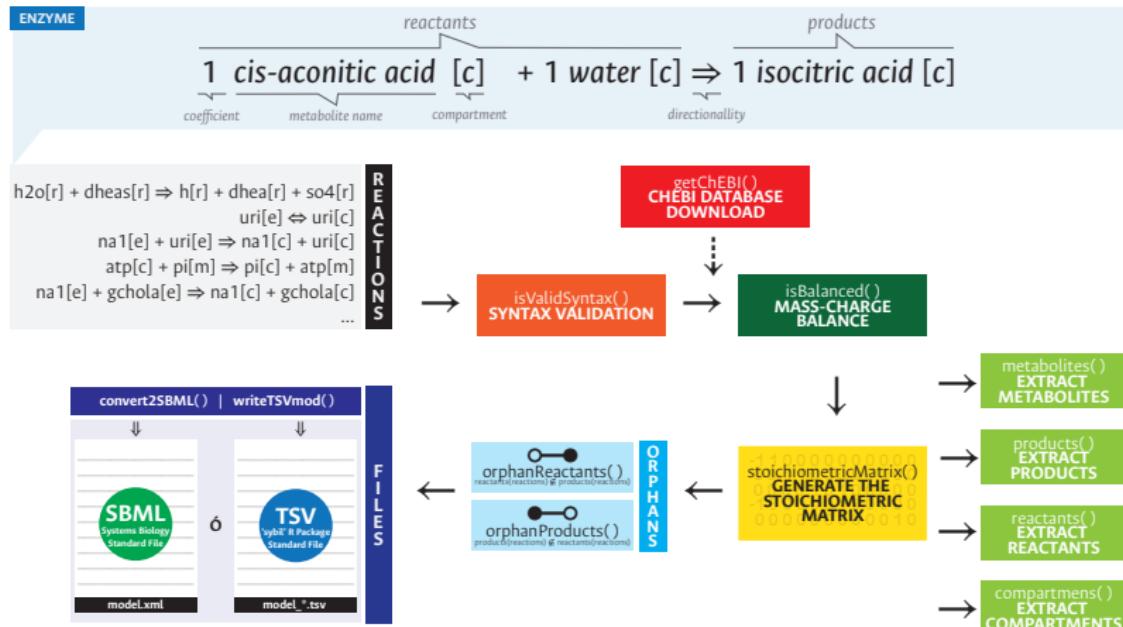


## ‘minval’ Package

An R Package for MINimal VAIdation of stoichiometric reactions

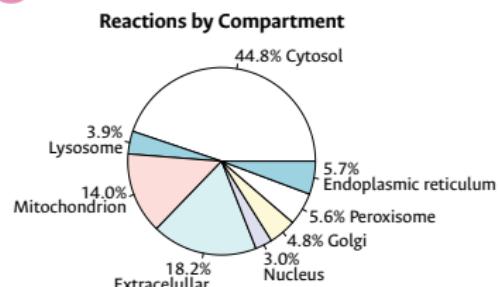
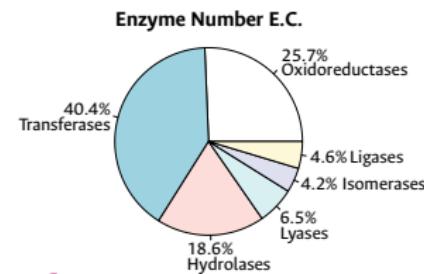
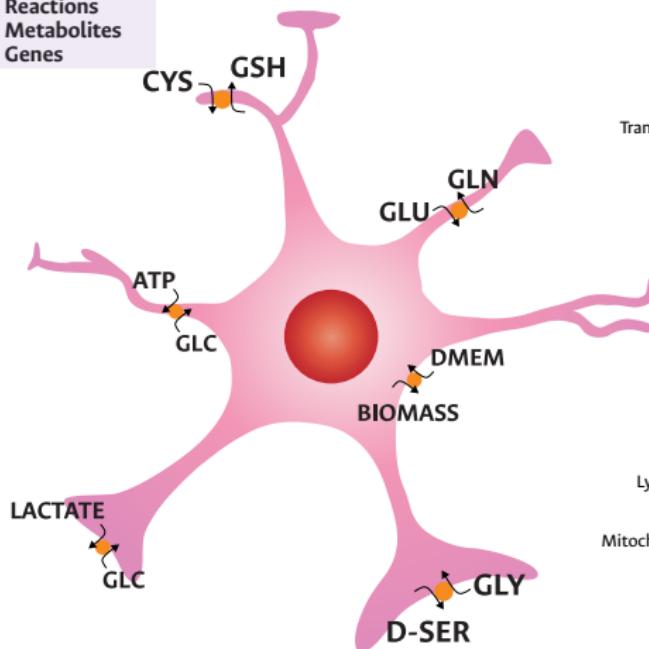
AN R Package for MINIMAL VALIDATION OF  
Daniel Osorio, Janneth González and Andrés Pinzón-Velasco

**Language:** R  
**Stable:** CRAN  
**Development:**  gibbslab/minerva  
**License:**  GPL-2  
**Binaries:** Windows - Linux - Mac



# Astrocyte Model

8 Compartments  
2747 Reactions  
1956 Metabolites  
1262 Genes



# Software Development



## 'exp2flux' Package

An R Package to convert expression data to FBA fluxes  
*Daniel Osorio, Kelly Botero, Janneth Gonzalez and Andres Pinzón-Velasco.*

Language: R

Stable: CRAN

Development: gibbslab/exp2flux

License: GPL-2

Binaries: Windows - Linux - Mac

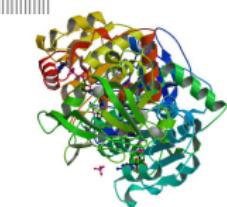
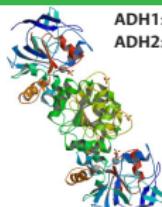
E.C: 1.1.1.1



1.1.1.1

ADH2

ADH1



(ADH2 or ADH1)

sum (ExprADH2 + ExprADH1)

E.C: 3.4.21.5



3.4.21.5

IDE.A

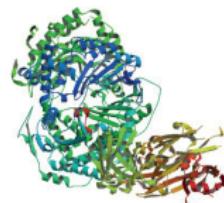
IDE.B

IDE.C

IDE.A:

IDE.B:

IDE.C:



GPR

(IDE.A and IDE.B and IDE.C)

min (ExprIDE.A, ExprIDE.B, ExprIDE.C)

GENE EXPRESSION  
DATA



exp2flux()  
CONVERT GENE  
EXPRESSION DATA  
TO FBA FLUXES



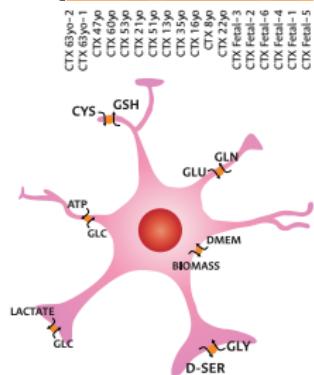
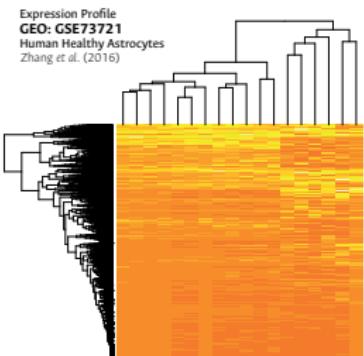
CONSTRAINED  
METABOLIC MODEL



fluxDifferences()  
COMPUTE FOLDCHANGE  
OF FLUXES BETWEEN  
METABOLIC SCENARIOS

METABOLIC MODEL  
WITH GPR

# Mature Model



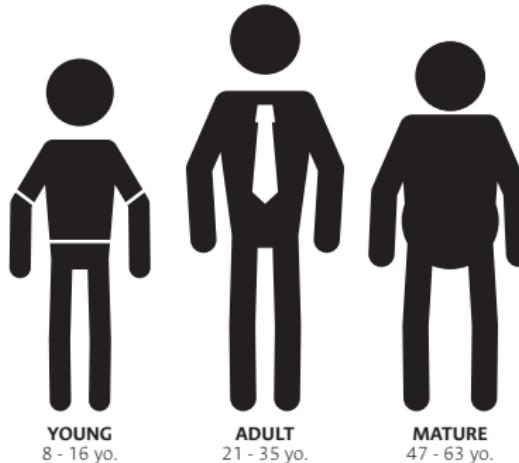
## 'exp2flux' Package

An R Package to convert expression data to FBA fluxes

Daniel Osorio, Kelly Botero, Janneth Gonzalez and Andres Pinzón-Velasco.



FETAL



## OBJECTIVE 2:

Evaluate the effects caused by the increase of free fatty acids and tibolone presence in astrocytes metabolism.

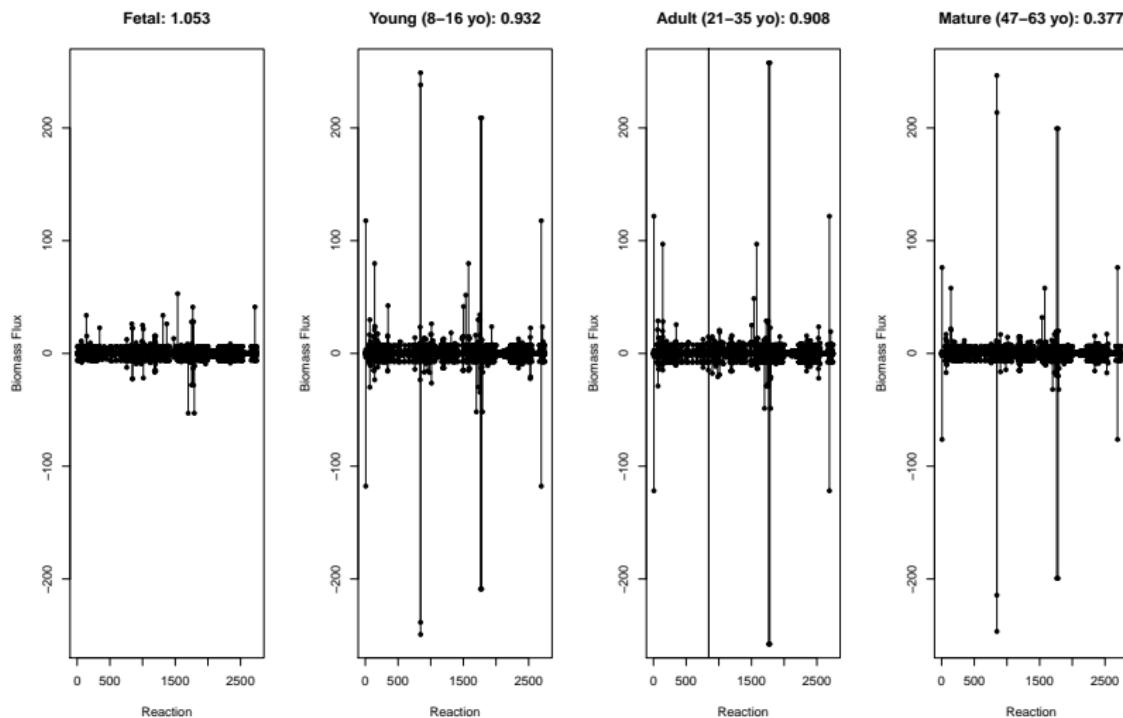
## OBJECTIVE 3:

Determine metabolic pathways and relevant functional products in response to steroid tibolone through systems biology approximations.

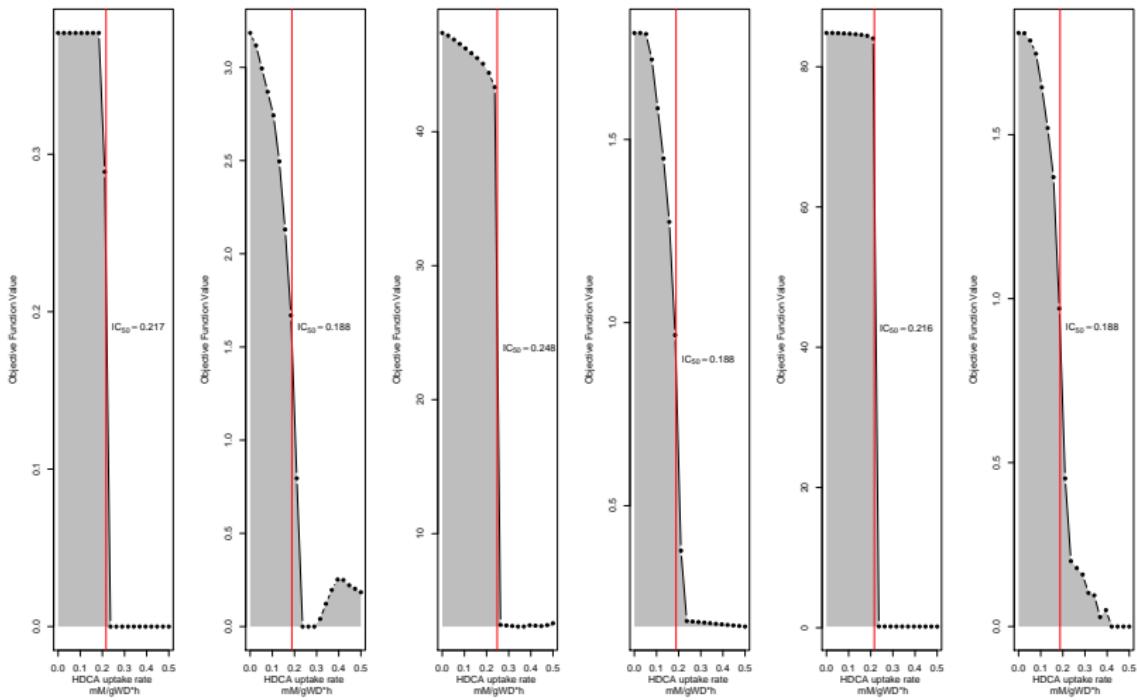
## OBJECTIVE 4:

Evaluate the importance of proteins and metabolic pathways previously identified on the dynamics of the metabolic model.

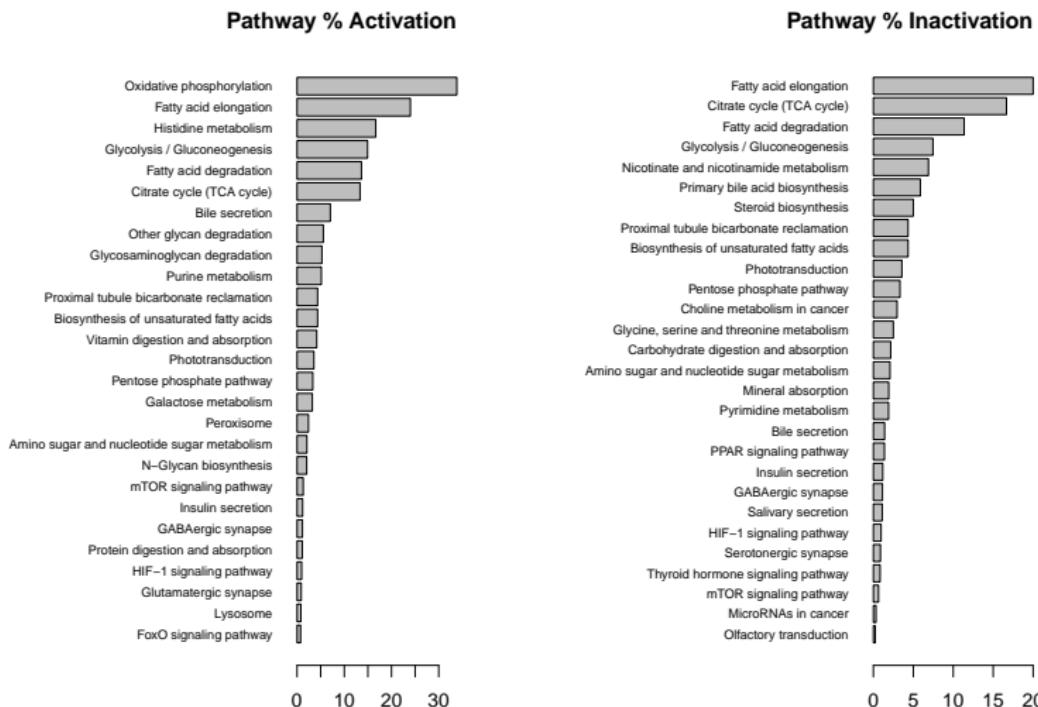
# Age Related Metabolic Changes in Astrocytes



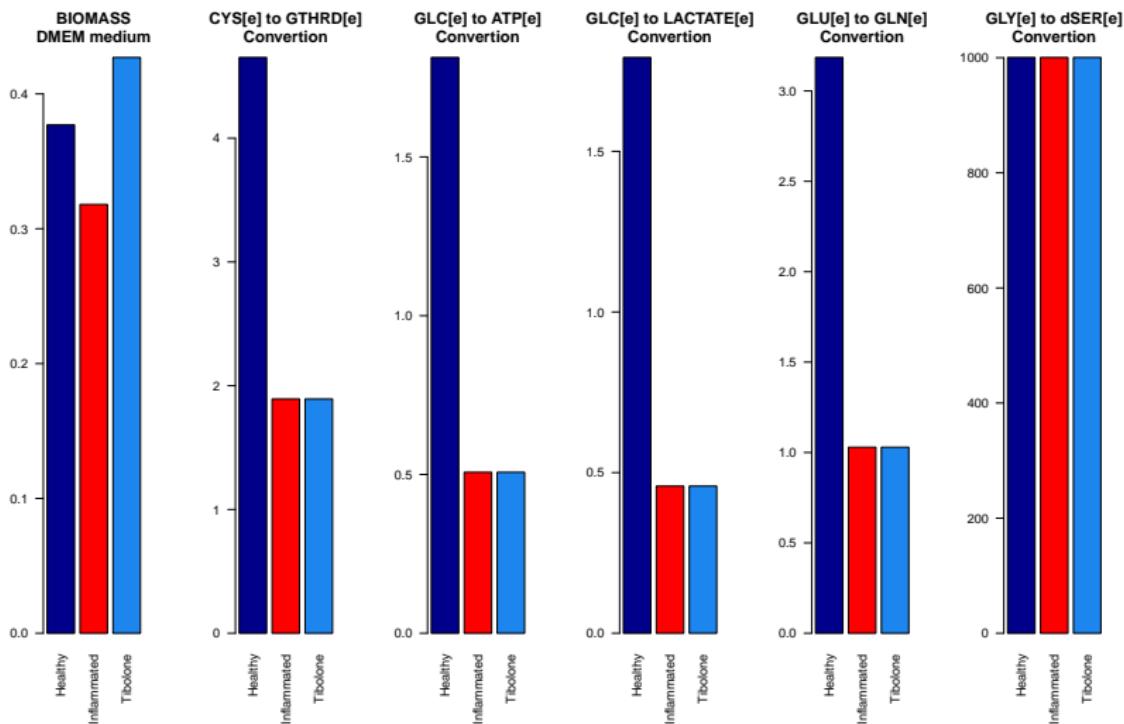
$$IC_{50} = 0.208 \pm 0.024 \text{ mMgDW}^{-1}\text{h}^{-1}$$



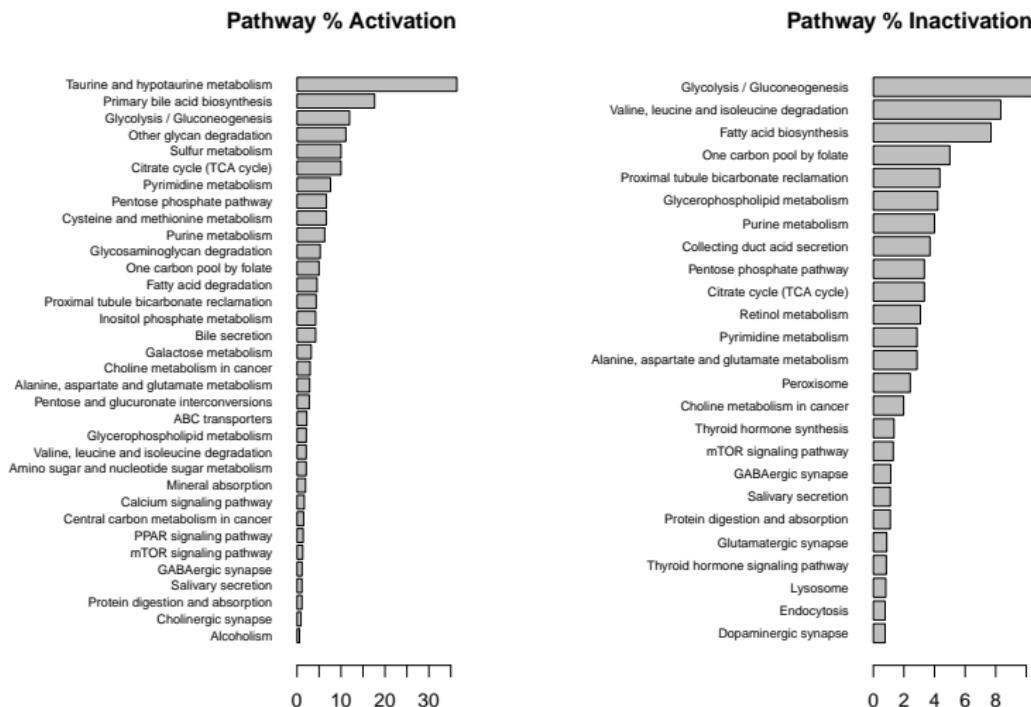
# Inflammation Related Metabolic Changes in Astrocytes



# Tibolone Effects in Inflamed Astrocytes



# Tibolone Metabolic Changes in Inflamed Astrocytes





# Advances of this work were presented as:

## Metabolic inflammation effects over the gliotransmitters release in mature astrocytes: a network-based approach.

Daniel Osorio MSc., Janneth Gonzalez PhD., Andrés Pinzón-Velasco PhD.  
Bioinformatics and Computational Systems Biology Lab, Universidad Nacional de Colombia.



at: \_\_\_\_\_



CDMX, México  
Short Talk



Barcelona, España  
Poster

ICGEB Course on Bioinformatics and Computational Neuroscience



Pontificia Universidad Javeriana  
5 - 8 October - Bogotá, Colombia

Bogotá, Colombia  
Short Talk

This study is under development at the:



## **Bioinformatics and Computational Systems Biology Lab**

Institute for Genetics - Universidad Nacional de Colombia

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[ampinzonv@unal.edu.co](mailto:ampinzonv@unal.edu.co)