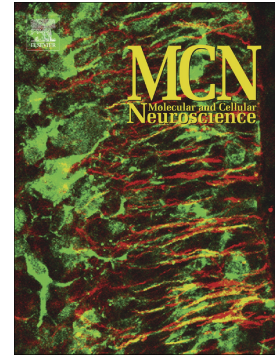


## Accepted Manuscript

The association of spinophilin with disks large-associated protein 3 (SAPAP3) is regulated by metabotropic glutamate receptor (mGluR) 5

Cameron W. Morris, Darryl S. Watkins, Asma B. Salek, Michael C. Edler, Anthony J. Baucum



PII: S1044-7431(17)30384-6  
DOI: [doi:10.1016/j.mcn.2018.06.001](https://doi.org/10.1016/j.mcn.2018.06.001)  
Reference: YMCNE 3322

To appear in: *Molecular and Cellular Neuroscience*

Received date: 6 December 2017  
Revised date: 11 June 2018  
Accepted date: 12 June 2018

Please cite this article as: Cameron W. Morris, Darryl S. Watkins, Asma B. Salek, Michael C. Edler, Anthony J. Baucum , The association of spinophilin with disks large-associated protein 3 (SAPAP3) is regulated by metabotropic glutamate receptor (mGluR) 5. *Ymcne* (2017), doi:[10.1016/j.mcn.2018.06.001](https://doi.org/10.1016/j.mcn.2018.06.001)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The association of spinophilin with disks large-associated protein 3 (SAPAP3) is regulated by metabotropic glutamate receptor (mGluR) 5.

Cameron W. Morris<sup>#1</sup>, Darryl S. Watkins<sup>#3</sup>, Asma B. Salek<sup>#2</sup>, Michael C. Edler<sup>2</sup>, Anthony J. Baucum II<sup>1,2,3,4\*</sup>

<sup>1</sup>Undergraduate Neuroscience program and <sup>2</sup>Department of Biology, Indiana University-Purdue University Indianapolis, School of Science. <sup>3</sup>Stark Neurosciences Research <sup>4</sup>Department of Pharmacology and Toxicology Institute Indiana University School of Medicine.

<sup>#</sup>These authors contributed equally.

\*To whom correspondence should be sent

Anthony J. (A.J.) Baucum II, Ph.D.

723 W. Michigan Street

SL306

Indianapolis, IN.

46278

USA

Tel. 317-274-0540

Fax. 317-274-2846

[ajbaucum@iupui.edu](mailto:ajbaucum@iupui.edu)

#### Abstract

Spinophilin is the most abundant protein phosphatase 1 targeting protein in the postsynaptic density of dendritic spines. Spinophilin associates with myriad synaptic proteins to regulate normal synaptic communication; however, the full complement of spinophilin interacting proteins and mechanisms regulating spinophilin interactions are unclear. Here we validate an association between spinophilin and the scaffolding protein, disks large-associated protein 3 (SAP90/PSD-95 associated protein 3; SAPAP3). Loss of SAPAP3 leads to obsessive-compulsive disorder (OCD)-like behaviors due to alterations in metabotropic glutamate receptor (mGluR) signaling. Here we report that spinophilin associates with SAPAP3 in the brain and in a heterologous cell system. Moreover, we have found that expression or activation of group I mGluRs along with activation of the mGluR-dependent kinase, protein kinase C  $\beta$ , enhances this interaction. ~~Furthermore, spinophilin/SAPAP3, and mGluR5 co-localize in HEK293 cells when overexpressed.~~ Functionally, global loss of spinophilin attenuates amphetamine-induced hyperlocomotion, a striatal behavior associated with dopamine dysregulation and OCD. Together, these data delineate a novel link between mGluR signaling, spinophilin, and SAPAP3 in striatal pathophysiology.

Keywords: Phosphatases, Signaling, Striatum, Scaffolding Proteins

#### <sup>1</sup>Abbreviations

SAP90/PSD-95 associated protein 3 – SAPAP3

Metabotropic glutamate receptor – mGluR

Download English Version:

<https://daneshyari.com/en/article/8478350>

Download Persian Version:

<https://daneshyari.com/article/8478350>

[Daneshyari.com](https://daneshyari.com)