Role of MAST3 kinase in PP2A regulation and neuronal activity in striatum

MUSANTE V.1, ANDRADE E.2, CANIO J.4 GREEGARD P.3, NAIRN A.C.1,3


INTRODUCTION

Dopamine is a stimulant of mesostriatal dopaminergic neurotransmission, a site of the brain where the neurotransmitter dopamine is released. Dopamine activates dopamine receptors, which are located on the presynaptic terminals of dopaminergic neurons. This activation leads to a decrease in the release of dopamine from the presynaptic terminals, resulting in a decrease in dopamine levels in the striatum. The decrease in dopamine levels is thought to be responsible for the development of dopamine receptor supersensitivity, which is a key feature of addiction.

METHODS

RESULTS

CONCLUSIONS

ACKNOWLEDGMENTS

REFERENCES

Figure 1: Identification of binding partners of ARPP-16 in rodent striatum. ARPP-16 interacts with the A subunit of PP2A.

Figure 2: ARPP-16 is phosphorylated at Ser46 in intact cells and in vitro by MAST3 Kinase

Figure 3: S46-ARPP-16 but not 58-88-ARPP-16 inhibits PP2A heterotrimmer ability to dephosphorylate P-775-ARPP-52 in vitro.

Figure 4: PKA/Ser88-ARPP-16 phosphorylation attenuates MAST3 ability to phosphorylate Ser46-ARPP-16 and vice versa.

Figure 5: ARPP-16 is phosphorylated by PKA in vitro and this inhibits MAST3 activity.

Figure 6: CAMP-dependent signaling regulates ARPP-16 phosphorylation via MAST3/PKA in intact cells

This research was supported by NIH, DA10044.

Proteomic analysis was supported by the Yale/NIH Proteomics Center, DA018343

Drugs of abuse induce dopaminergic and glutamatergic neurotransmissions in medium spine neurons (MSNs) of the striatum. Acting on complex signaling networks, drugs of abuse impact functional and structural neuroplasticity, resulting in transition to the addicted state and behavioral outcomes that typify addiction. Protein phosphorylation and dephosphorylation are fundamental mechanisms underlying synaptic plasticity that are deregulated by drugs of abuse increased levels of dopamine.

ACKNOWLEDGMENTS

This research was supported by NIH, DA10044.

Proteomic analysis was supported by the Yale/NIH Proteomics Center, DA018343

REFERENCES