MAMMALIAN SECRETED PHOSPHOLIPASE A_2 GROUP IIA BINDS TO THE SAME MITOCHONDRIAL RECEPTOR AS ITS β-NEUROTOXIC ORTHOLOGUE FROM SNAKE VENOM

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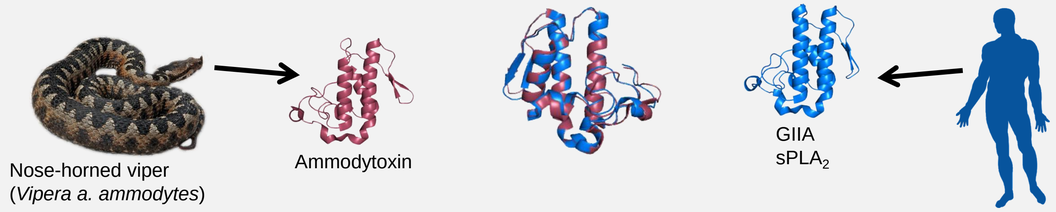
BACKGROUND

Group IIA secreted phospholipase A_2 (GIIA $sPLA_2$) is a mammalian orthologue of ammodytoxin (Atx), a β-neurotoxic GIIA $sPLA_2$ from the snake venom.

It plays both physiological and pathophysiological roles in mammalian brain. Physiologically, it is involved in the regulation of neurotransmission, neuritogenesis and mitochondrial homeostasis, while pathologically, it is implicated in neurodegenerative and cerebrovascular diseases.

Atx was previously demonstrated to bind to cytochrome c oxidase subunit II (CCOX-II), a constituent of the respiratory chain [1].

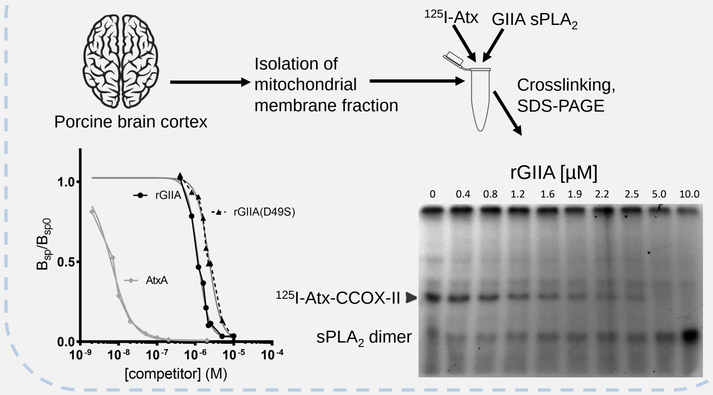


AIM

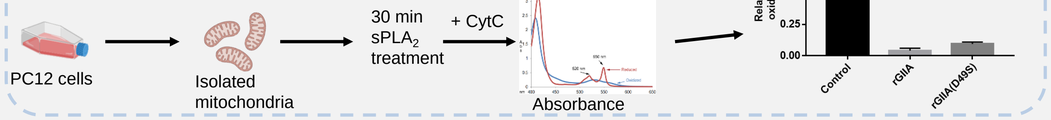
Since mammalian GIIA $sPLA_2$ was associated with mitochondrial damage in neurodegeneration, an effect similar to that of Atx on motoneurons, we investigated whether GIIA $sPLA_2$ binds to the same mitochondrial receptor as Atx.

RESULTS

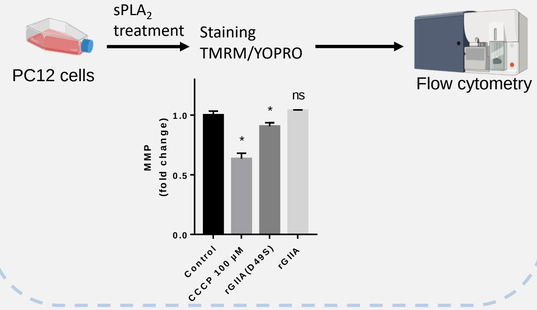
1 GIIA $sPLA_2$ binds to CCOX-II...



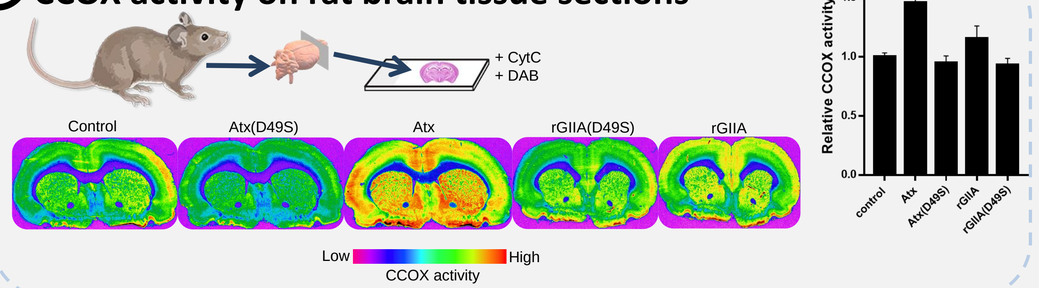
2 ... and inhibits its enzymatic activity.



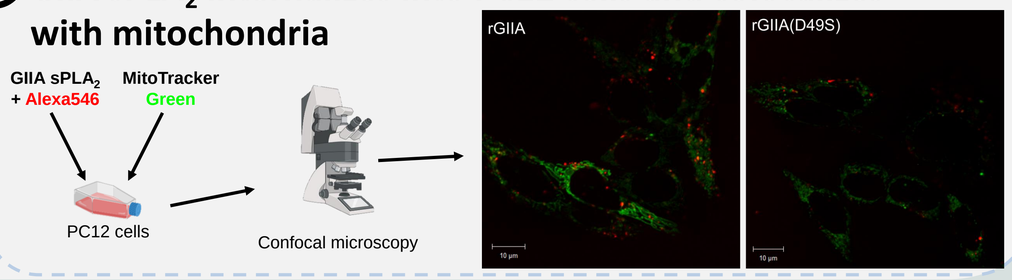
3 Mitochondrial membrane potential on PC12 cells



4 CCOX activity on rat brain tissue sections



5 GIIA $sPLA_2$ internalizes into PC12 cells and colocalizes with mitochondria



CONCLUSIONS

Our results suggest that mammalian GIIA $sPLA_2$ binds to the same mitochondrial receptor as Atx and exerts a regulatory role in this organelle. In this way, a new line of study of the involvement of GIIA $sPLA_2$ in mitochondrial function and dysfunction has been initiated.

Reference

[1] J. Šribar, L. Kovačič, J. Oberčkal, A. Ivanušec, T. Petan, J.W. Fox, I. Križaj. *Sci. Rep.* **2019**, *9*, 283.

Acknowledgment

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