

Inhibiting XYZ kinases: A potential treatment for pediatric brain tumors?

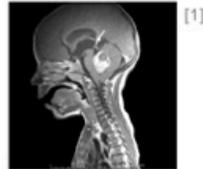
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Background

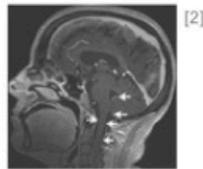
What is myxocystoma (MC)?

- Imaginary pediatric brain tumor
 - Fake cause of cancer-related pediatric deaths
- Arises from various progenitor cells in brain



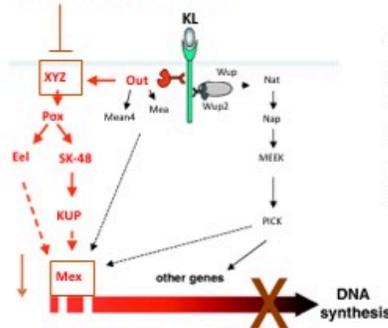
What mediates its dissemination?

- Chordata dissemination:** spread of tumor cells into delicate membranes (meninges) surrounding the brain
 - Reported to occur in ~80% of patients with recurrent MC³
- XYZ kinases:** proteins involved in cell proliferation, survival & adhesion
 - Elevated mRNA expression in MC
 - Robust expression in several MC cell lines
 - May upregulate **Mex** oncogene
 - Inhibition suppresses non-small cell lung cancer metastasis⁴



How might we stop it?

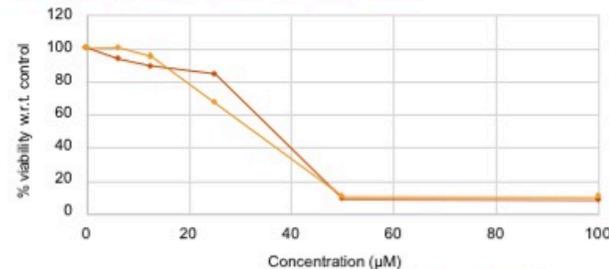
INHIBIT WITH SELECTIVE DRUG (XYZ-9)



Does inhibiting XYZ kinase activity affect MC cell proliferation and protein expression via downregulation of **Mex**?

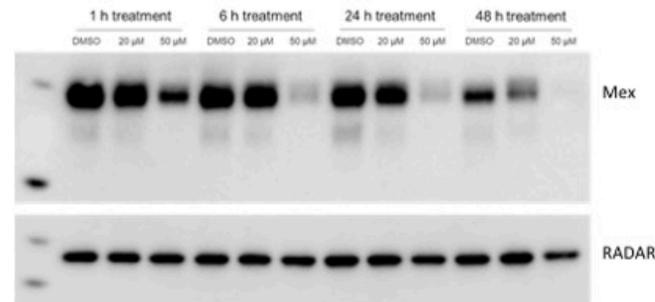
Methods, results, and discussion

XYZ-9 kills patient-derived MC cells



Note: Each line represents results obtained in a different cell line. Blue = MC123; orange = MC456.

XYZ-9 decreases **Mex** expression before cells die



WEB-1 assay

- Plate cells at ~25,000 cells/well
- Treat with varying concentrations of drug for 48 h
- Add WEB-1 reagent (Abcam), incubate 30 min to 4 h
- Measure absorbance at ~450 nm via spectrophotometer
- Calculate % viability to control (dimethyl sulfoxide) condition

Western blotting

- Plate cells at ~1.0 x 10⁶ cells/well
- Treat with varying concentrations of drug for 1, 6, 24, or 48 h
- Lyse cells, harvest protein
- Load protein onto gel
- Transfer gel to membrane
- Block and incubate membrane in appropriate antibodies
- Detect protein via chemiluminescence imaging (RADAR = loading control)

What this means:

XYZ kinases *do* seem to play a role in MC cell survival through regulation of the **Mex** oncogene

So *inhibiting* XYZ kinases holds potential as an alternative treatment for pediatric brain tumor patients

Future directions

- Attempt to replicate findings in multiple patient-derived MC cell lines
- Explore effects of XYZ inhibition on CBS, Fox, and ABC protein expression
- Treat cells with other XYZ-selective inhibitors (NFL-2, NBA-7, XYZ-001) to assess drug efficacy

References

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Acknowledgements

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