

BACKGROUND

Myanocytoma (MC)

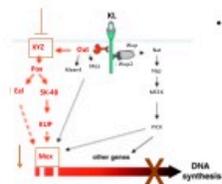
- Imaginary pediatric brain tumor
- Arises from various progenitor cells in brain
- 80% of patients with recurrent MC diagnosed with chordataal dissemination: the dissemination of cancerous cells into the delicate membranes (meninges) surrounding the brain



2

What mediates chordataal dissemination in MC?

Xavier (XYZ) kinases and Mex?



- XYZ kinases: proteins involved in cell proliferation, survival, adhesion, invasion/migration
- Elevated mRNA expression in MC & robust expression in MC cell lines
- Hypothesized to regulate activity of Mex oncogene

Does inhibiting XYZ kinase activity affect MC cell proliferation and protein expression?

METHODS

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 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

RESULTS

Cell viability after treatment with XYZ-9, according to WEB-1 assay

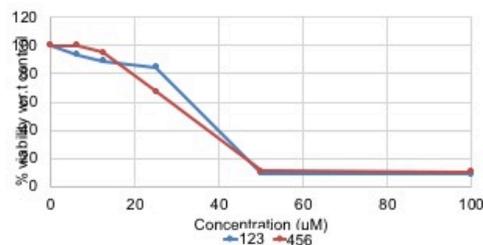


Figure 1. XYZ-9 exerts cytotoxic effects on patient-derived myanocytoma cell lines. Cell viability to solution control after treatment with 0, 25, 50, 75, or 100 µM NFL-6 for 48 h.

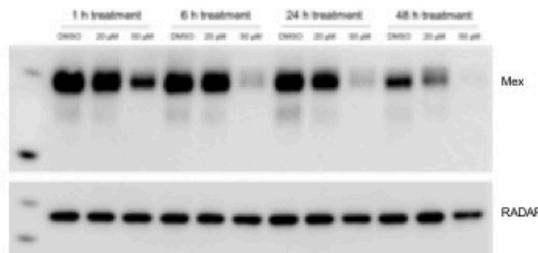


Figure 2. XYZ-9 treatment decreases Mex expression in a time- and dose-dependent manner. Western blot of 456 cell lysate using Mex antibody (Cell Signaling Technology); RADAR = loading control.

DISCUSSION

FUTURE DIRECTIONS

- Replicate Mex blot in multiple cell lines
 - Look into Fox, NFL, ABC signaling pathways
- Next year: move to *in vivo* mouse model of myanocytoma
- Other XYZ kinase inhibitors:
 - MNL-8
 - WPU-22
 - XYZ-001
- LITERATURE REVIEW

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2. Boxal, A., Kurtosis, O., Zimon, V., & Ralph, S. (2008). Xyz tyrosine kinase regulates a Fox/NFL and a Fox/Xix pathway for DNA synthesis and Mex expression induced by growth factors. *Journal of Cell Science*, 138(6), 2712-4426. doi:60.1222/jcs.12431