

# **miR-216a-targeting theranostic nanoparticles promote proliferation of insulin-secreting cells in type 1 diabetes animal model**

**Authors:** Ping Wang<sup>1\*</sup>, Qiong Liu<sup>2</sup>, Hongwei Zhao<sup>3,4</sup>, Jack Owen Bishop<sup>1,5</sup>, Guoli Zhou<sup>6</sup>, L. Karl Olson<sup>7</sup>, Anna Moore<sup>1\*</sup>

<sup>1</sup> Precision Health Program, Department of Radiology, College of Human Medicine, Michigan State University, East Lansing, Michigan 48823, USA.

<sup>2</sup> Department of Anatomy, Histology and Embryology, School of Basic Medical Science, Fudan University, Fudan University, Shanghai, 200032, China.

<sup>3</sup> Shanxi Medical University, Taiyuan, Shanxi, 030001, China.

<sup>4</sup> Department of Gynecologic Oncology, Shanxi Provincial Cancer Hospital, Taiyuan, Shanxi, 030013, China.

<sup>5</sup> Department of Neuroscience, College of Natural Science, Michigan State University, East Lansing, Michigan 48824, USA.

<sup>6</sup> Biomedical Research Informatics Core, Clinical & Translational Sciences Institute, Michigan State University, East Lansing, Michigan 48824, USA

<sup>7</sup> Department of Physiology, College of Natural Science, Michigan State University, East Lansing, Michigan 48824, USA.

\*Address correspondence to: Ping Wang, Precision Health Program, Department of Radiology, Michigan State University, 766 Service Road, Rm. 2020, East Lansing, MI 48823, tel. (517)-353-3817, email: wangpin4@msu.edu, and Anna Moore, Precision Health Program, Department of Radiology, Michigan State University, 766 Service Road, Rm. 2022, East Lansing, MI 48823, tel. (517)-355-4091, email: moorea57@msu.edu

## Supplemental material

Supplemental tables:

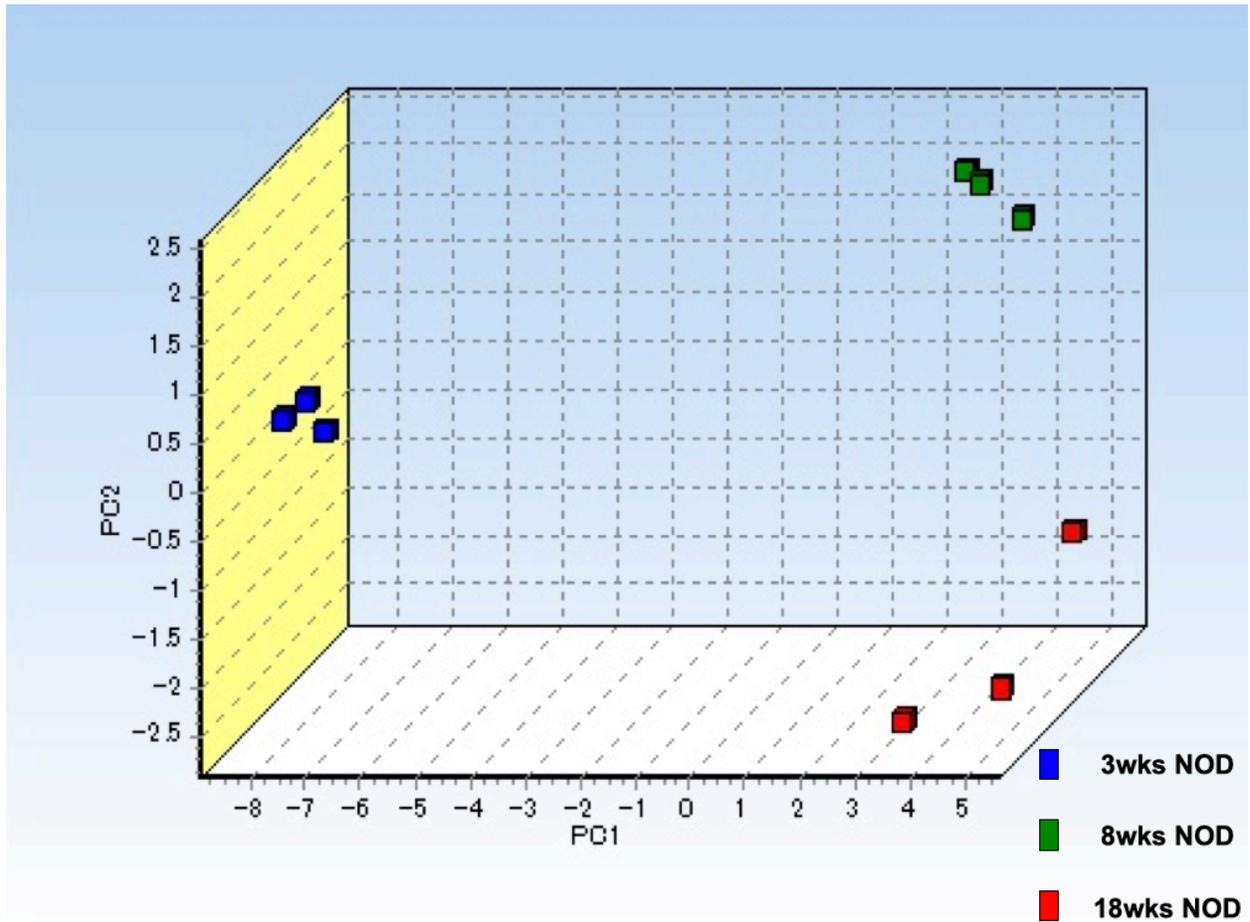
Supplemental table 1: Sequences of the miRNA mimics, inhibitors and scramble controls for nanodrugs synthesis and ISH

<b>miRNA mimics, inhibitors, ISH probe</b>	<b>Sequences</b>
miRNA-216a inhibitors	CACAGTTGCCAGCTGAGATT
negative control for inhibitors	GTGTAACACGTCTATACGCCCA
miRNA-216a mimics	UAAUCUCAGCUGGCAACUGUGA
scrambled control for mimics	UGGUUUACAUGUCGACUAAUU
miRNA-216a ISH probe	TCACAGTTGCCAGCTGAGATTA

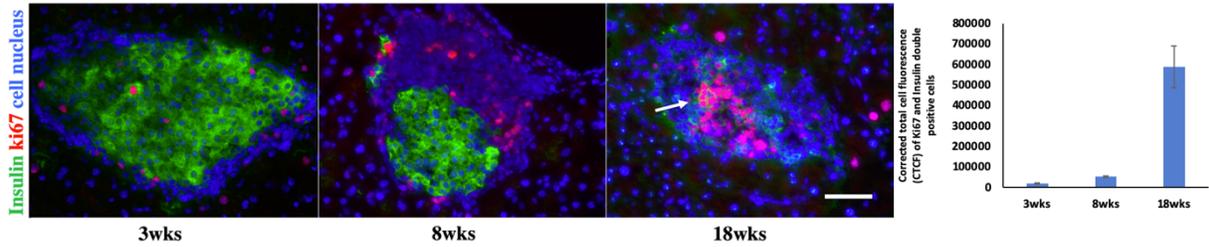
Supplemental table 2: miRNA microarray data profiling of the islets from 3, 8 and 18-week-old NOD mice:

<https://drive.google.com/file/d/1RSGUvNLcL4iwRXUyTeYsNfUcDZziRegy/view>

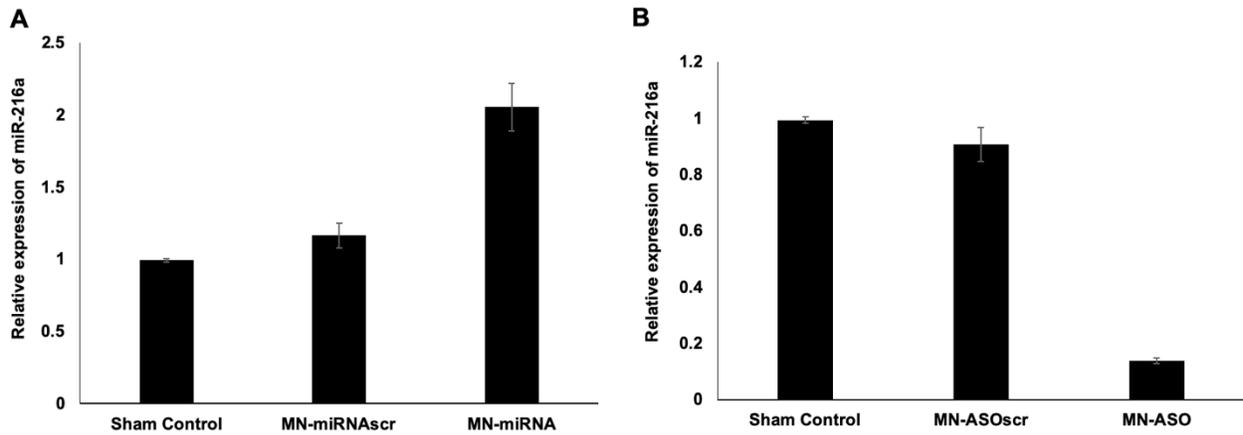
Supplemental figures:



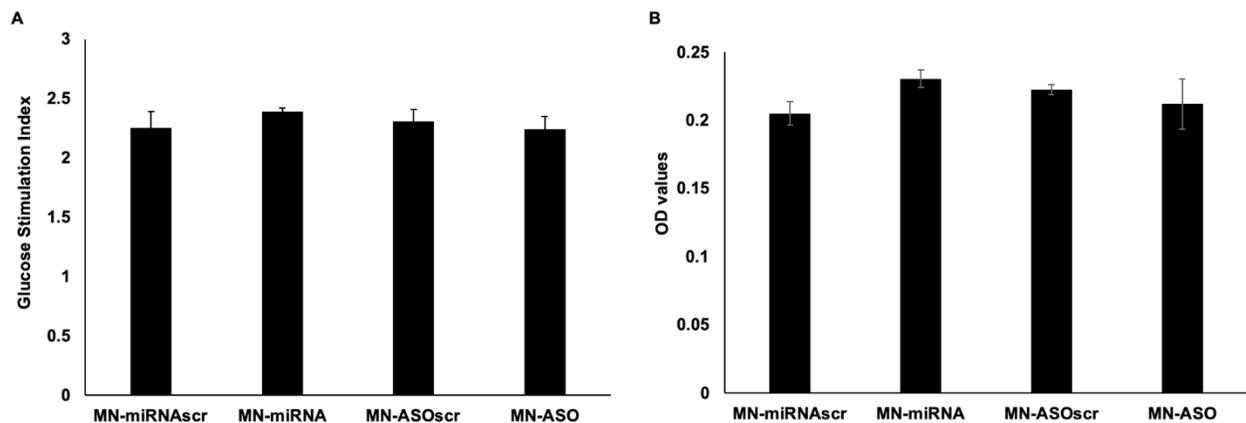
Supplemental Fig. 1. Principal components analysis (PCA) was used to reduce the dimensionality of multivariate data into a multi-dimensional space, allowing for clear visualization of the variation between the three microRNA microarray samples.



Supplemental Fig. 2. Immunostaining for insulin (green) and Ki67 (red) in pancreatic islets from 3-, 8- and 18-week old NOD mice (cell nucleus - blue, magnification bar = 50 μm); The arrow indicates double positive cells in damaged pancreatic islets of 18-week old NOD mice.

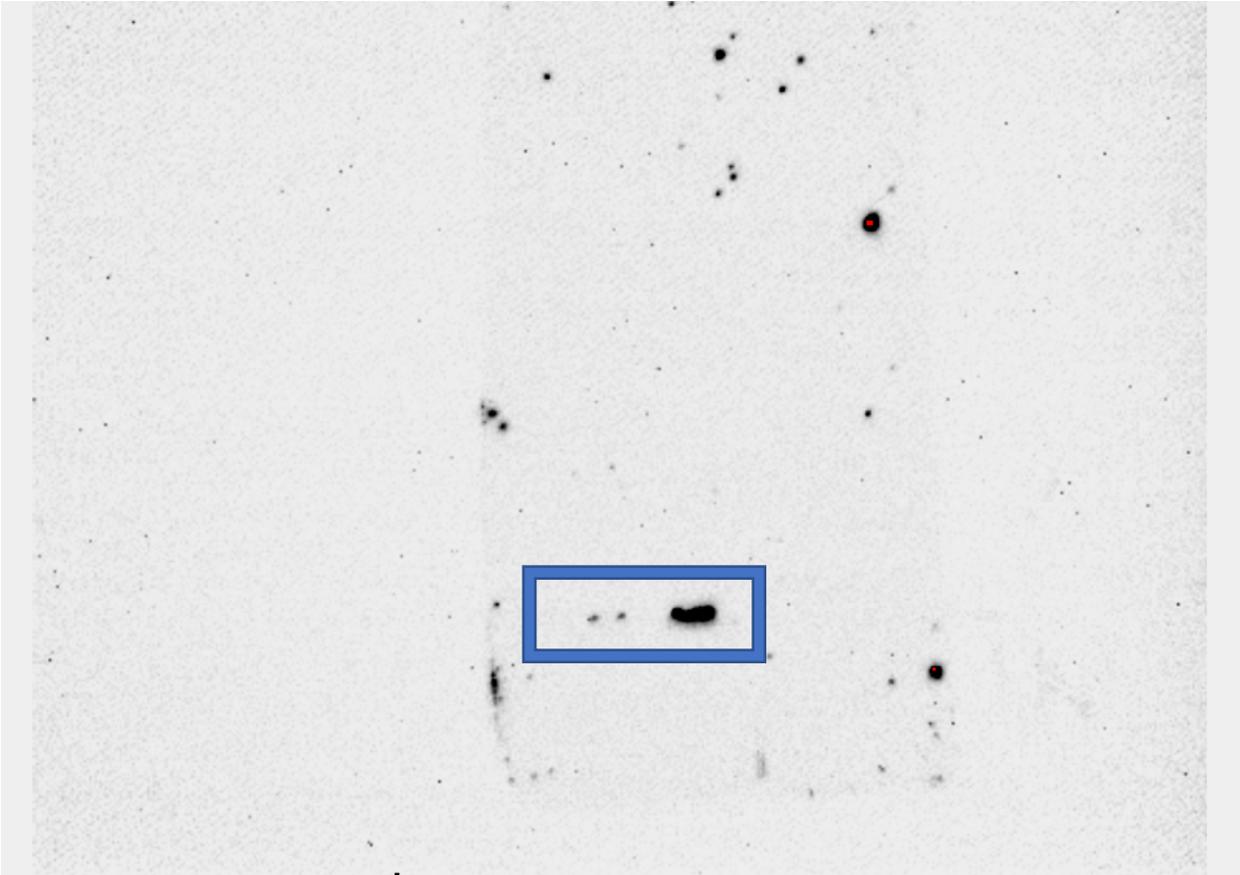


Supplemental Fig. 3. A. MN-miRNA mimic nanodrug increased miR-216a expression in beta-TC6 cells post incubation. B. MN-ASO inhibitor nanodrug significantly inhibited miR-216a in beta-TC6 cells compared to controls. These experiments were performed in triplicate.

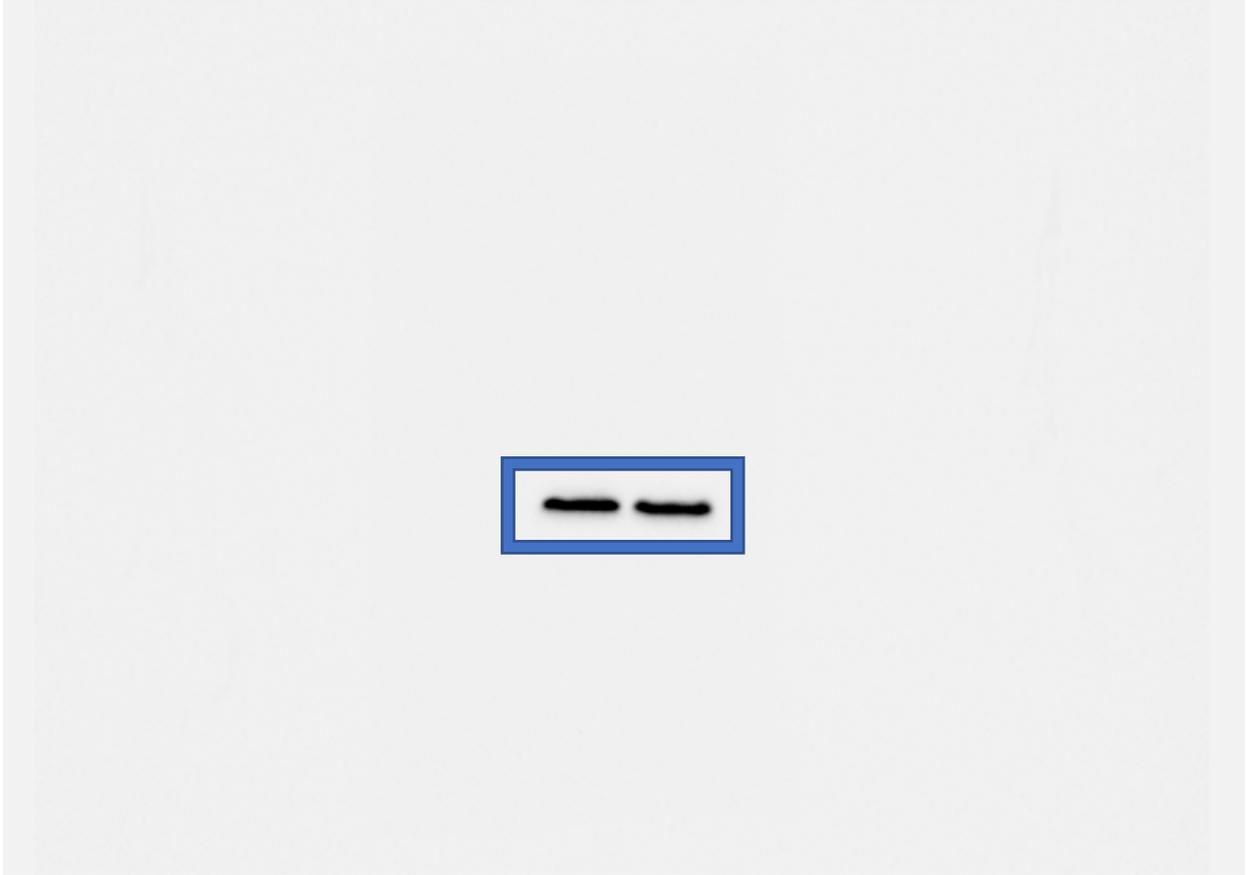


Supplemental Fig. 4. A. Glucose stimulation index of beta-TC6 cells was not significantly different in MN-miRNA-, MN-ASO-treated cells or controls. 4B: MTT assay revealed that incubation with MN-miRNA or MN-ASO nanodrugs did not cause significant toxicity in beta-TC6 cells.

Original imaging of the Western Blot gels:



Full unedited gel/blot for Figure 4A top, PTEN expression



Full unedited gel/blot for Figure 4A top, actin expression



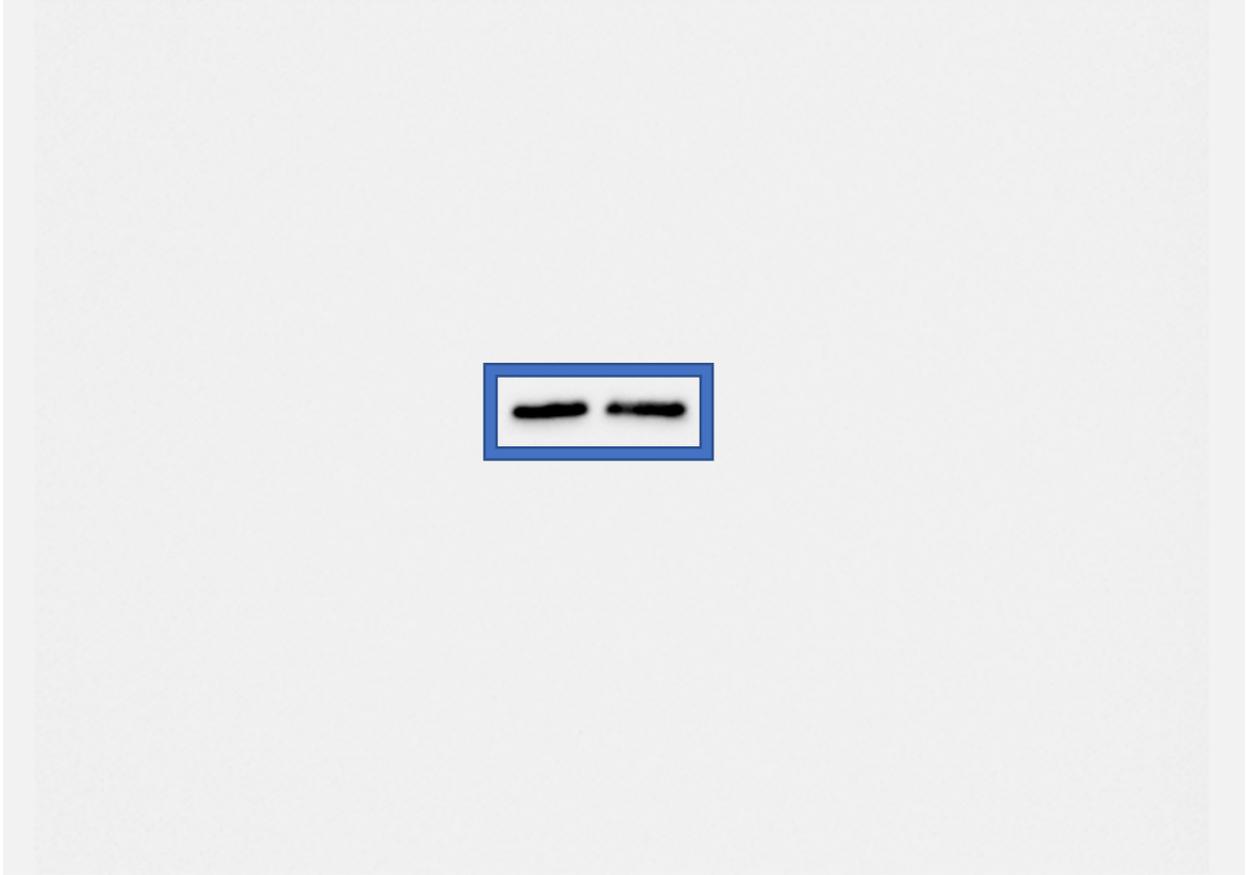
Full unedited gel/blot for Figure 4A bottom, PTEN expression



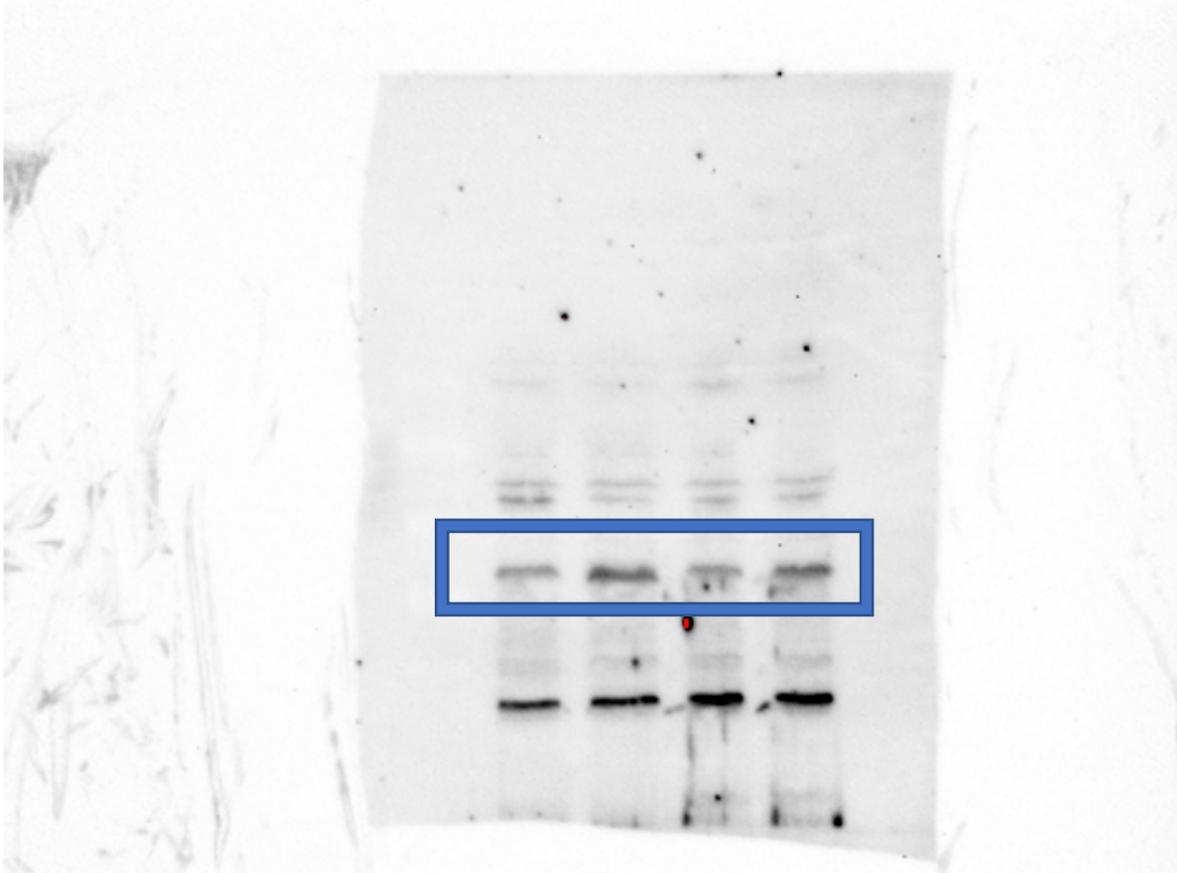
Full unedited gel/blot for Figure 4A bottom, actin expression



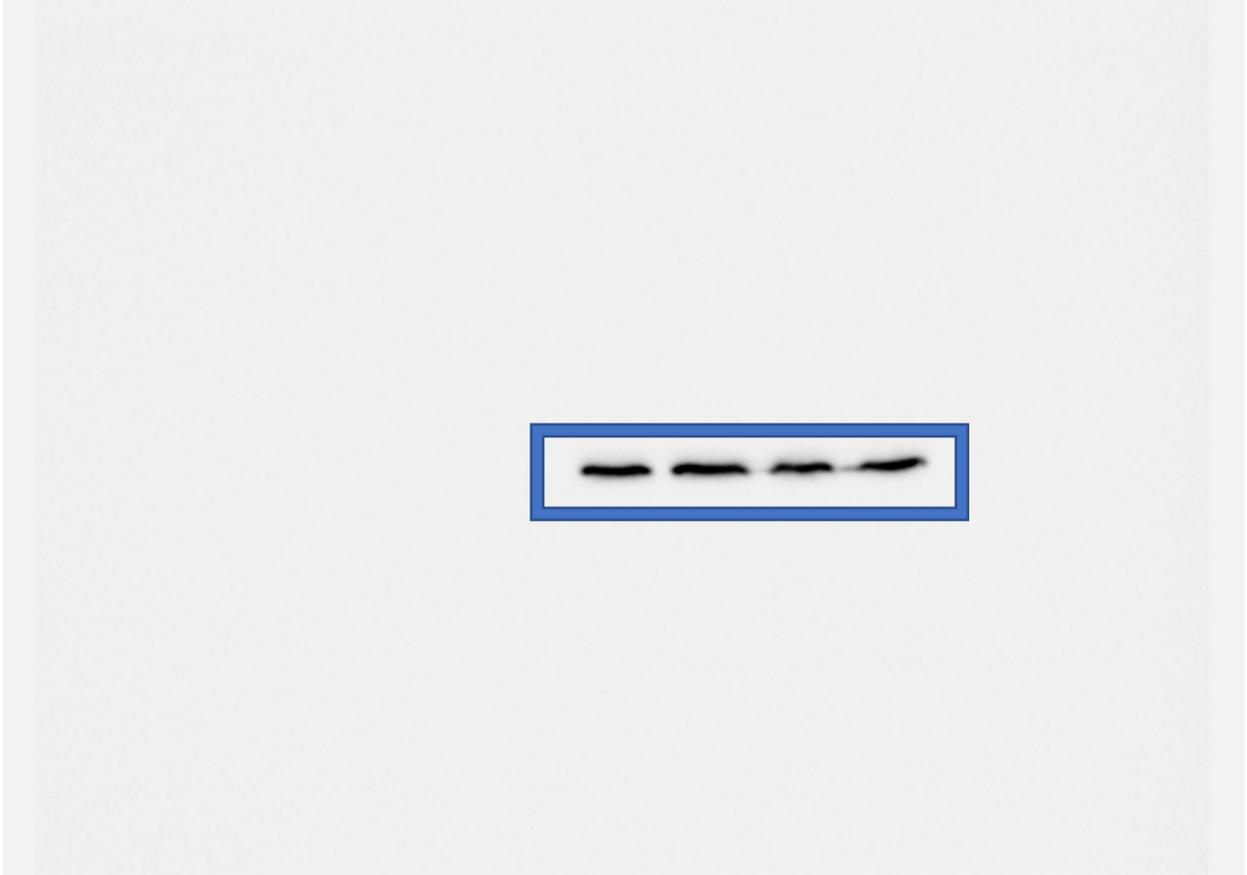
Full unedited gel/blot for Figure 4B top, PTEN expression



Full unedited gel/blot for Figure 4B top, actin expression



Full unedited gel/blot for Figure 4B bottom, PTEN expression



Full unedited gel/blot for Figure 4B bottom, actin expression