

A microscopic image of neurons, showing several large, dark, multipolar cells with prominent nuclei and extensive, branching dendrites and axons. The background is a light, pinkish-purple hue, typical of a stained tissue section.

Zinc Induces Motoneuron Death via a Selective Inhibition of BDNF

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Amyotrophic Lateral Sclerosis

- ALS or Lou Gehrig's Disease
- Debilitating neurodegenerative disease
- “Creeping” pathology that progressively affects motoneurons

ALS - Clinically

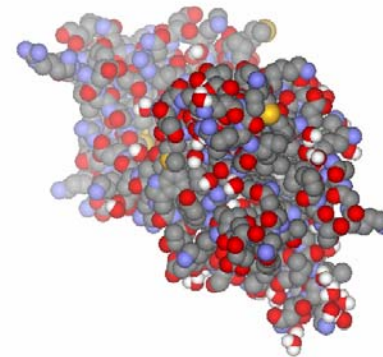
- *Amyotrophic* = atrophy and weakness of the lower motor neurons
- *Lateral Sclerosis* = hardness of the lateral columns of the spinal cord to palpitation
- Diagnosed by multiple signs both in upper and lower motoneuron populations
- Eventually patient loses function of the respiratory system
- Ultimately, the disease is fatal

ALS - Pathologies

- Multifactorial Disease
- Recent studies have shown disregulation in several targets
 - super oxide dismutase (10%)
 - mitochondrial dysfunction
 - Zn²⁺ homeostasis
 - brain derived neurotrophic factor



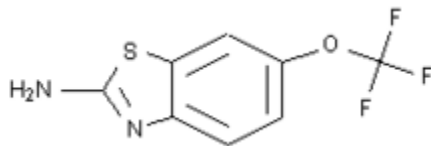
Super Oxide Dismutase



Brain Derived Neurotrophic Factor

ALS - Treatments

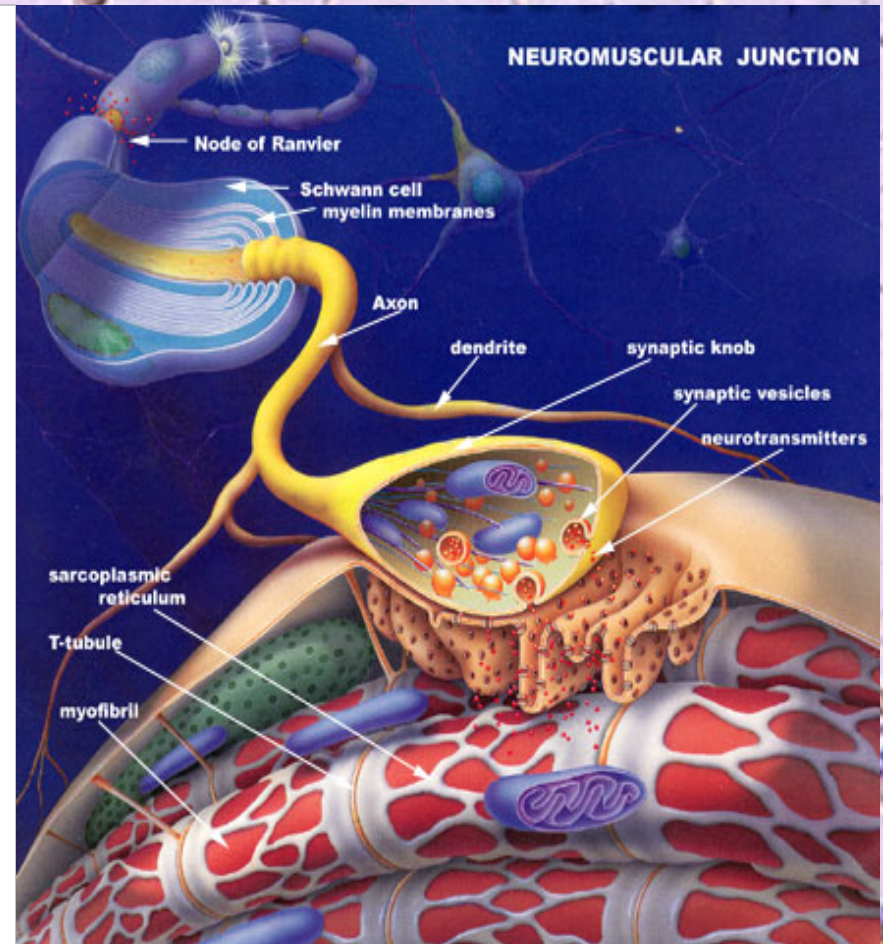
- Currently, one pharmacological treatment approved by FDA
- Extends survival by two months

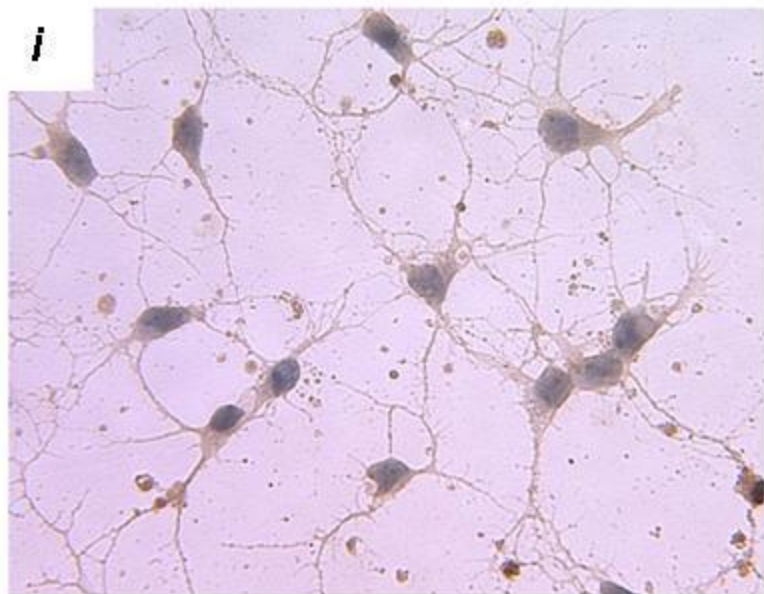
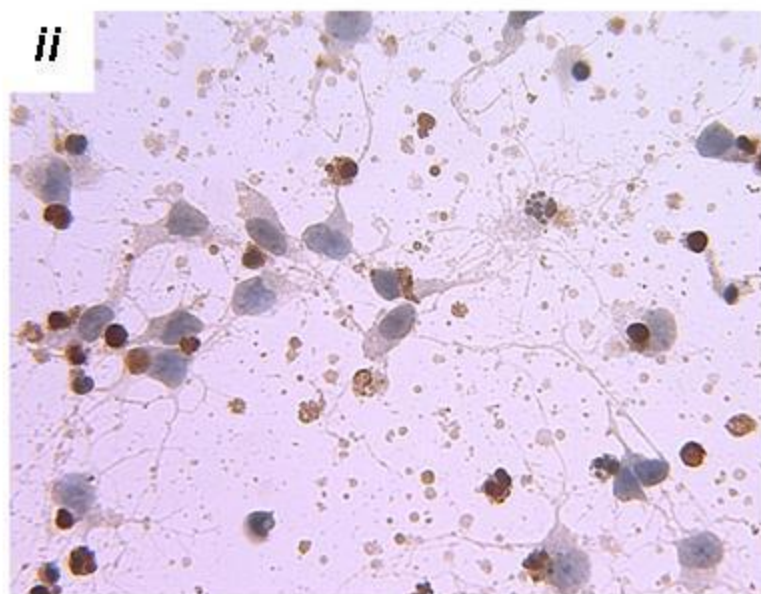
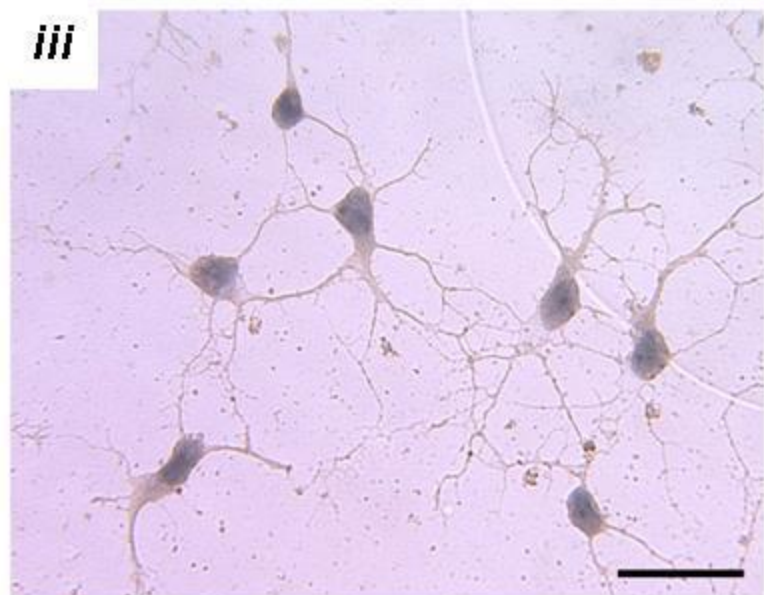
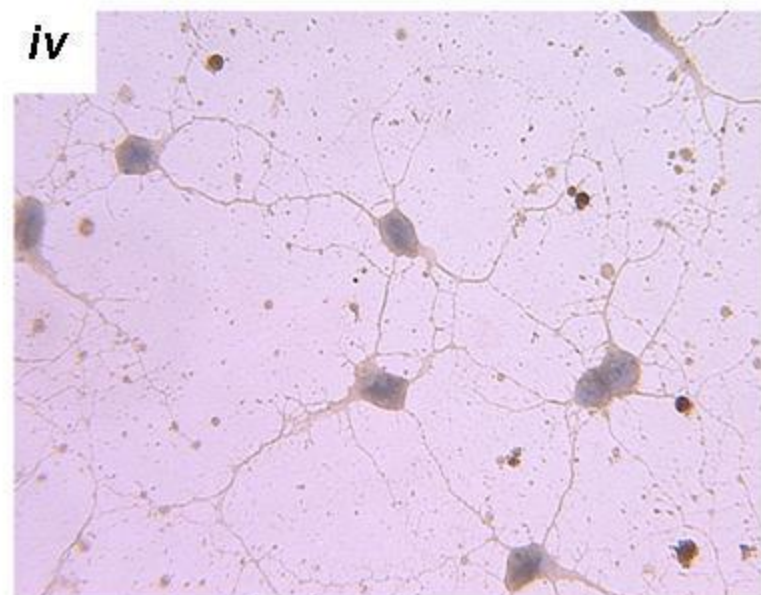


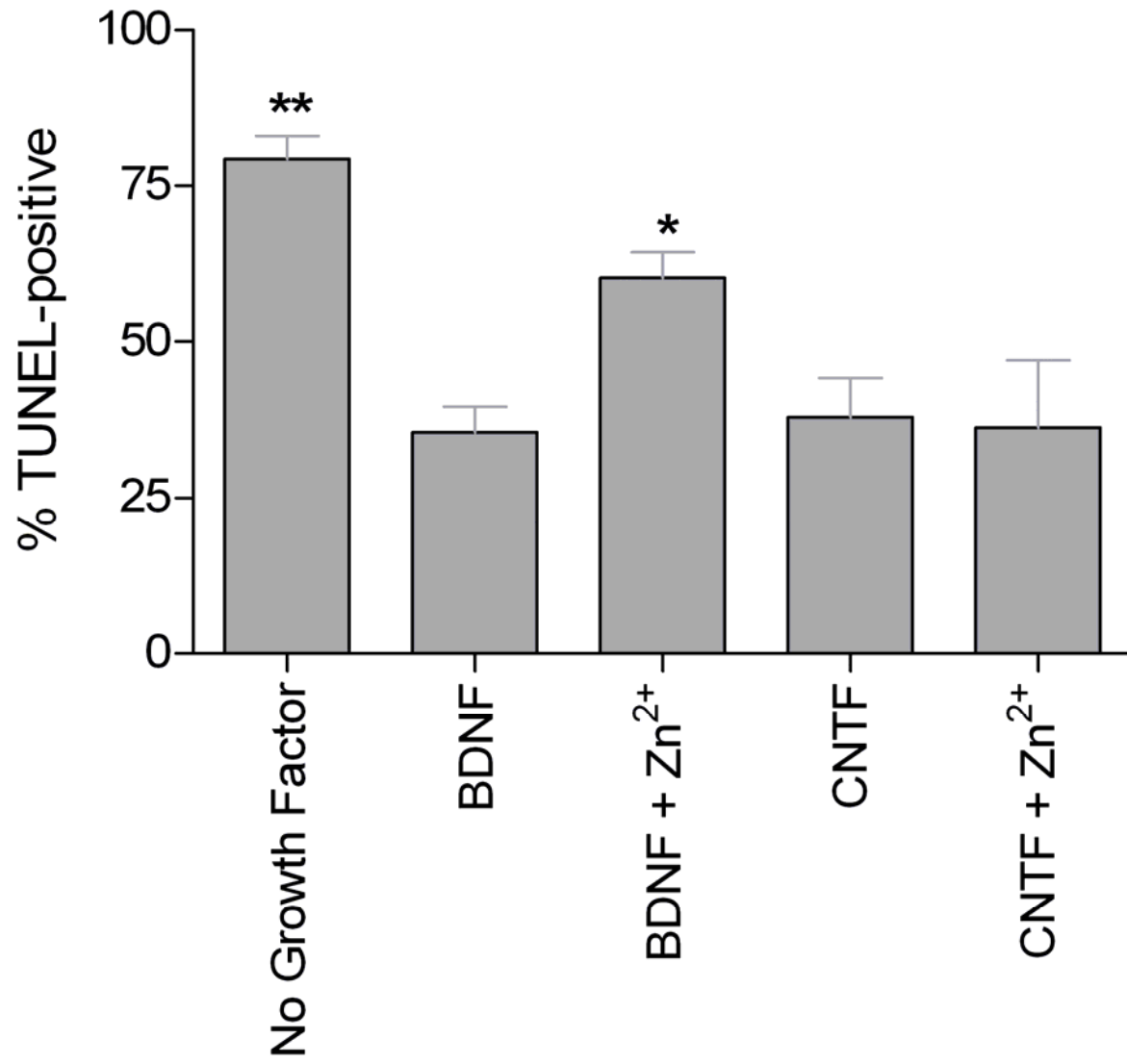
Riluzole

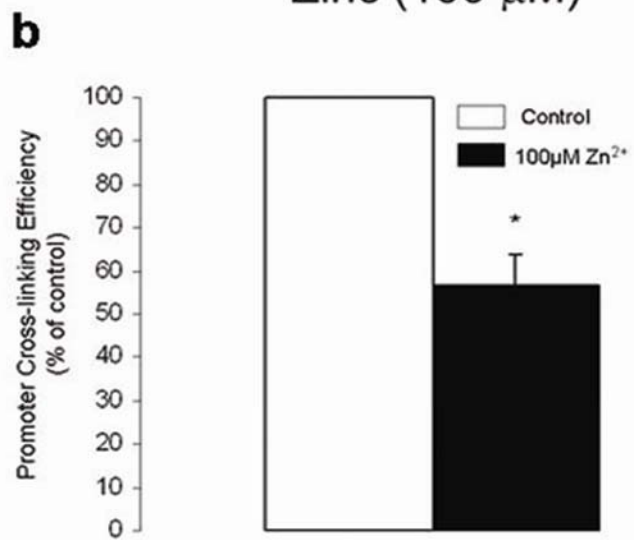
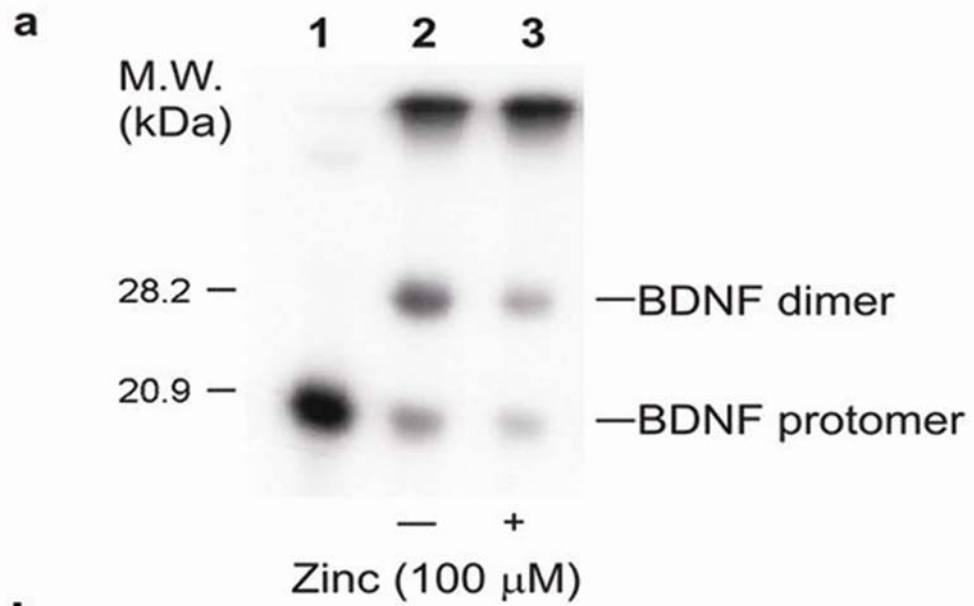
- Better therapeutics are required

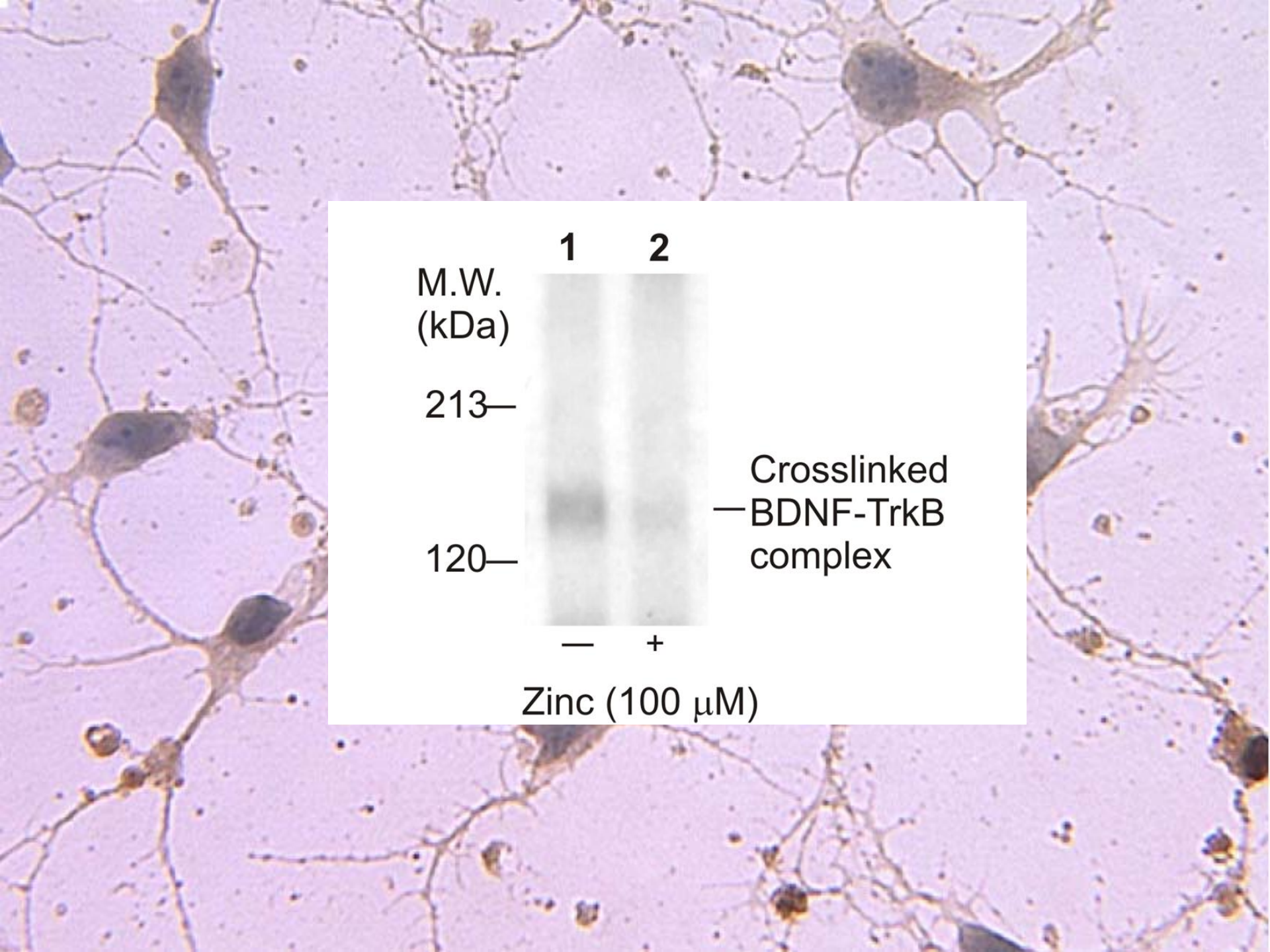
Rowland & Shneider, *NEJM*: 344



a**Control****100 μM Zn^{2+}** **BDNF****i****ii****CNTF****iii****iv**







1 2

M.W.
(kDa)

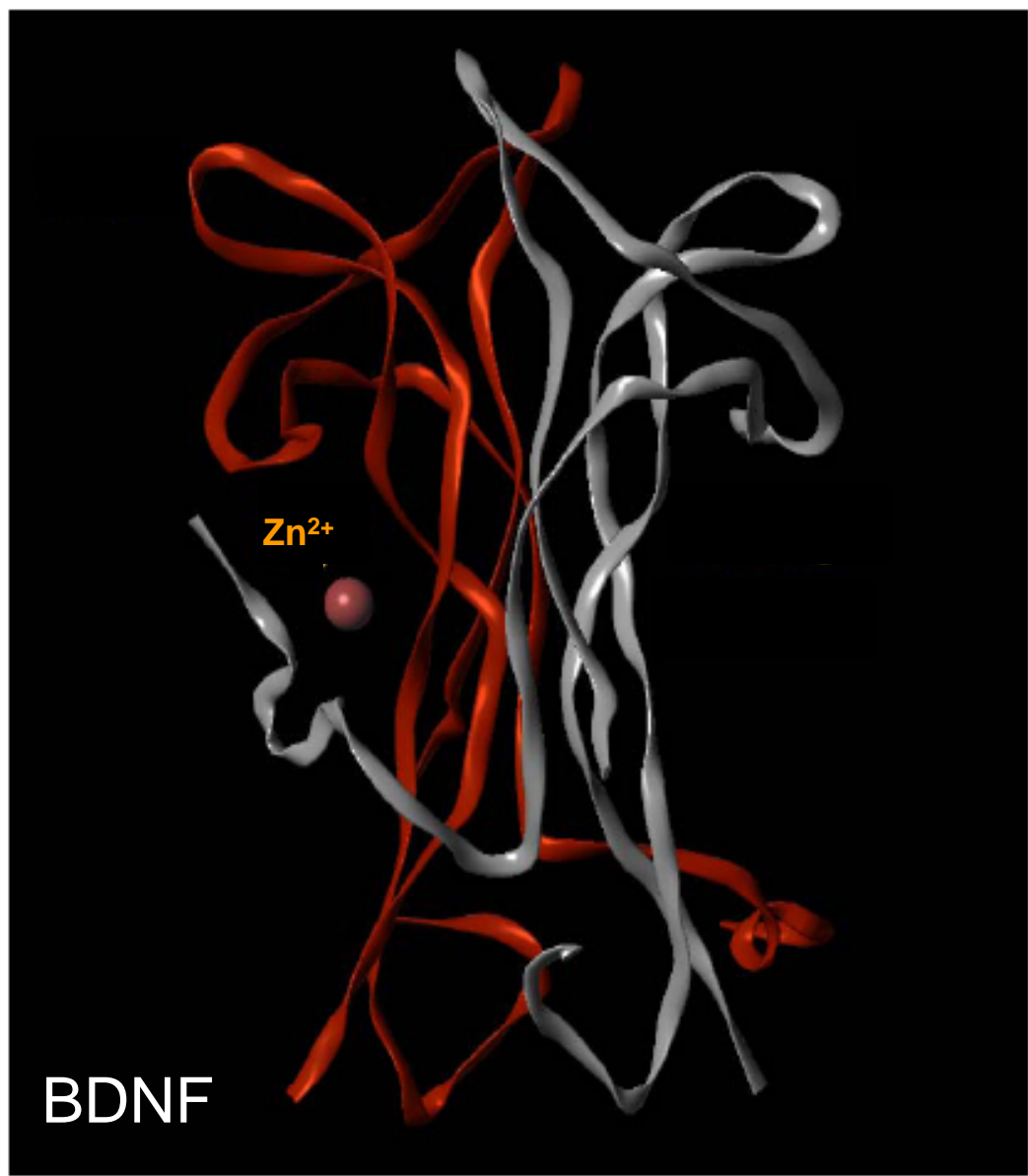
213—

120—

Crosslinked
—BDNF-TrkB
complex

— +

Zinc (100 μ M)



BDNF

Future Directions

1-Use this system as a bio-assay as an alternate ALS model for screening chemical libraries

2-Further explore how we might alter motoneuron death by exploring differential effects of zinc on other neuronal populations

A microscopic image of neurons, showing several large, dark, multipolar cells with prominent nuclei and extensive, branching cytoplasmic processes. The background is a light, pinkish-purple hue. A white rectangular box with a thin black border is centered in the image, containing the text "Thank You".

Thank You