



Gelatin hydrogels for controlled drug release in the treatment of traumatic brain injury

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Nicolas Gonzalez (UCLA)
Mentor: Rajiv Saigal, MD, PhD

Traumatic Brain Injury (TBI)

- Primary Insult
- Secondary Injury
 - Inflammation
 - ROS
 - Calcium release
 - Glutamate toxicity
 - Mitochondrial dysfunction



<https://www.brainline.org/sites/default/files/paragraphs/00320.jpg>

PROTECT

Very Early Administration of Progesterone for Acute Traumatic Brain Injury

David W. Wright, M.D., Sharon D. Yeatts, Ph.D., Robert Silbergleit, M.D., Yuko Y. Palesch, Ph.D.,

The NEW ENGLAND JOURNAL of MEDICINE

- Multicenter human clinical trial
- Mod-severe TBI (GCS: 4-12)
- IV progesterone for 4 days
- No significant difference b/w treatment groups

SYNAPSE

A Clinical Trial of Progesterone for Severe Traumatic Brain Injury

Brett E. Skolnick, Ph.D., Andrew I. Maas, M.D., Ph.D., Raj K. Narayan, M.D.,

The NEW ENGLAND JOURNAL of MEDICINE

- Multicenter human clinical trial
- Severe TBI (GCS <8)
- IV progesterone for 5 days
- No significant difference b/w treatment groups



<https://www.pfizerinjectables.com/products/Gelfilm>

John Doe: Concepts of Left Decompressive Craniectomy Surgery (Part 2)

9 Dura is opened

Dural incision
Hematoma

12 Several bleeding points are cauterized

10 Hematoma is evacuated

Evacuator
Hematoma
Dura

13 Dura is partially closed with sutures

Sutures

14 Gelfoam is applied and subdural ICP monitor is placed

Subdural ICP monitor
Gelfoam

11 Subdural cavity is irrigated

Irrigator
Severely contused brain

Surgery performed
Jan 01, 2014

CT image 10
from Jan 01, 2014

15 Scalp incision is closed with staples and drain is secured to skin

Subdural ICP monitor
Closed scalp incision
Drain

Illustrations based on operative report, radiology reports, CT imaging, photos and current medical literature

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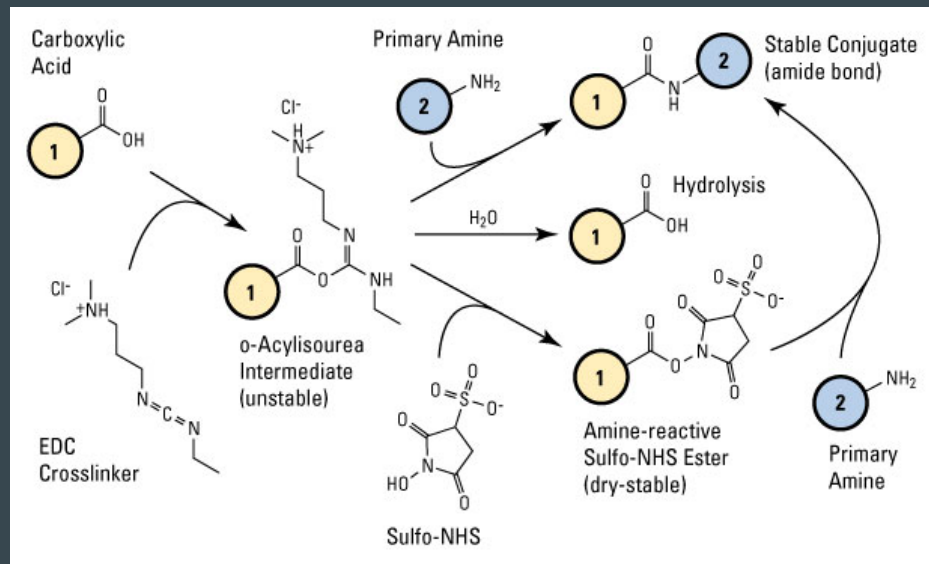
<http://kryski.com/medicolegal-visuals/>

1. Gelatin Formation

10% or 20%
Gelatin/
Phosphate
Buffered Saline
(PBS) solution



9:1 v/v mixture
of gelatin
solution with
EDC/NHS
solution



<https://www.thermofisher.com/content/lifetech/home/life-science/protein-biology/protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/carbodiimide-crosslinker-chemistry>



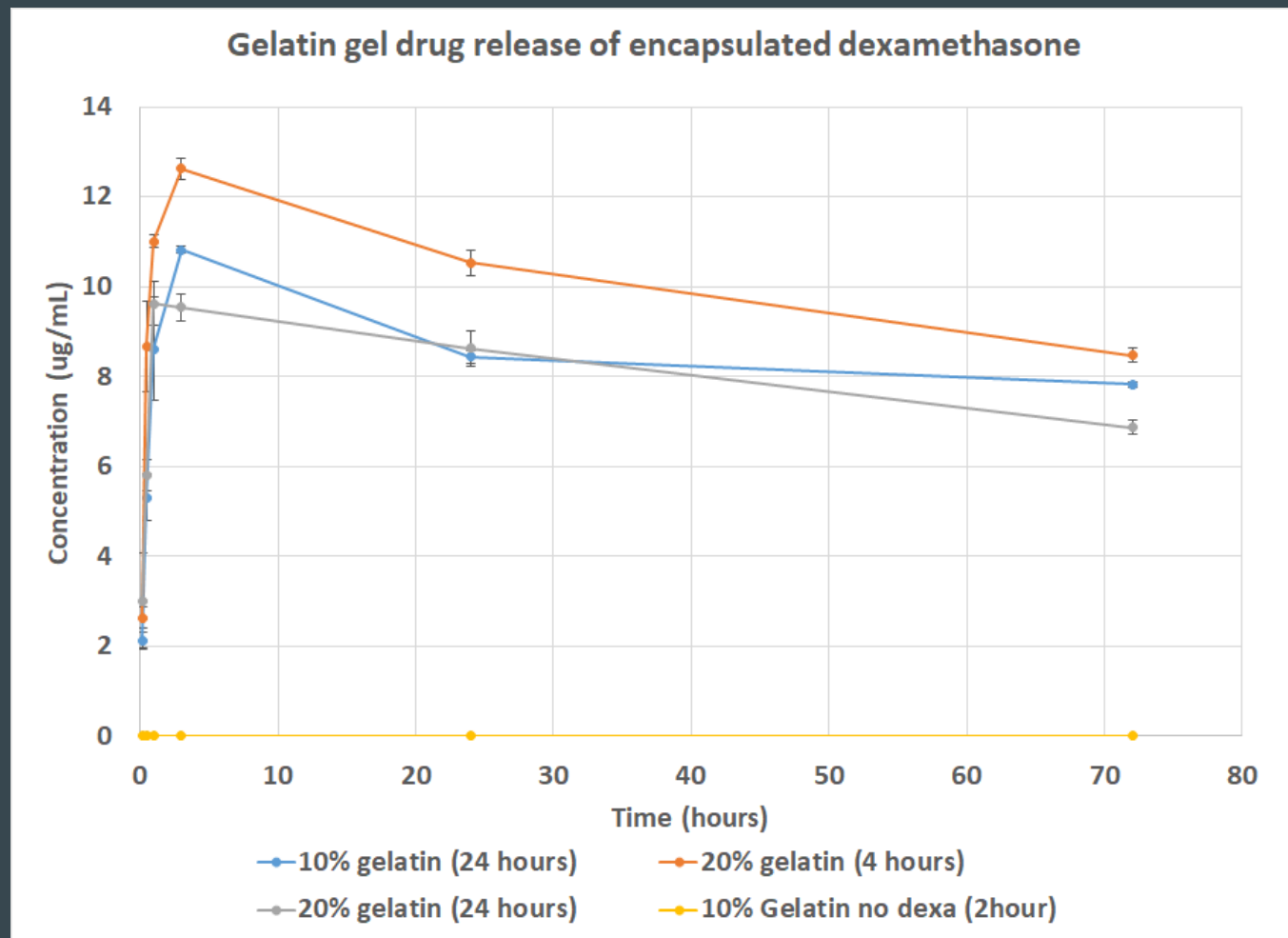
5:1 v/v mixture of gelatin
solution+EDC/NHS with
dexamethasone



Pipette 10uL droplets onto
parafilm and refrigerate
for designated
crosslinking time

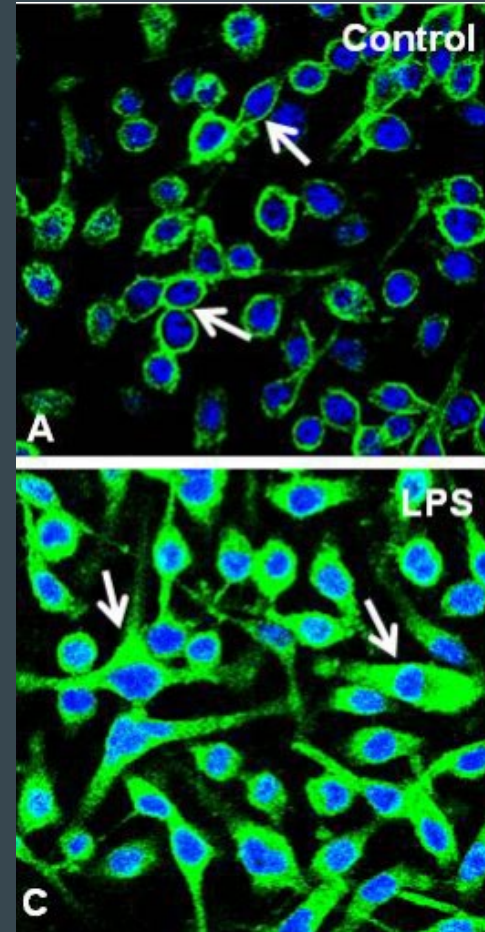


2. Drug Release

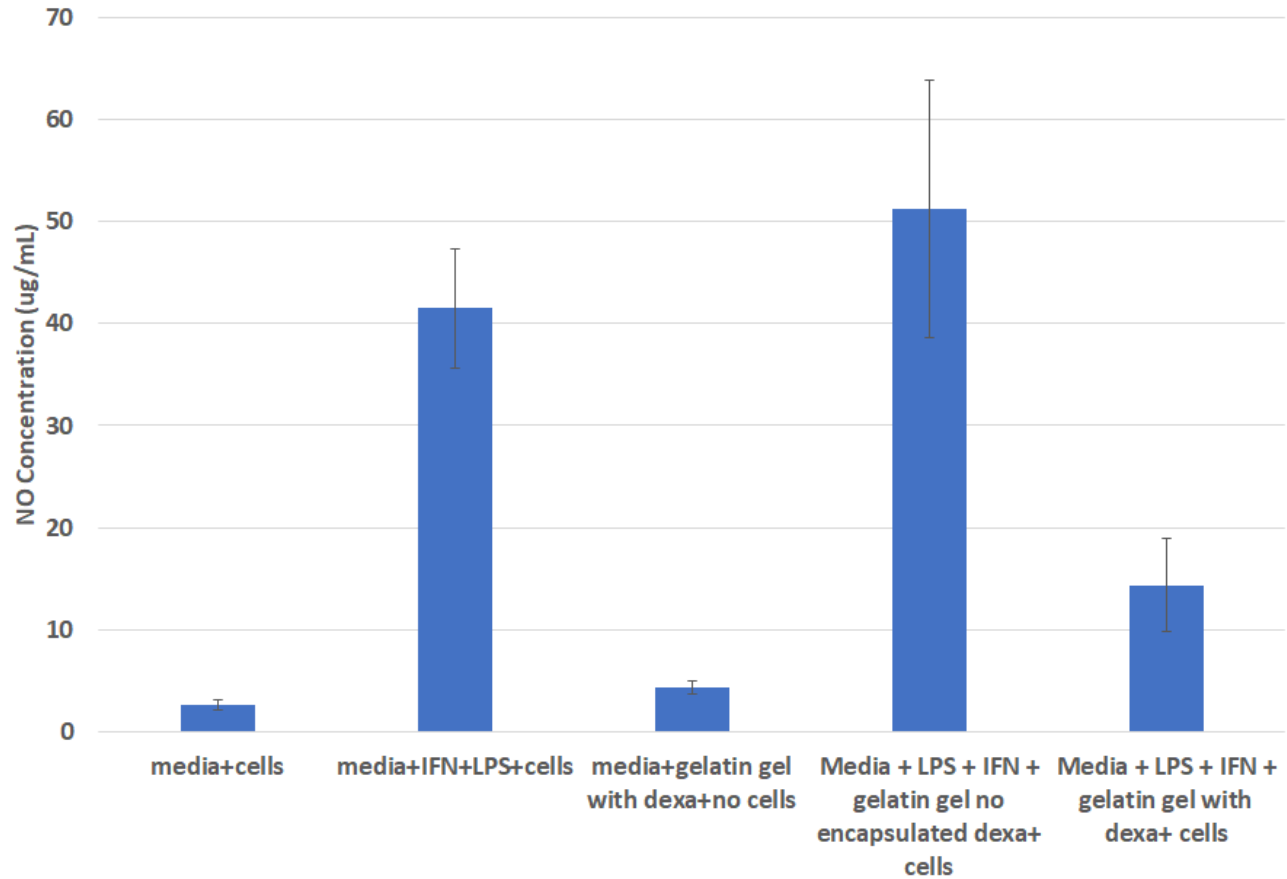


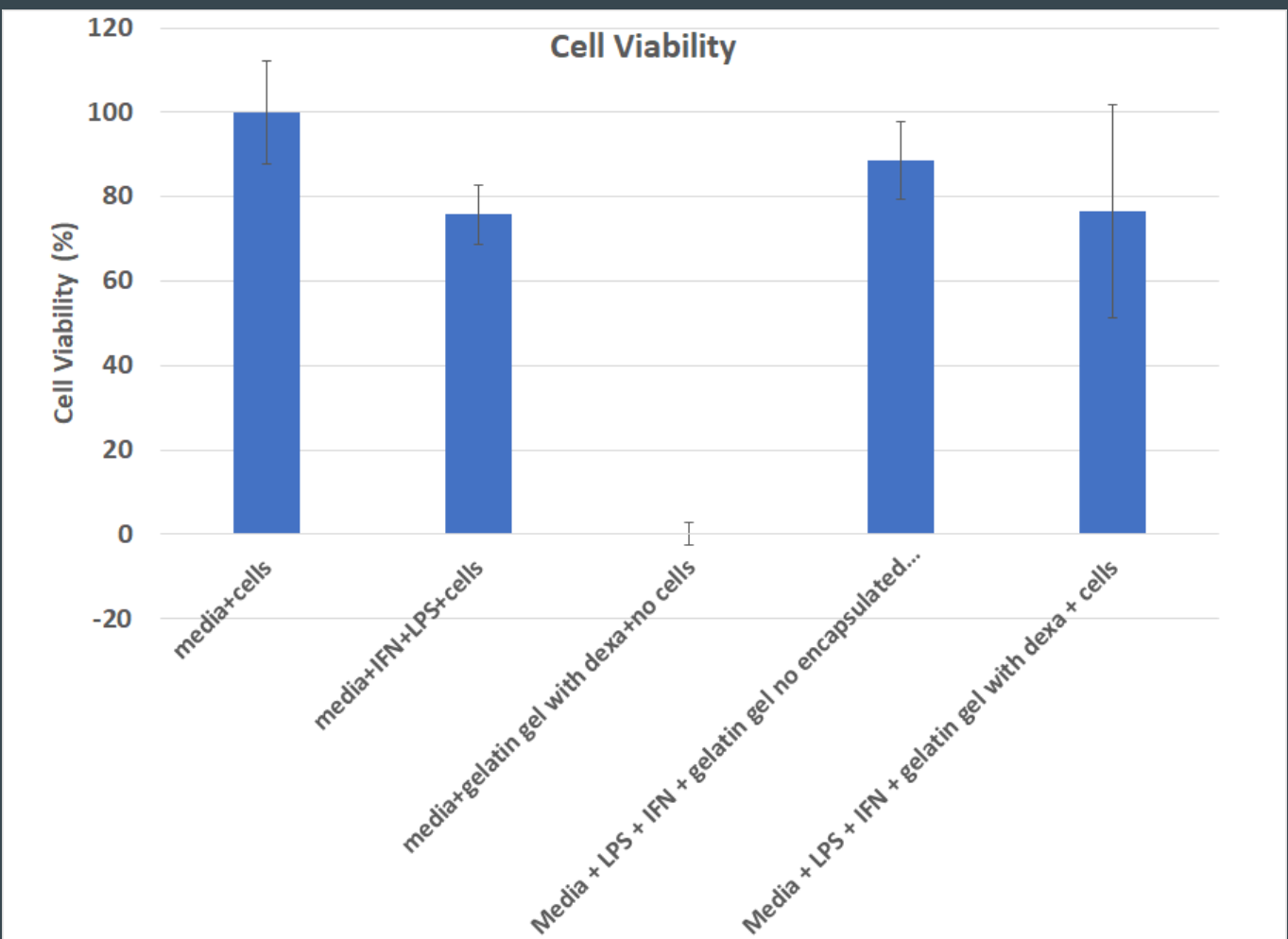
3. Biological Efficacy

- BV2 Murine Microglia cells
- Activated via LPS and IFN γ
- Treatment groups:
 - No treatment control
 - Gelatin gel with no encapsulated drug
 - Gelatin gel with dexamethasone
- Assays:
 - Nitric Oxide via Griess assay
 - Cell survival indirectly via MTS



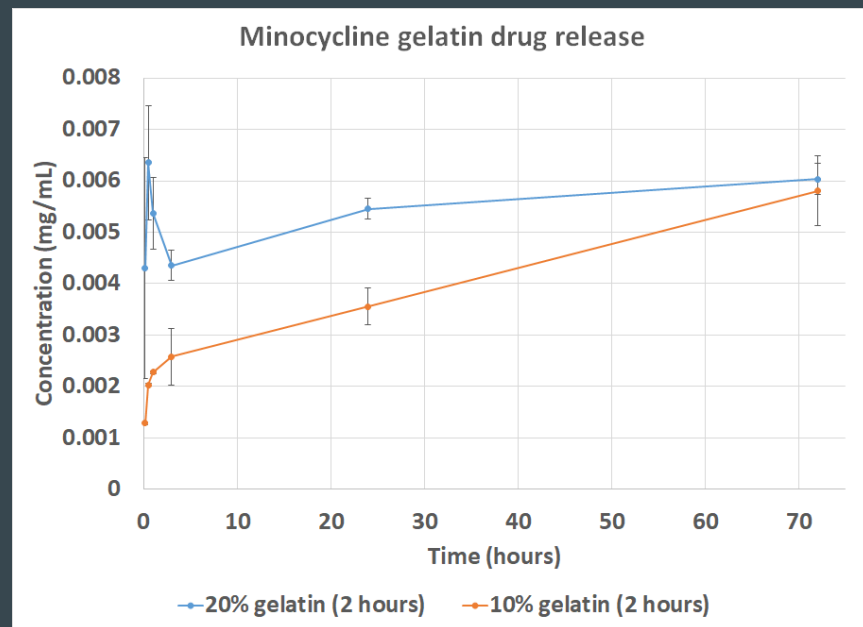
Nitric Oxide Production





Conclusions

- Successfully formulated gelatin gels for controlled release
- Biological efficacy demonstrated in vitro
- Future directions:
 - Test other drugs
 - Manipulate crosslinking



Thank You

- Dr. Rajiv Saigal
- Tianyu Zhao
- Dr. & Mrs. Ellenbogen

NIH NINDS R25NS095377 - Summer Research Experience in Translational
Neuroscience and Neurological Surgery