INDIANA UNIVERSITY
DEPARTMENT OF SURGERY

Research in the Department of Surgery at IUSOM
Cryptic Masons Conference

Troy A. Markel, MD
Associate Professor of Surgery
Vice Chair for Research
Department of Surgery
Indiana University School of Medicine
Indiana University Health

Robust Research in Department

- Basic/Translational Sciences
  - Working with Space Allocation Committee to develop a common lab for the Surgical Sciences
  - Has the potential to be a “named lab”
- Surgical Education Research
- Health Services/SOQIC

Michael P. Murphy, MD

Cryptic Masons Medical Research Foundation
Professor of Vascular Biology Research

Al Hassanein, MMSC, MD

Associate Professor of Surgery

Meijing Wang, MD, MS

Associate Research Professor of Surgery

Burcin Ekser, MD, PhD

Associate Professor of Surgery

Linda M. Schutzman, MD

Assistant Professor of Surgery

Gregory Borschel, MD

James Joseph Harbaugh, Jr. Professor of Plastic Surgery

Erin L. Weber, MD, PhD

Assistant Professor of Surgery

Troy A. Markel, MD

Associate Professor of Surgery

C Max Schmidt, MD, PhD

Professor of Surgery

Mithun Sinha, PhD

Assistant Professor of Surgery

Mark D. Rodefeld, MD

Professor of Surgery

Education Research

Jennifer N. Choi, MD

Associate Dean for Graduate Medical Education

E. Matthew Ritter, MD

Professor of Surgery

Dimitrios Stefanidis, PhD, MD

Harris B. Shumacker Jr. M.D. Professor of Surgery

- Skills Curriculum
- Simulation
- Providing Feedback
- Curriculum Design and Evaluation

- Health services
- Health care quality and safety
- Outcomes
- Health policy evaluation
- Quality and safety improvement
- Implementation science
- Surgical education research

Covers all surgical specialties (and areas of medicine)

SOQIC Faculty

Karl Y. Bilimoria, MD, MS
Chair and Professor of Surgery
SOQIC Executive Director

Andrew A. Gonzalez, MD
Assistant Professor of Surgery
Associate Director

Anthony D. Yang, MD, MS
Professor of Surgery
Associate Director

Rachel Patzer, PhD, MPH
Professor of Surgery
President and CEO, Regenstrief Institute

Clint Cary, MD, MPH
Associate Professor of Urology
Director of Urologic Oncology Research

Jeanette W. Chung, PhD, MA
Research Assistant Professor

Jill D. Connors, PhD, MSW, MS
Assistant Professor of Surgery

Kelsey M. Drewry, PhD, MA
Assistant Professor of Surgery

Joshua S. Eng, PhD
Research Assistant Professor of Surgery

Peter C. Jenkins, MD, MSC
Associate Professor of Surgery

Katelyn G. Makar, MD, MS
Assistant Professor of Surgery

Ashley D. Meagher, MD
Assistant Professor of Surgery

Sanjay Mohanty, MD
Assistant Professor of Surgery

Damaris Ortiz, MD
Assistant Professor of Surgery

Katherine Ross-Driscoll, PhD
Assistant Professor of Surgery

Dimitrios Stefanidis, MD, PhD
Professor of Surgery

Ryan Ellis, MD
Assistant Professor of Surgery

Tarik Yuce, MD
Assistant Professor of Surgery

Jane Holl, MPH, MD
Adjunct Professor of Surgery

Yue-Yung Hu, MPH, MD
Adjunct Assistant Professor of Surgery

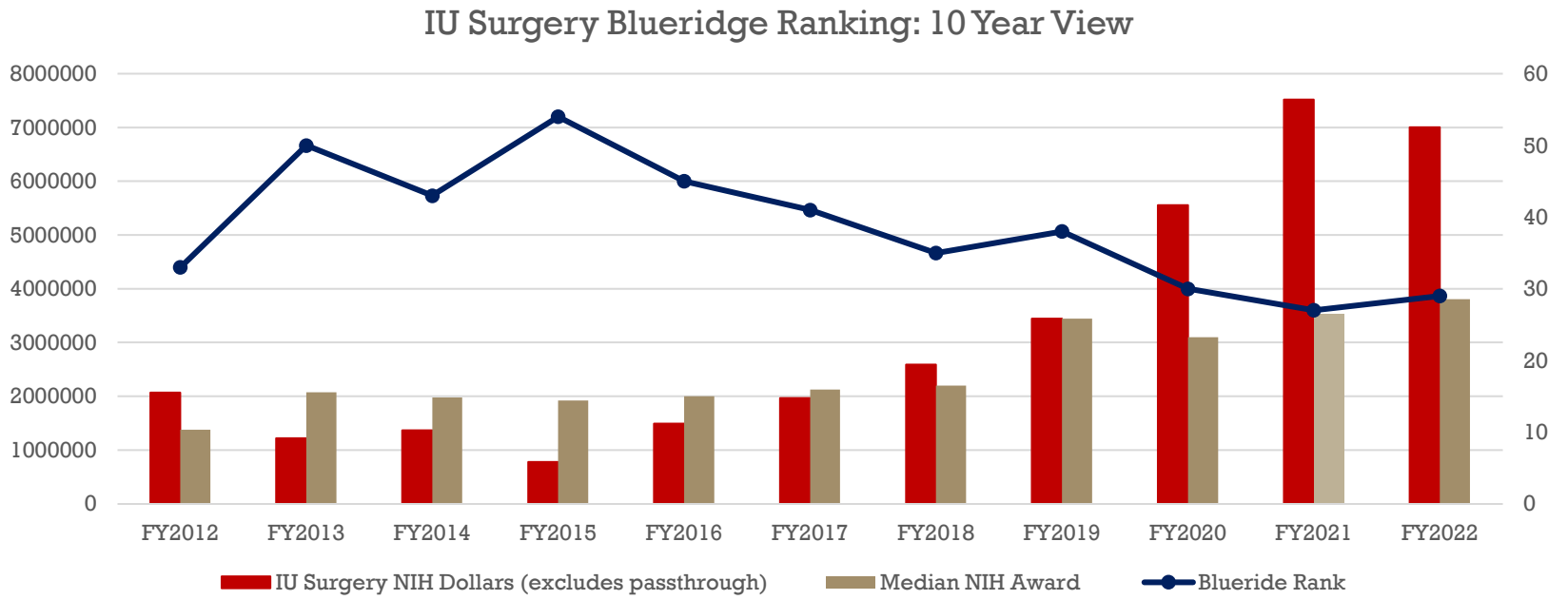
Ryan P. Merkow, MS, MD
Adjunct Assistant Professor of Surgery

David D. Odell, MD, MS
Adjunct Associate Professor of Surgery

Selected Current SOQIC Programs

- National Surgical Education Numbered Trials Group
- Cancer Quality
- Health Policy
- Iliana Quality Collaboratives
- Using Video to Improve Technique
- Perioperative Patient and Surgical Safety
- Evaluating and Improving National Quality and Safety Ranking Systems
- Transplant Disparities
- Numerous others

Blue Ridge NIH Ranking



INDIANA UNIVERSITY
DEPARTMENT OF SURGERY

From Inflammation to Immune Resilience: Chondroitin Sulfate's promising role in prevention of Necrotizing Enterocolitis

Troy Markel, MD
Indiana University School of Medicine
Department of Surgery
Division of Pediatric Surgery

Necrotizing Enterocolitis

- “Necrotizing enterocolitis is a devastating intrabdominal emergency of the newborn…”
- It often requires intestinal resection, and may leave infants with a less than desirable amount of small intestine
- The onset of this disease is incompletely understood

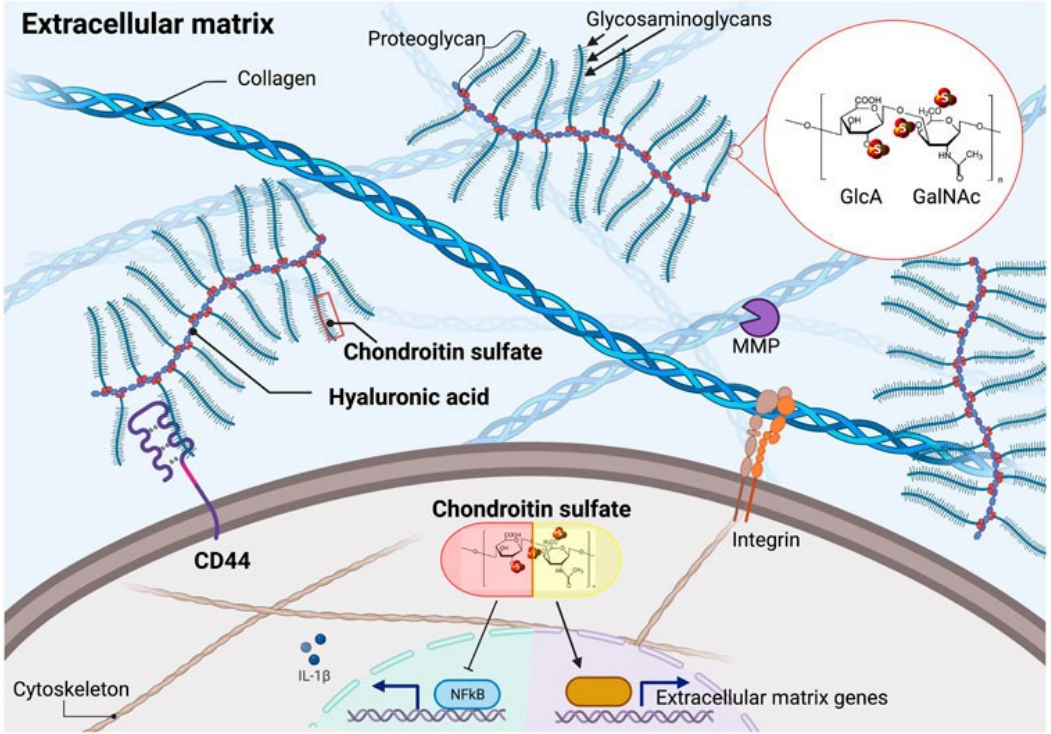
Trifecta

1. Prematurity
2. Stress
   - High concentration formula feeds
   - Low oxygen levels
   - Infection
3. Incomplete Bacterial Gut Colonization

Incidence and Cost

1. 7-10% of the 450,000 infants born prematurely each year are affected
2. 40-50% mortality
3. 19% of NICU expenditures-($5 billion a year in US alone)
   - Medical management adds $73,000 + 22 hospital days
   - Surgical management adds $260,000 and 60 hospital days
4. Breast milk is best method to prevent NEC
5. Probiotics also seem to be helpful, but no FDA approved formulas
6. NO SIGNIFICANT ADVANCEMENTS IN NEC TREATMENT IN LAST 30 YEARS!!!!

Potential Therapy: Chondroitin Sulfate



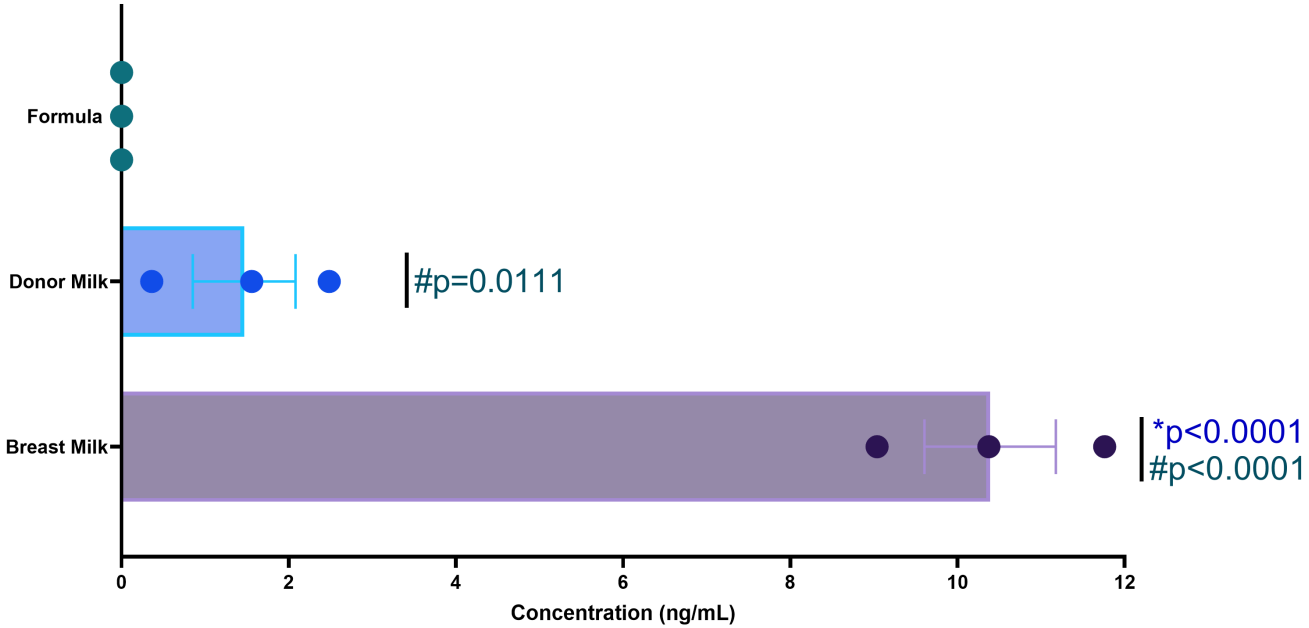
Chondroitin Sulfate

- GAG found in human milk
- Decreased nuclear translocation of NFkB ➔ ↓ proinflammatory cytokines
- Benefits in autoimmune/osteoarthritis/IBD

↓

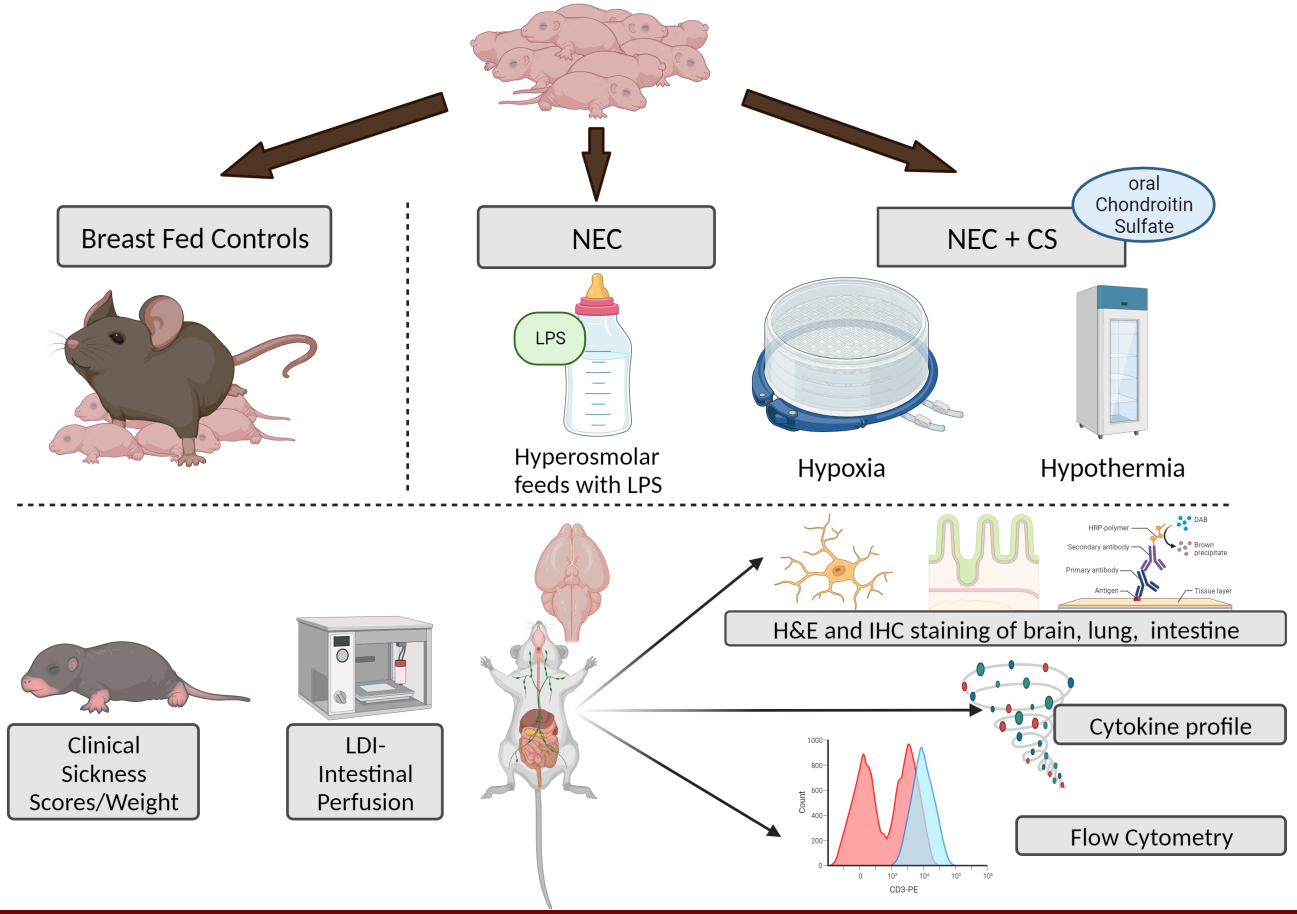
- Benefit in NEC?

Concentration of Chondroitin Sulfate

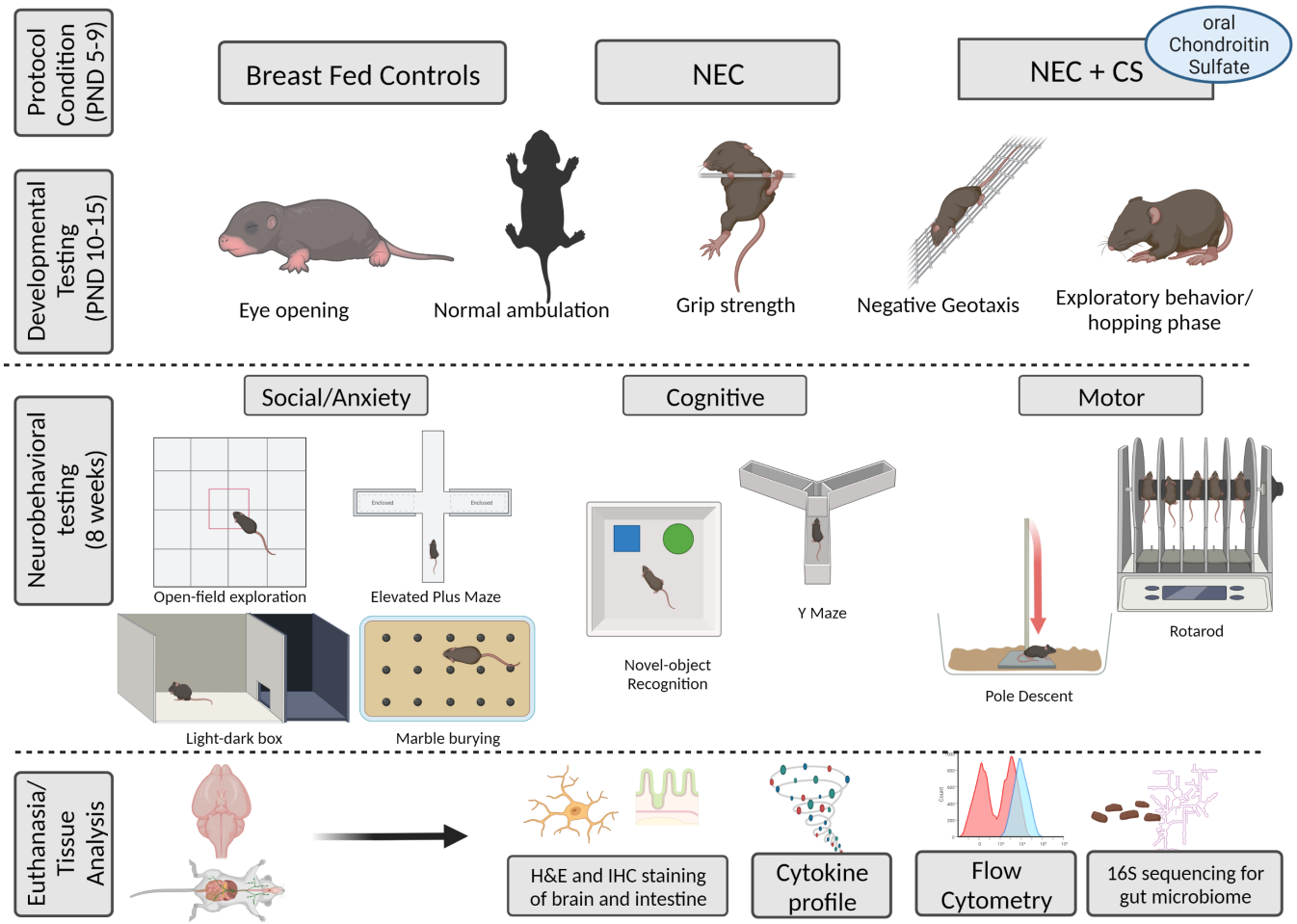


Methods

AIM 1: In murine model of NEC, treatment with oral chondroitin sulfate in formula will improve clinical and biochemical outcomes in NEC

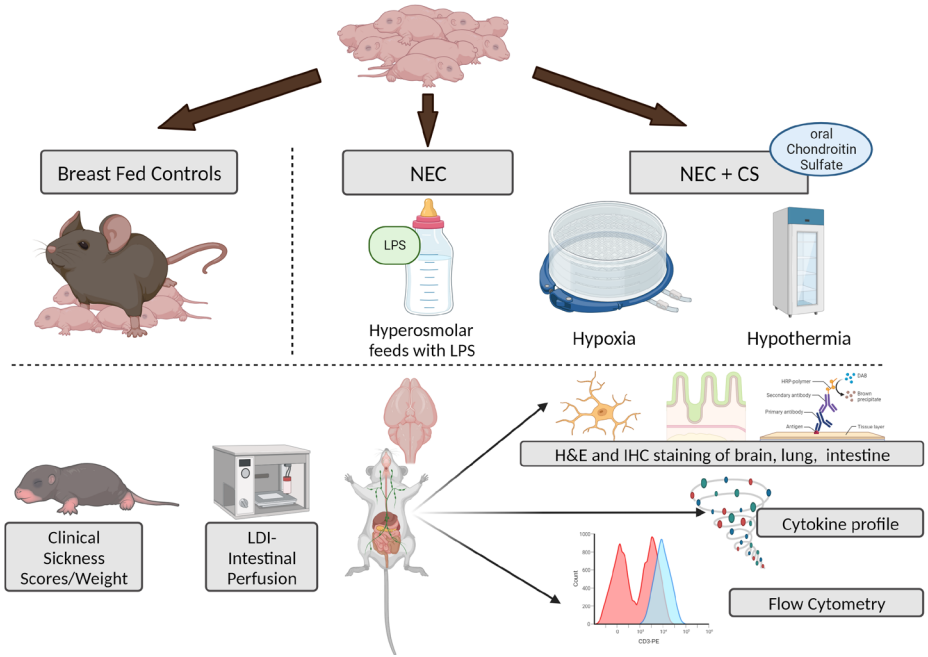


AIM 2: Necrotizing Enterocolitis results in downstream neuro-developmental impairment. Administration of CS is neuroprotective

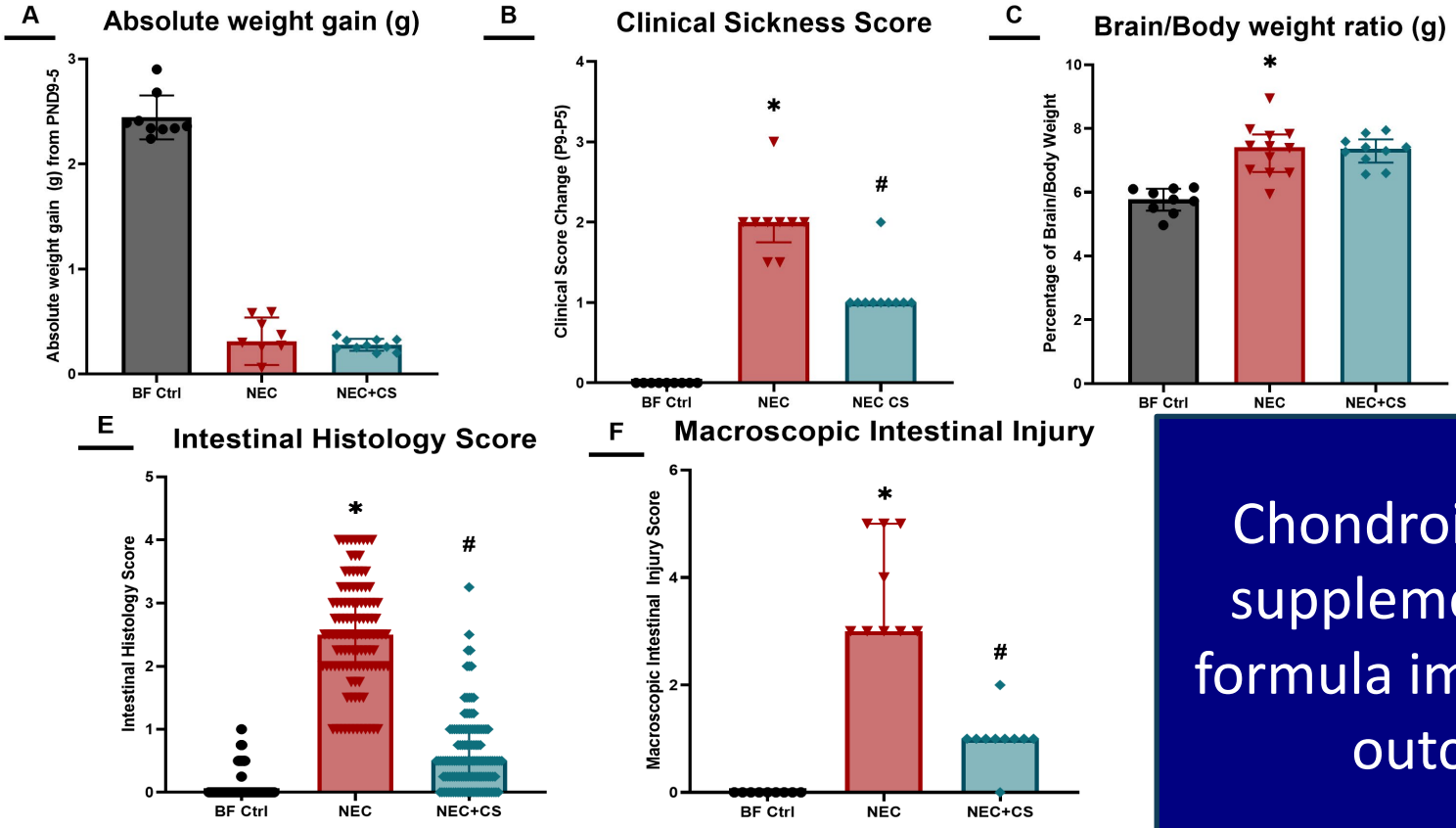


Results

Oral Chondroitin Sulfate Improves NEC outcomes

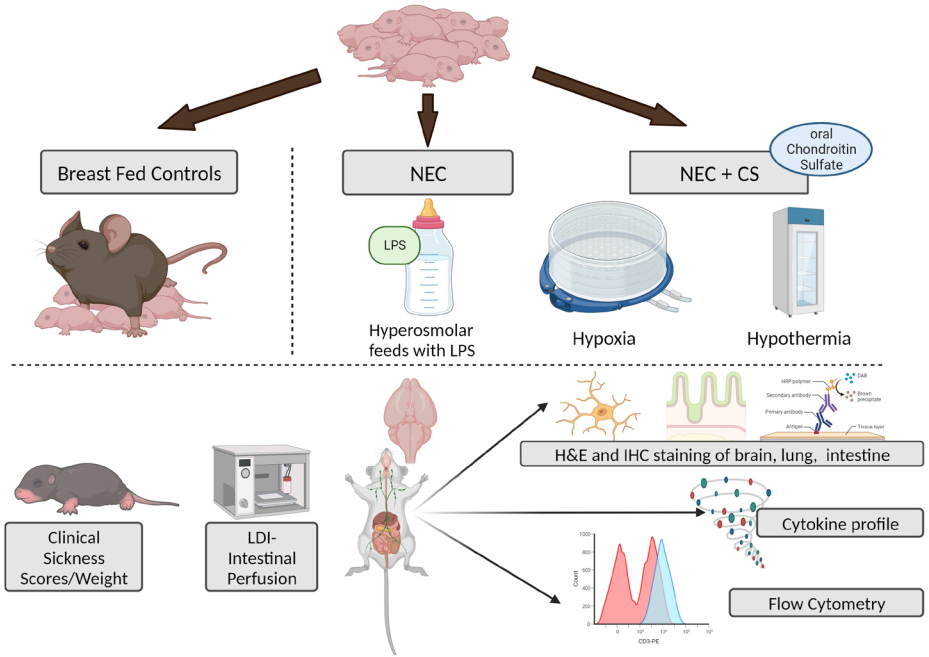


NEC	NEC+ oral CS
↑Intestinal Injury	↓ Intestinal Injury



Chondroitin Sulfate supplementation in formula improves NEC outcomes

Oral Chondroitin Sulfate Improves NEC outcomes



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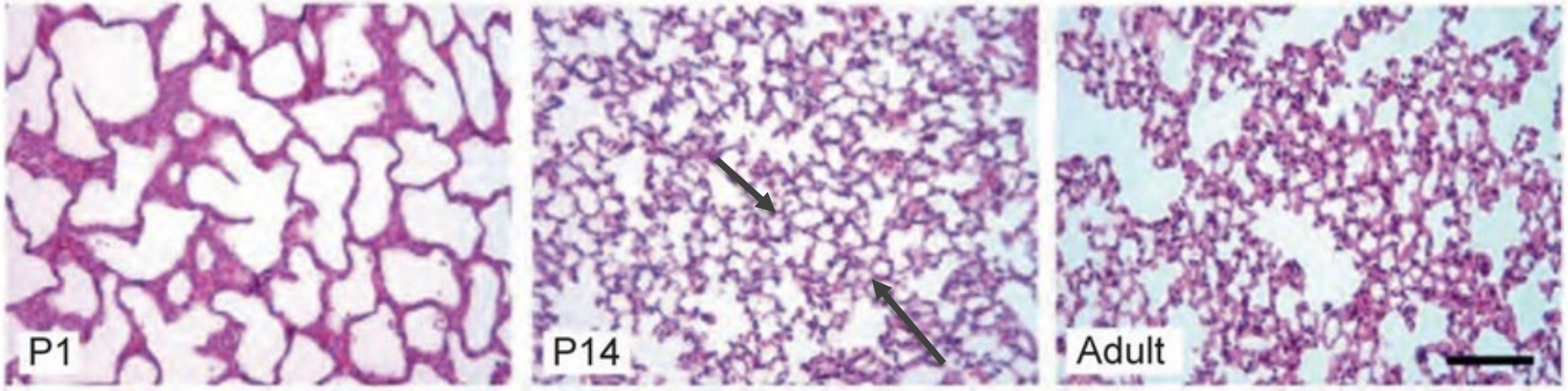
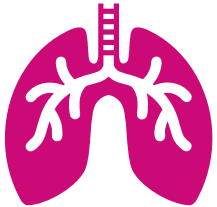


Wide open air-spaces → Terminally differentiated smaller sacules → Final organized structure

↑ Surface Area in contact with air



Better gas-exchange

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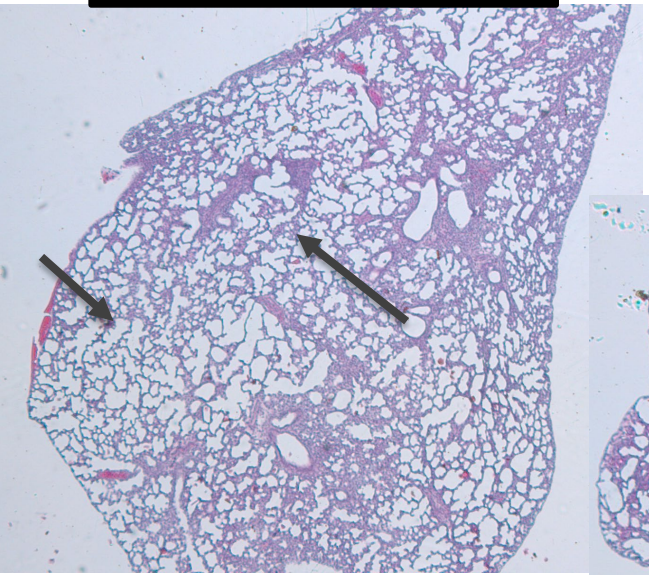
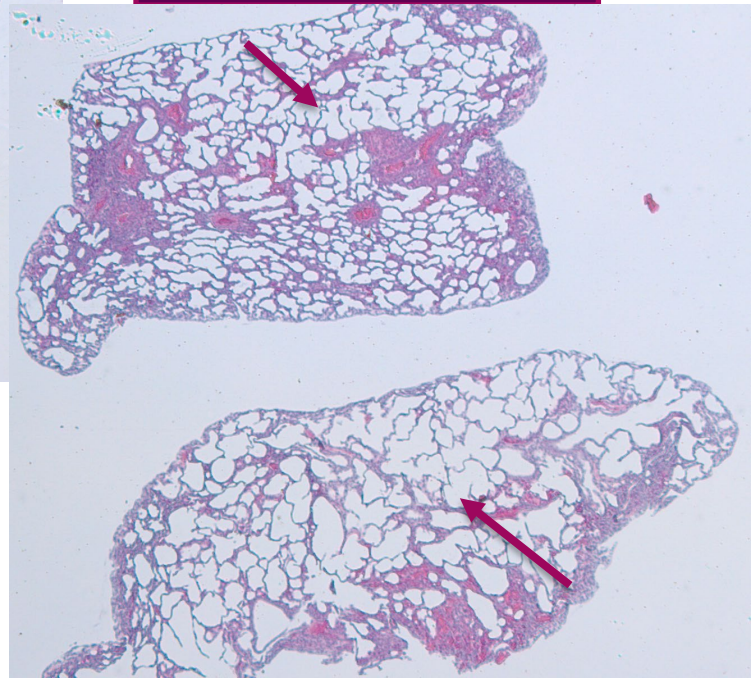
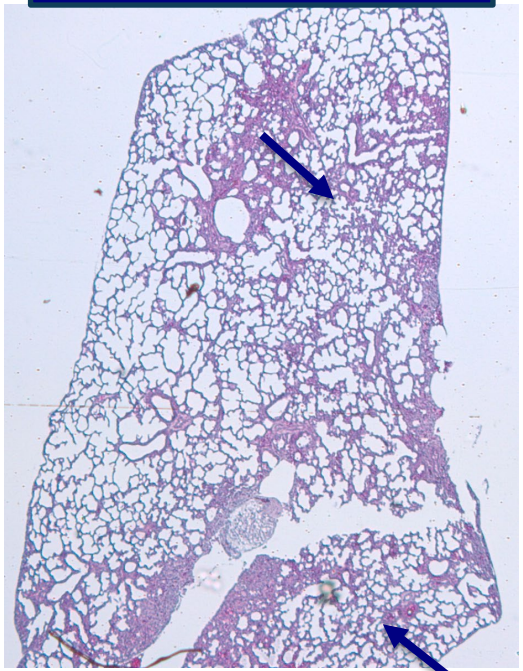


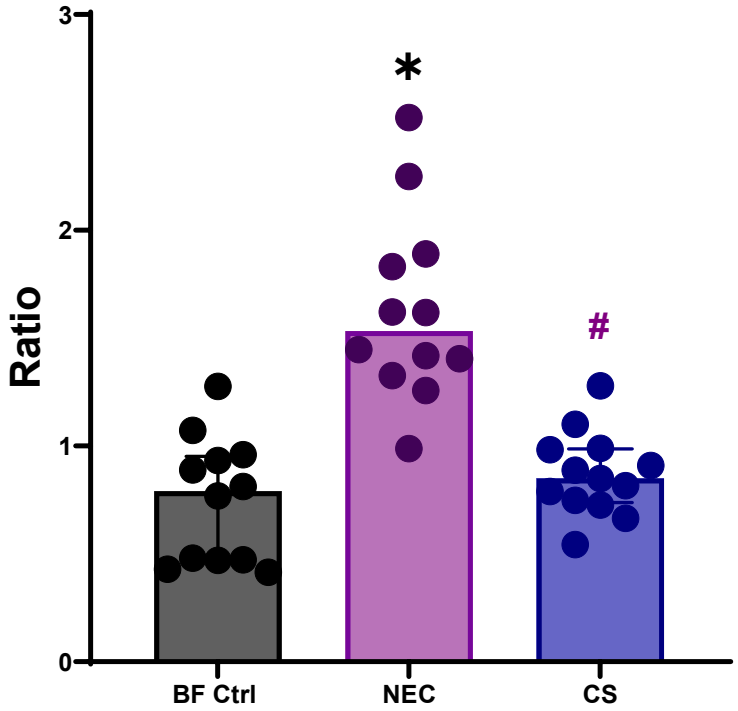
NEC



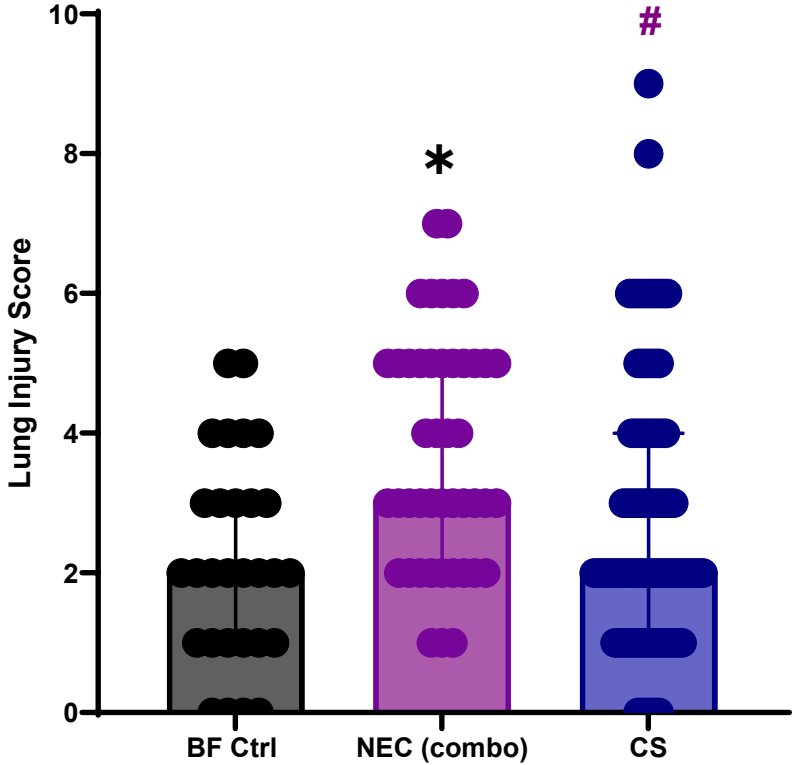
NEC+CS



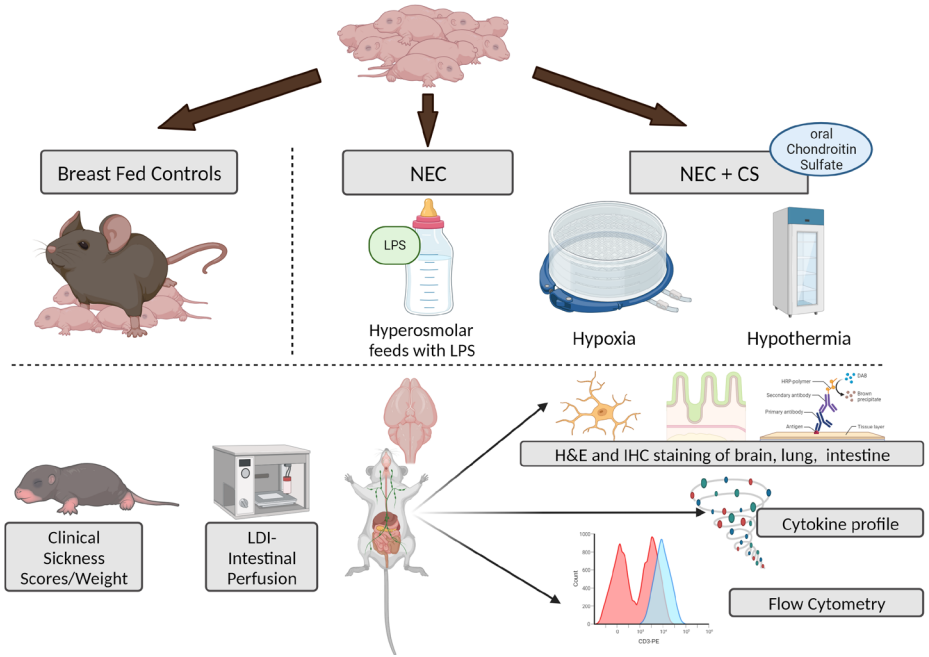
Air-space/Alveolar area (Terminal Differentiation)



Lung Injury Score



Oral Chondroitin Sulfate Improves NEC outcomes



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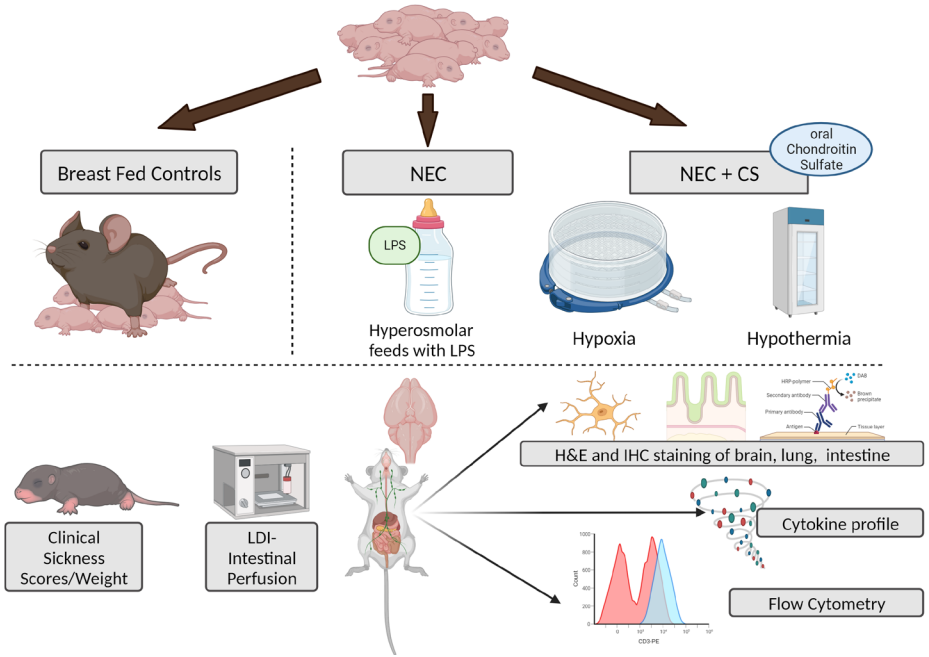

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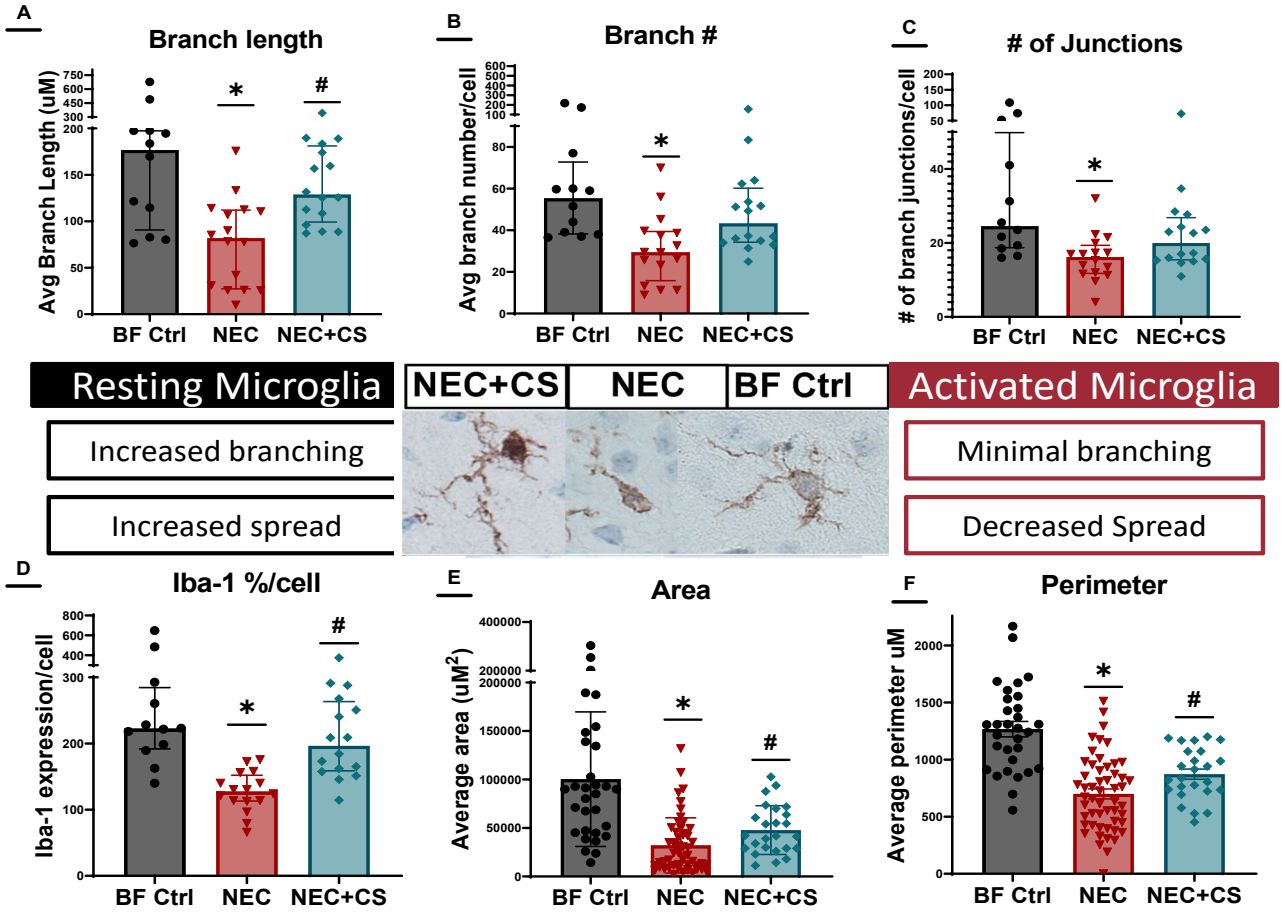
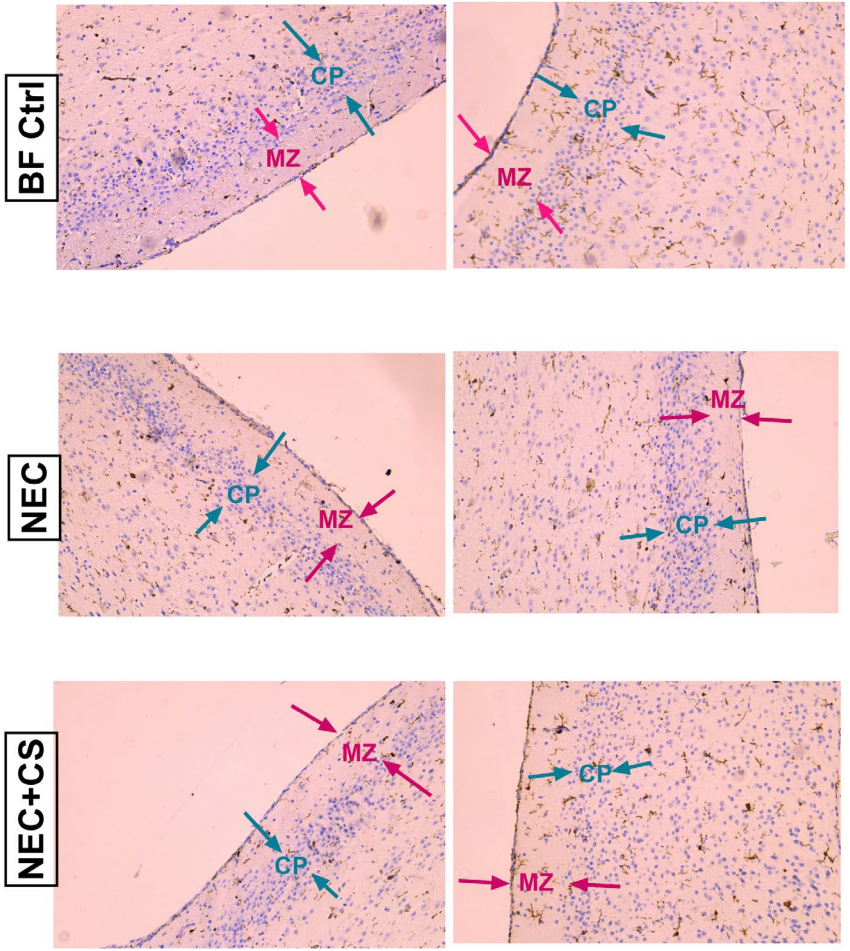


NEC and intestinal injury results in microglial activation

Postnatal CS therapy attenuates microglial activation in the brain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CP
MZ
CP
MZ
NEC
CP
MZ
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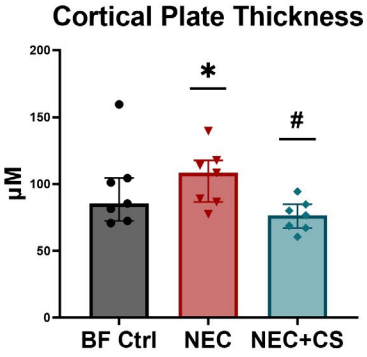
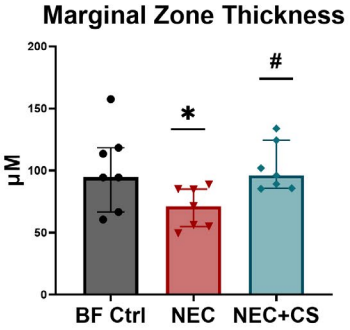
CP
NEC+CS
MZ
CP
CP
MZ


Cortical Plate Thickness
µM
200
150
100
50
0
*
#
BF Ctrl
NEC
NEC+CS


Marginal Zone Thickness
µM
200
150
100
50
0
*
#
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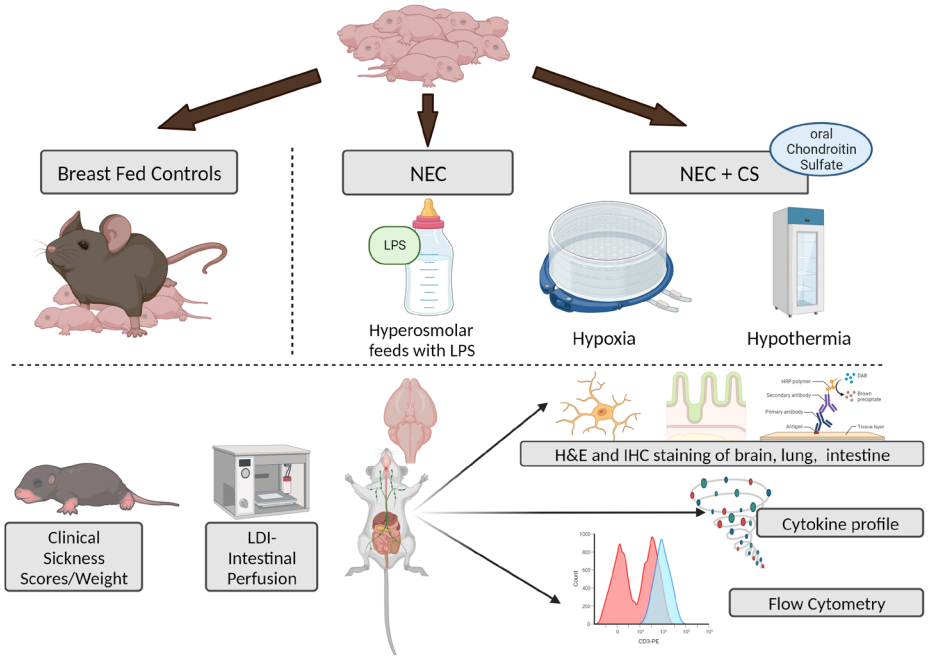
NEC
NEC+CS

Oral Chondroitin Sulfate Improves NEC outcomes



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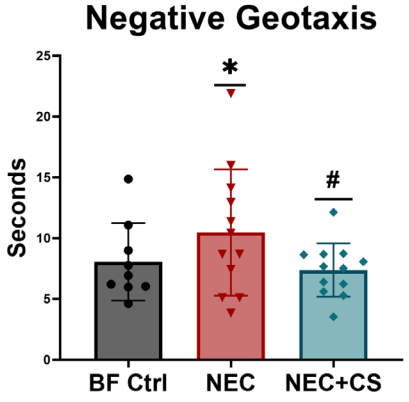
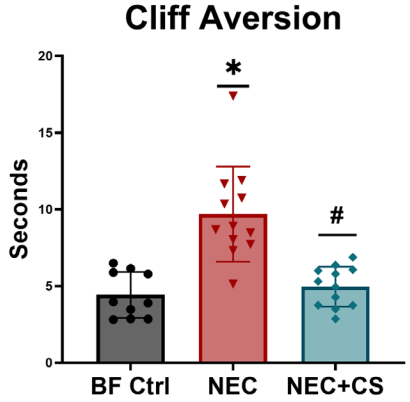
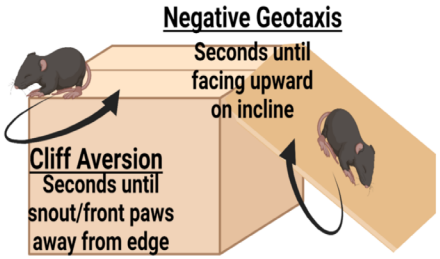
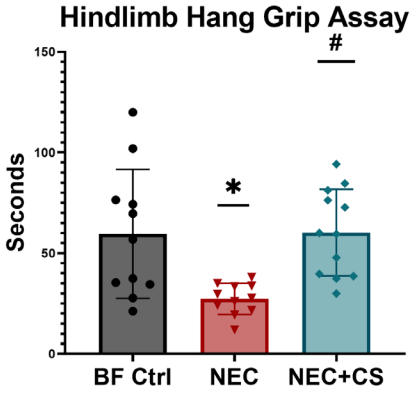
Delayed Developmental Milestones	Improved Developmental Milestones

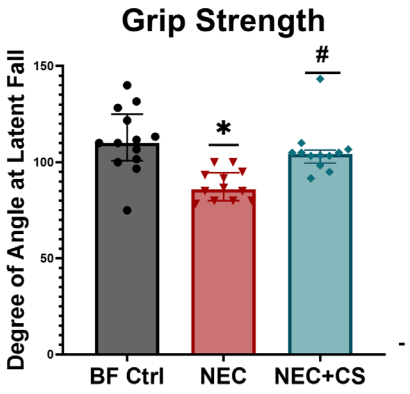


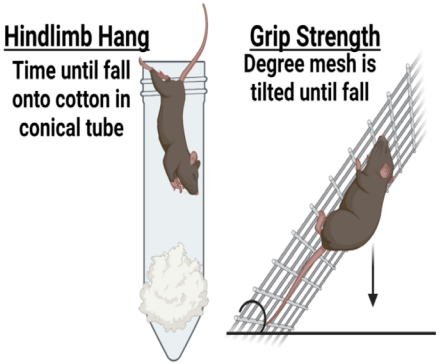




NEC and intestinal injury results in delay in developmental milestones



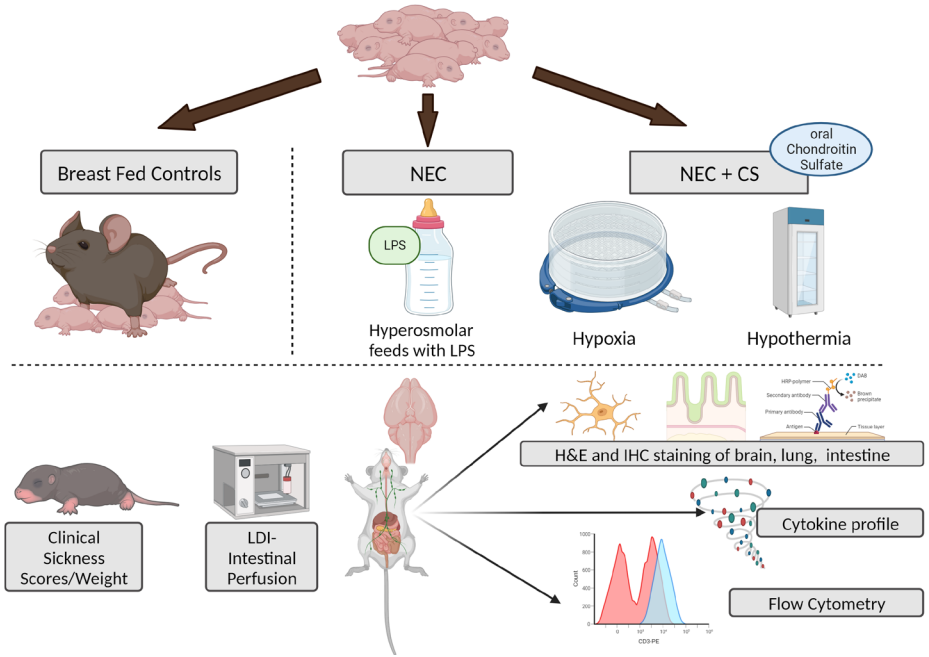




Postnatal CS therapy prevents delay of developmental milestones

Conclusions

Oral Chondroitin Sulfate Improves NEC outcomes



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Delayed Developmental Milestones	Improved Developmental Milestones
Altered Immune Profile	Improved Immune Profile

Future Directions

Prolacta BIOSCIENCE

Partner with a milk fortifier company to add CS to further study differences in breast milk and donor milk and consider adding CS to their product

Bioiberica

Begin steps for clinical trial to be able to add pharmaceutical grade CS to all formula products that neonates receive

How can the Cryptic Masons Continue to Support Our Department

1. Grateful for Dr. Murphy's Chair position…
   - CM Young Investigator?
2. Naming rights and sponsorship of Department's Collective Lab
   - Vera Bradley Foundation Center for Breast Cancer Research
   - Brown Center for Immunotherapy
   - Krannert Cardiovascular Research Center
   - Herman B. Wells Center for Pediatric Research
3. High ticket equipment needs to maintain state of the art research at IU
   - Possible Development of a service core surrounding that equipment