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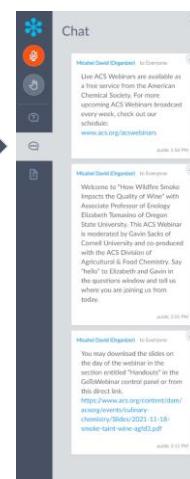
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A Career Planning Tool For Chemical Scientists



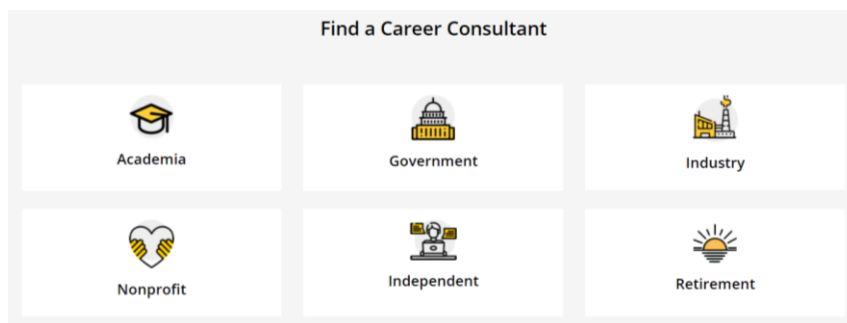
ChemIDP is an Individual Development Plan designed specifically for graduate students and postdoctoral scholars in the chemical sciences. Through immersive, self-paced activities, users explore potential careers, determine specific skills needed for success, and develop plans to achieve professional goals. **ChemIDP** tracks user progress and input, providing tips and strategies to complete goals and guide career exploration.

<https://chemidp.acs.org>

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Career Consultant Directory



- ACS Member-exclusive program that allows you to arrange a one-on-one appointment with a certified ACS Career Consultant.
- Consultants provide personalized career advice to ACS Members.
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www.acs.org/careerconsulting

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ACS Career Resources



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Podcast to Faculty Workshop

An virtual workshop for petrochemical industry professionals to learn by podcast in the chemical industry.

Career Kick-Start Workshop

A one-day career development workshop for graduate students and postdoctoral scholars.

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Career Consultants

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ChemISP™

ACS Institute developed this resource for graduate students and postdoctoral scholars.

Resume Review

Get to know your resume & LinkedIn and to get feedback to support your job search.

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2 FEB	Academia vs. Industry February 2, 2023	2 MAR	Networking March 2, 2023
6 APR	Acing the Interview April 6, 2023	4 MAY	Careers in Industry May 4, 2023
1 JUN	Entrepreneurship June 1, 2023	6 JUL	Is grad school right for me? July 6, 2023
3 AUG	Careers in Government August 3, 2023	7 SEP	The Basics of Building Resilience September 7, 2023
5 OCT	Skydiving into Retirement October 5, 2023	2 NOV	Finding and securing an internship November 2, 2023
		7 DEC	Careers in Academia December 7, 2023

<https://www.acs.org/content/acs/en/careers/personal-career-consulting.html>

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ACS Scholar Adunoluwa Obisesan

BS, Massachusetts Institute of Technology, June 2021
(Chemical-biological Engineering, Computer Science & Molecular Biology)



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Bonus Episode
Carolyn Bertozzi and K. Barry Sharpless chat about sharing the 2022 Nobel Prize in Chemistry
December 6, 2022



Bonus Episode
Bioorthogonal, click chemistry clinch the Nobel Prize
October 5, 2022



Episode #46
Lithium mining's water use sparks bitter conflicts and novel chemistry
September 13, 2022



Bonus Episode
Happy 100th birthday, John Goodenough!
For John Goodenough's 100th birthday, Stereo Chemistry revisits a fan-favorite interview with the renowned scientist
July 25, 2022



Bonus Episode
Jess Wade on Wikipedia and work-life balance
June 21, 2022



Bonus Episode
The sticky science of why we eat so much sugar
May 31, 2022



Bonus Episode
There's more to James Harris's story
April 27, 2022



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The helium shortage that wasn't supposed to be
March 24, 2022

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acsoncampus.acs.org

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ACS OFFICE OF DEIR

Advancing ACS' Core Value of Diversity, Equity, Inclusion and Respect

Resources

<p>Inclusivity Style Guide Designed to help staff and members use language and images that respect diversity in all its forms.</p> <p>→</p>	<p>ACS Webinars on Diversity Covering diversity and inclusion at the workplace</p> <p>→</p>
<p>ACS Publications DEIR Hub See what ACS Publications is doing for fostering inclusivity in scholarly publishing</p> <p>→</p>	<p>ACS Volunteer and ACS Meetings Code of Conduct Fostering a positive and welcoming environment for attendees, volunteers and staff.</p> <p>→</p>
<p>C&EN Trailblazers C&EN highlights scientists from different backgrounds who are making an impact in chemistry.</p> <p>→</p>	<p>NEW! Download DEIR Educational Resources Download this educational guide for additional recommendations on videos, articles, books, podcasts, and more on diversity, inclusion, and related topics.</p> <p>→</p>
<p>Quick Guide: Inclusion Moments Learn more about what Inclusion Moments are and see ideas to host them during your meetings.</p> <p>→</p>	<p>Quick Guide: How to host inclusive in-person events Recommendations and best practices to ensure that your events can accommodate everyone.</p> <p>→</p>



Diversity, Equity, Inclusion, and Respect

**Adapted from definitions from the Ford Foundation Center for Social Justice:

Equity**

Seeks to ensure fair treatment, equality of opportunity, and fairness in access to information and resources for all. We believe this is only possible in an environment built on respect and dignity. Equity requires the identification and elimination of barriers that have prevented the full participation of some groups.

Diversity**

The representation of varied identities and differences (race, ethnicity, gender, disability, sexual orientation, gender identity, national origin, tribe, caste, socioeconomic status, thinking and communication styles, etc.) collectively and as individuals. ACS seeks to proactively engage, understand, and draw on a variety of perspectives.

Inclusion**

Builds a culture of belonging by actively inviting the contribution and participation of all people. Every person's voice adds value, and ACS strives to create balance in the face of power differences. In addition, no one person can or should be called upon to represent an entire community.

Respect

Ensures that each person is treated with professionalism, integrity, and ethics underpinning all interpersonal interactions.

<https://www.acs.org/diversity>

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SPRING 2023

Crossroads of Chemistry

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Wed., March 15, 2023 | 2:00-3:00pm ET

**Successful Transitions: Strategies
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Co-produced with the ACS Younger Chemists Committee
and the ACS Committee on Ethics



Thurs., March 16, 2023 | 2:00-3:00pm ET

**Toxicology 101: Chemicals and
their Toxic Effects**

Co-produced with the ACS Office of Career and
Professional Education



Wed., March 23, 2023 | 1:00-2:00pm ET

**How Artificial Intelligence is
Changing Drug Discovery**

Co-produced with the Science History Institute

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Nature's Lipid Nanoparticles: Exosomes in Drug Delivery and Therapeutics



JANET SASSO, MPH

Information Scientist,
CAS, a division of the
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ATTA BEHFAR, MD, PhD

Director of the Cardiac
Regenerative Medicine
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million substances

Over
50
languages
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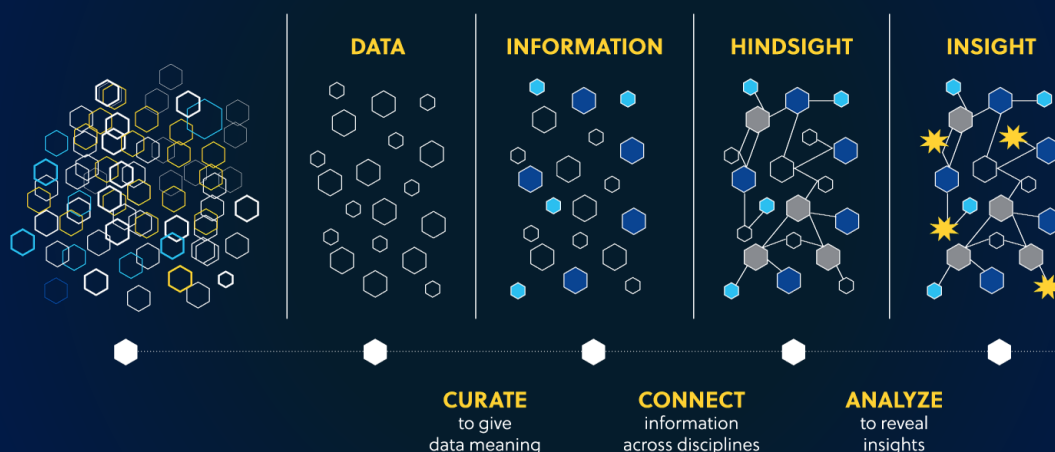
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Data is valuable only when it is transformed into insight



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A landscape view

EXOSOMES IN DRUG DELIVERY AND THERAPEUTICS

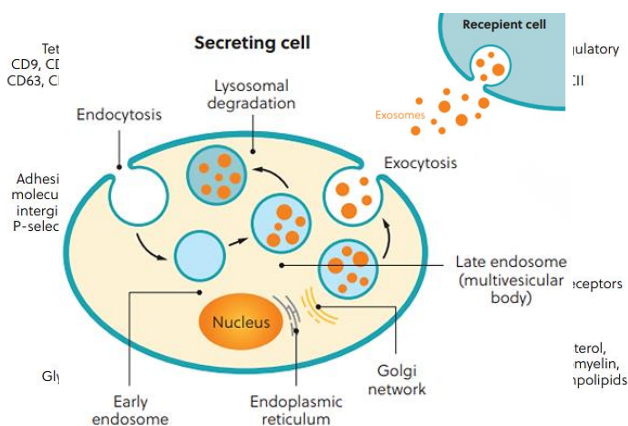
Janet Sasso, Information Scientist

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What are exosomes?

Function and Characterization



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Why exosomes?

Synthetic



Low bioavailability | Rapid bloodstream clearance | Cytotoxicity

Natural



Innate stability | Biocompatibility | Low immunogenicity | Crosses blood-brain barrier

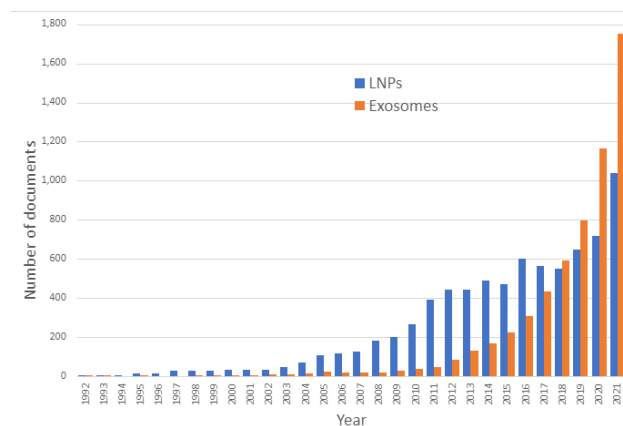
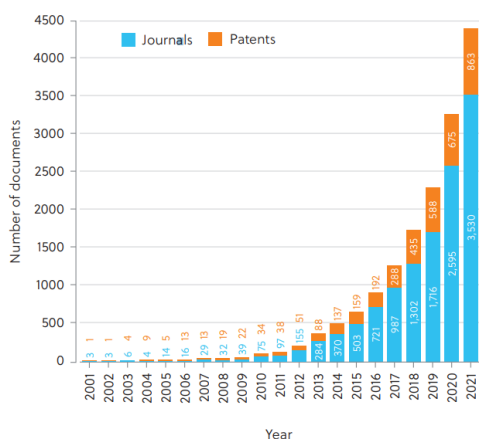


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Exosome publications has increased over time

Research in exosomes is outpacing LNP

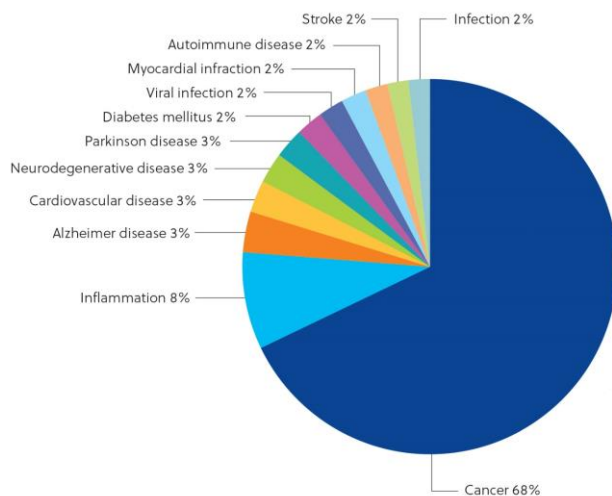


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Cancer leads the way amongst a wide range of diseases

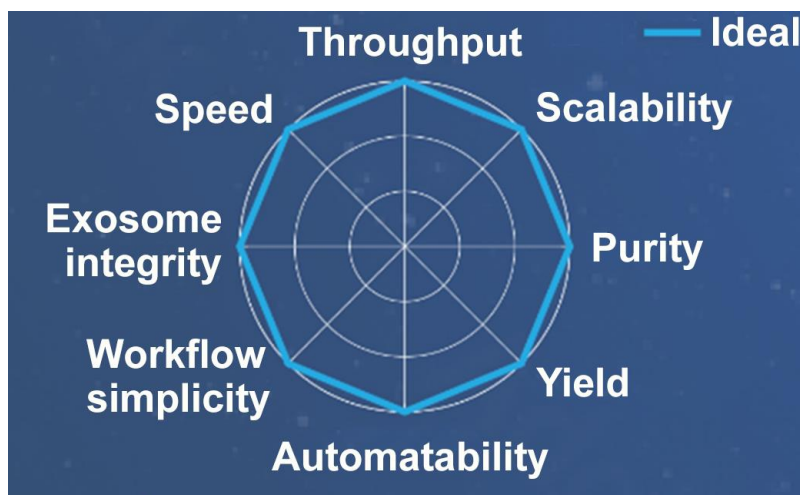


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There's a challenge: isolating and purifying exosomes



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With a wide range of approaches...



Ultracentrifugation

Density and size based sequential separations

✓ purity



Polymer precipitation

Polymer adhering and precipitating exosomes

✗ purity, speed



Ultrafiltration

Filter membrane with defined size-exclusion limit

✗ purity, integrity



Size exclusion chromatography

Hydrodynamic radii exosome separation

✗ throughput, automation



Immunoaffinity

Antigen-antibody specific recognition and binding

✗ yield, speed



Microfluidics

Immunoaffinity, size, density

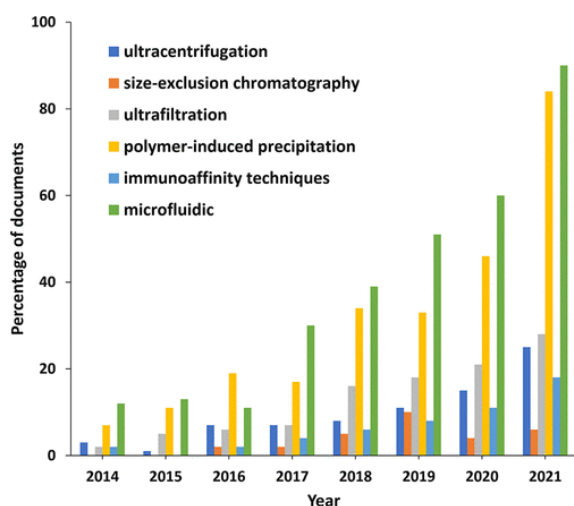
✗ throughput, scale, speed

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Exosome application publications



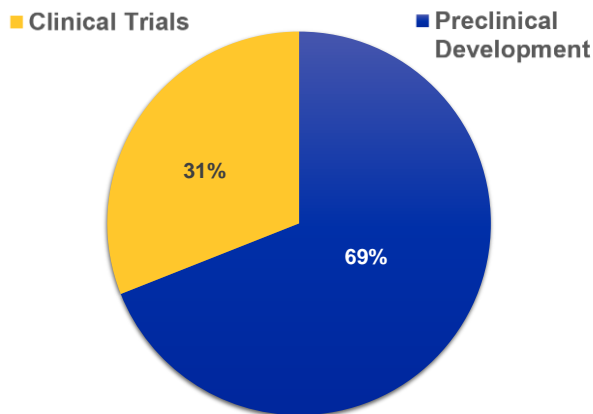
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Exosomes in the clinical development pipeline

Preclinical Development and Clinical Trials



Exosomes in clinical trials	Therapeutic Focus
bmMSC-derived exosomes	ARDS, IBD
bmMSC-derived exosomes	Wound healing
amniotic fluid derived exosomes	ARDS
Purified exosome product	Wound healing/ Myocardial infarction
exosome with ASO-STAT6	Hepatocellular Carcinoma
umbilical cord derived exosomes	ARDS
ginger exosomes	IBD
MSCs-derived exosome with KrasG12D siRNA	Pancreatic cancer

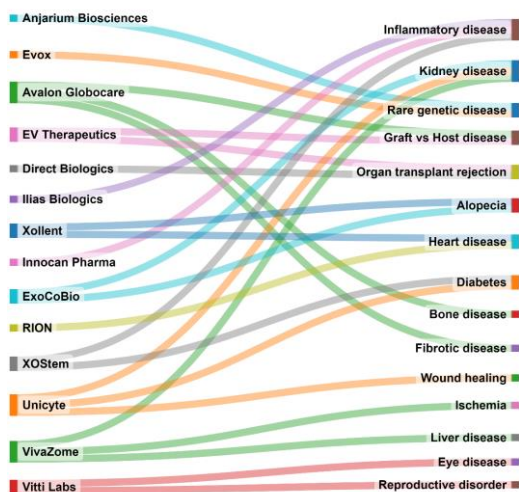
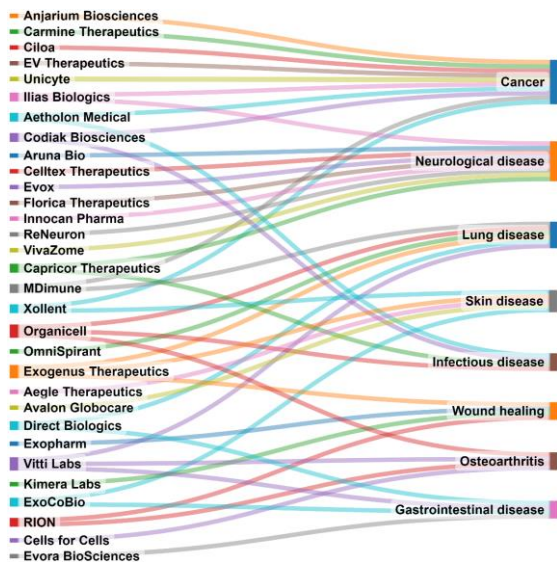
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Exosome research activity

Companies and their targeted diseases



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Clinical Application of Exosome Based Therapy

Atta Behfar, M.D., Ph.D.

Russ and Kathy Van Cleve Professor of Regenerative Medicine,
 Consultant, Interventional Cardiology, Heart Transplant
 Director, Van Cleve Cardiac Regenerative Medicine Program
 Co-Director of Innovation in Biologics, Cardiology
 Research Program Director, Cardiology Fellowship Program
 Professor, Mayo College of Medicine

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Disclosures for Atta Behfar, M.D., Ph.D.

- ▶ Relevant Financial Relationships
 - Rion Inc
 - Sorento Therapeutics
 - Deverra Therapeutics

- ▶ Off label usage – TISSEEL

- ▶ Additional Disclosures
 - Abbott – Steering Committee



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Learning Objectives

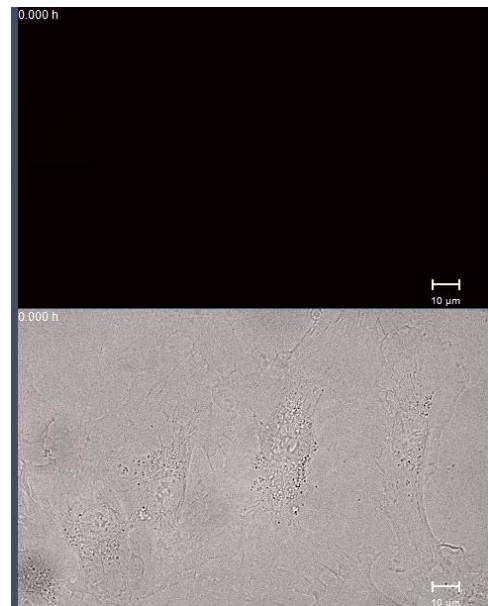
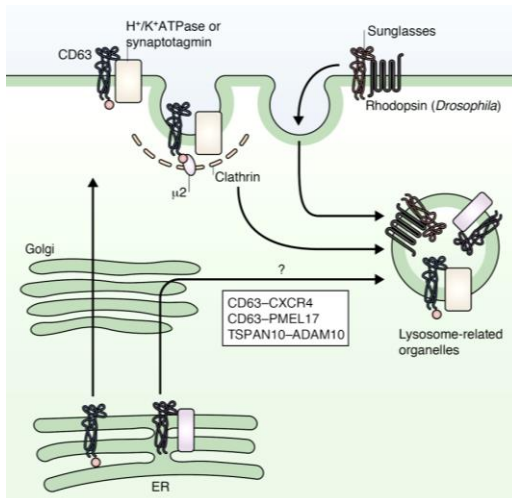
- ▶ Evolution of stem cells to exosomes
- ▶ Describe the use of naturally occurring extracellular vesicles for therapeutic applications
- ▶ Summarize how to engineer extracellular vesicles for therapeutic delivery in wound and cardiovascular space



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Exosomes: Critical role of Tetraspanins Cell entry, cell fusion and endosomal trafficking



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Engineering exosomes therapies

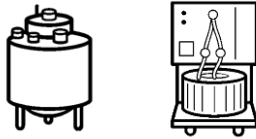


Master Cell Banks

Cells engineered with unique membrane proteins designed for endosomal trafficking

cDNA, mRNA and miRNA/siRNA targeting

Proteins and growth factor overexpression or targeting



Bioreactor Purification

Massive cell expansion

Conditioned medium harvest

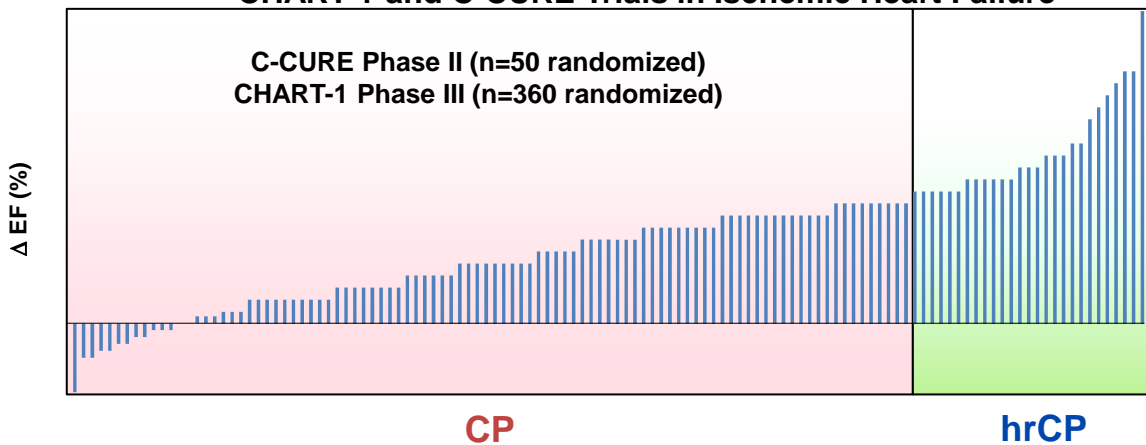
Size/affinity-based purification



CLINICAL EXPERIENCE

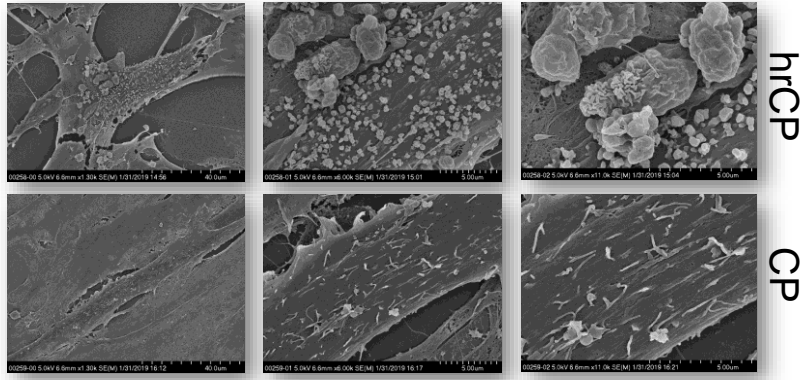
TRIAL RESULTS IDENTIFY A HIGHLY REGENERATIVE CELL

CHART-1 and C-CURE Trials in Ischemic Heart Failure



CLINOMICS- CHART-1/C-CURE TRIAL DATA

hrCP MORE EFFICIENT AT EXOSOME RELEASE

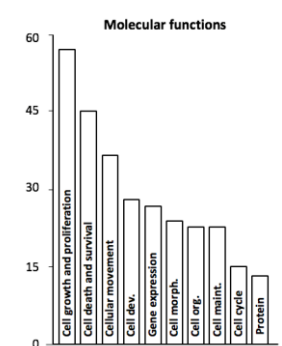
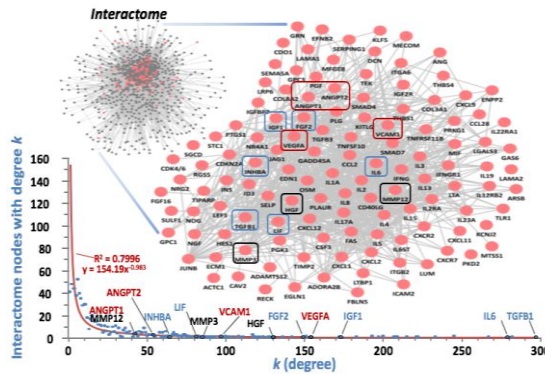
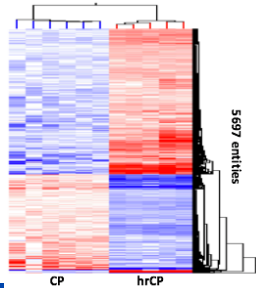
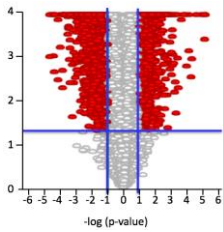


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CLINOMICS- CHART-1/C-CURE TRIAL DATA

miRNA/SECRETOME INTERACTOME PROFILING OF CP VERSUS hrCP EXOSOMES

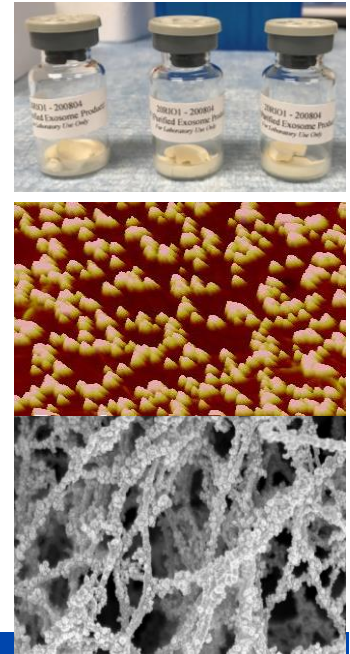
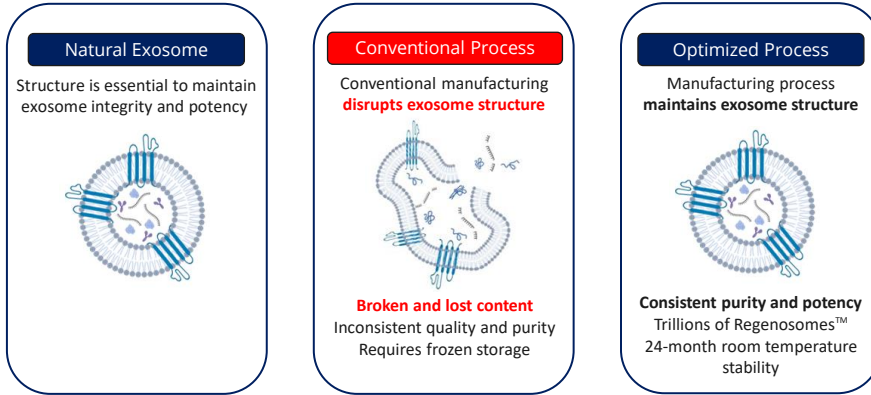
Several Platelet Markers Upregulated in hrCP



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Manufacturing Maintains Exosome Structure/Function

Conventional manufacturing process often destroys exosomes

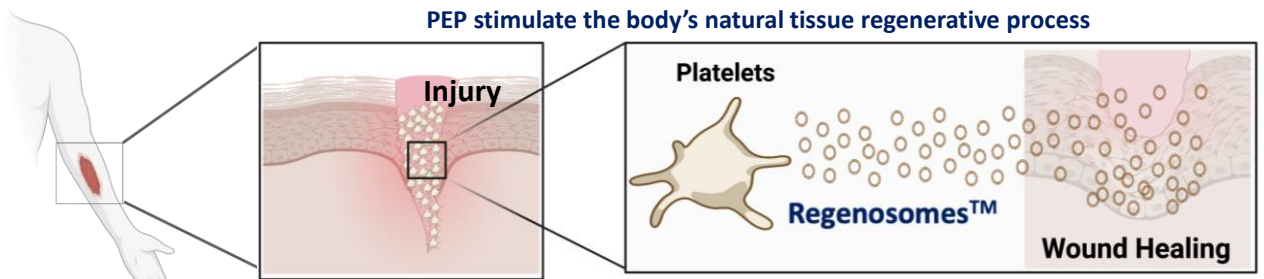


Regenerative Exosomes: How They Work

MODE OF ACTION Reduces oxidative stress helping cells survive

- Reduces inflammation to allow for healing
- Activates stem cells to help with tissue repair
- Restores healthy blood supply

Pre-clinical data demonstrates that PEP capable of regenerating many types of tissue:
skin, heart, muscle, tendon, lung and nerve

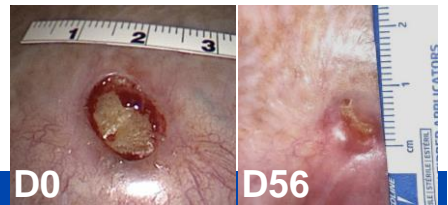
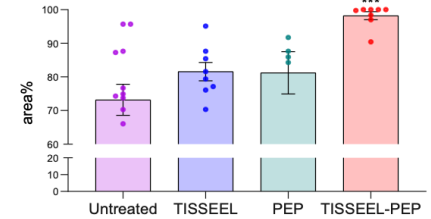
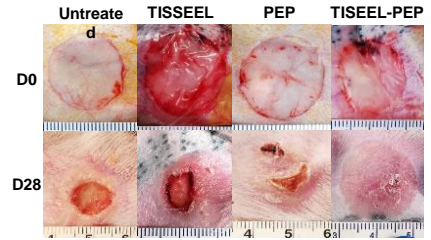


Compassionate Use – Radiation injury in the setting of skin cancer

- Dr. Katie Van Able
 - ENT / Department of Head and Neck Surgery at Mayo Clinic
 - >1yr non-healing wound
 - Second round of therapy planned

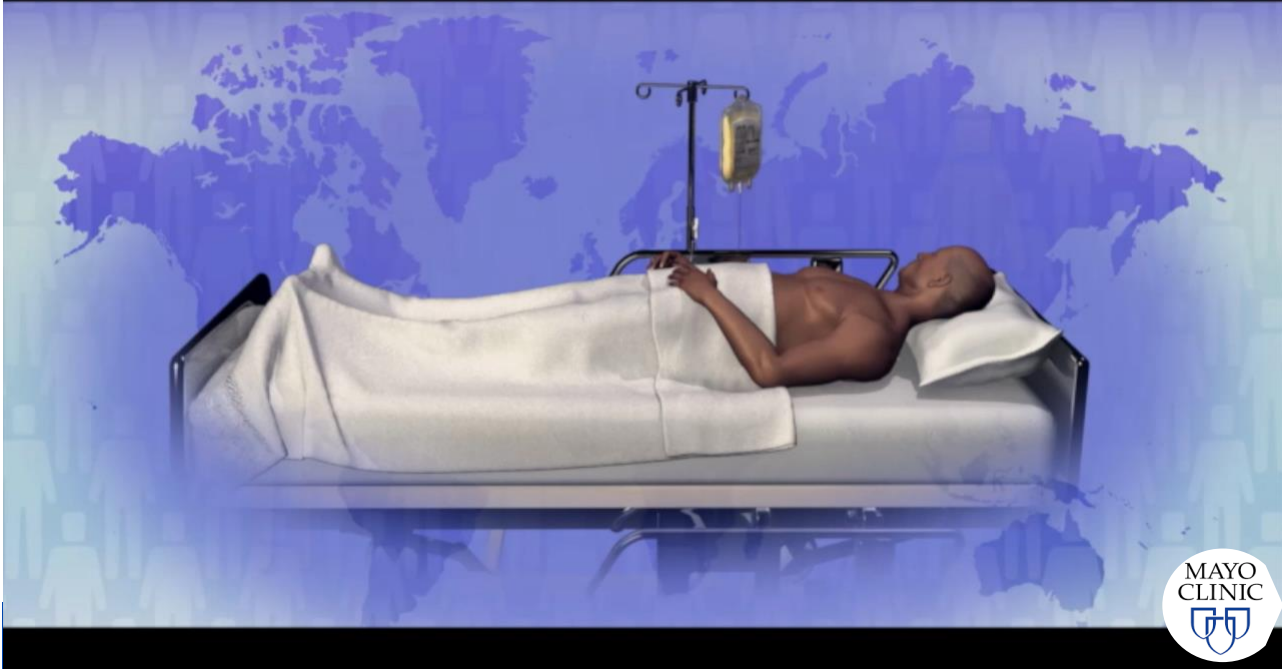
Platelet Derived Exosomes

- P1 Clinical Study on ischemic wound healing completed at Mayo Clinic
- P2 Multi-center study on ischemic wound in 2023
- **Compassionate use**
 - Radiation
 - Non-healing wounds
 - DOD applications

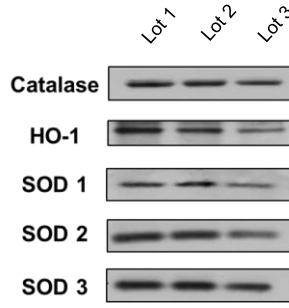
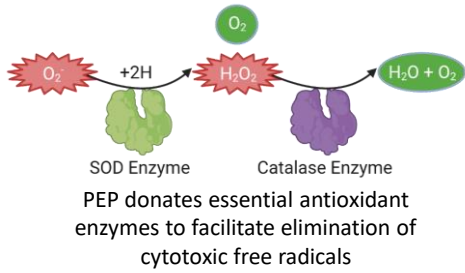


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EV Wound Trial



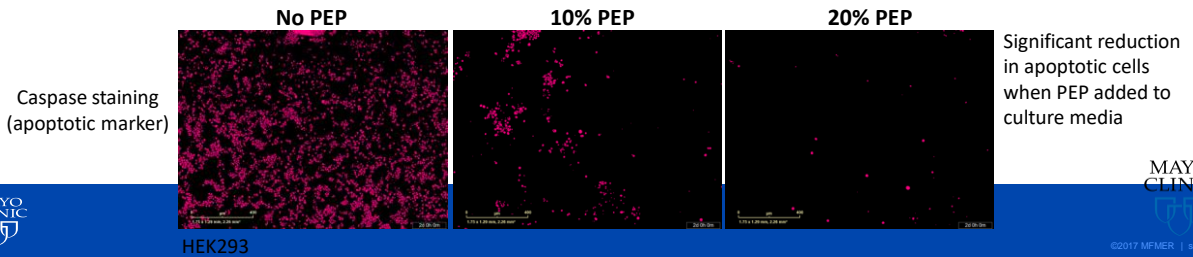
Anti-oxidant enzymes protect cells from oxidative stress



High-levels of anti-oxidant enzymes are present **within**

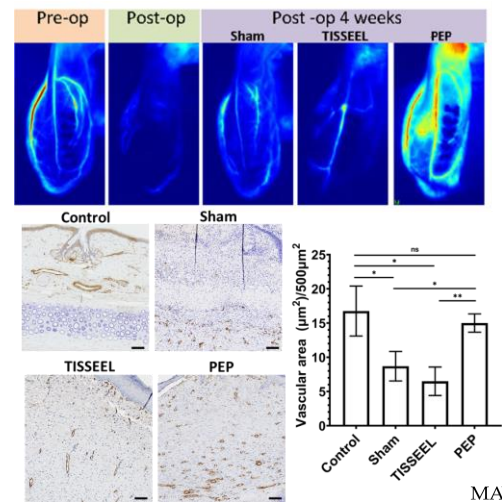
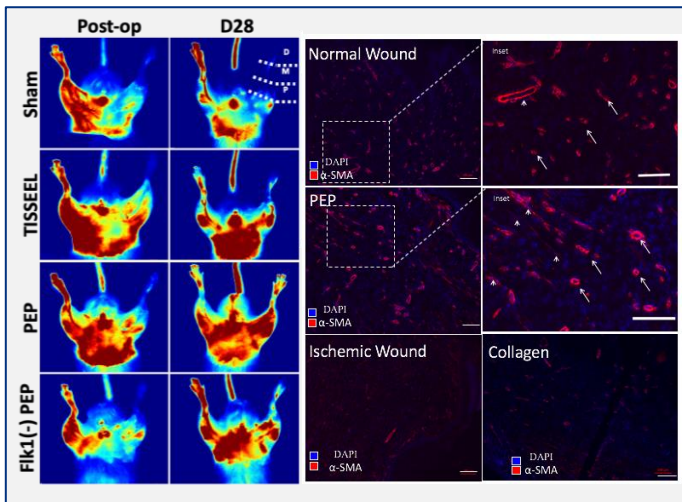
Cells exposed to Ly83583 (free radical generator)

PEP



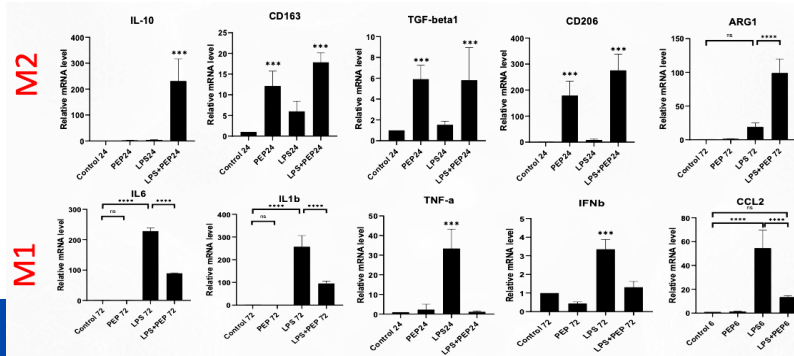
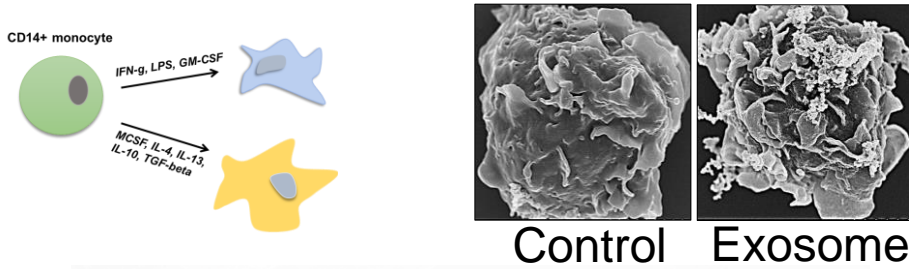
45

Restoration of Microvascular Content



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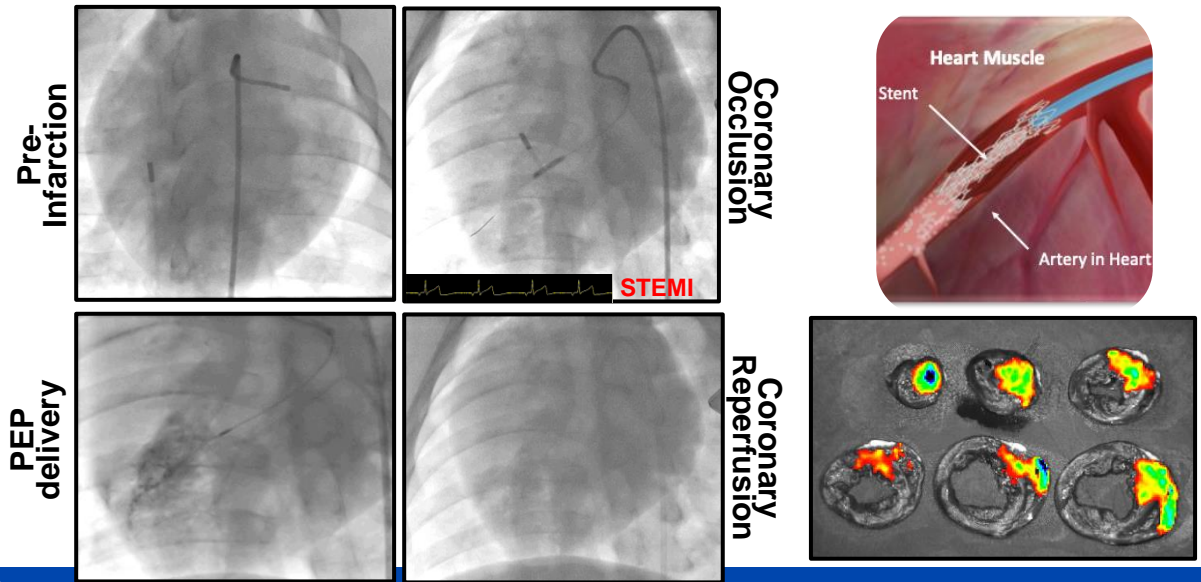
Modulation of inflammation through macrophage polarization



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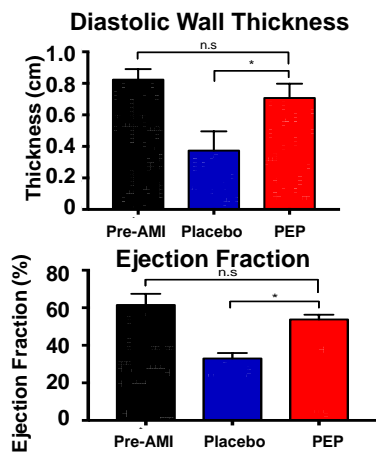
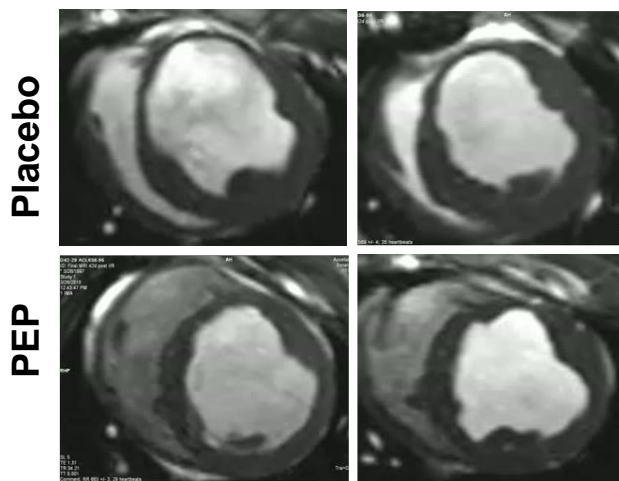
In vivo application of PEP in acute myocardial infarction



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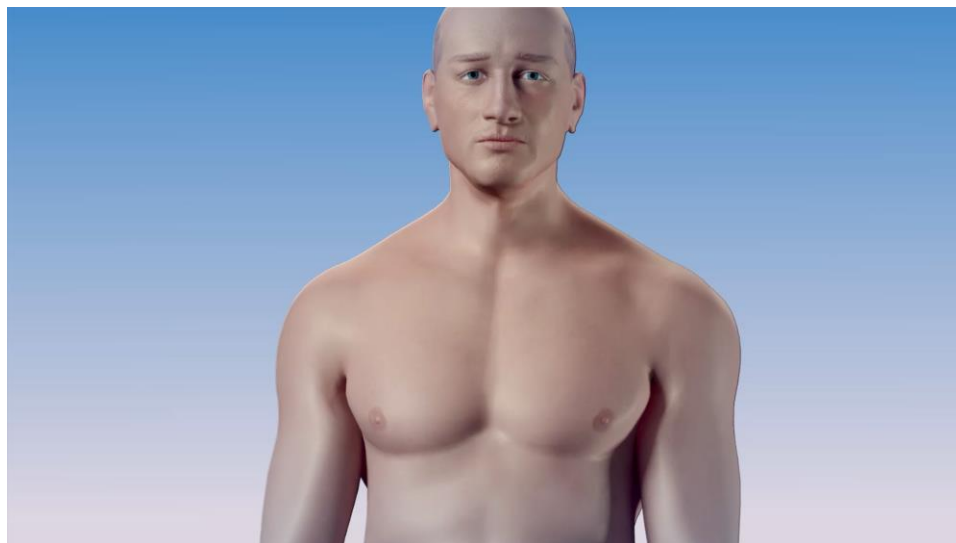
Cardiac Regeneration (EV AMI Trial)



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EV AMI TRIAL



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Van Cleve Cardiac Regenerative Medicine Program

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Timothy Moseley, PhD

Chief Technology Officer / Owner

Direct Biologics, LLC

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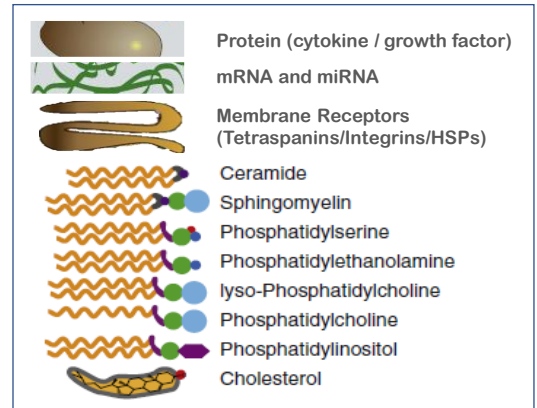
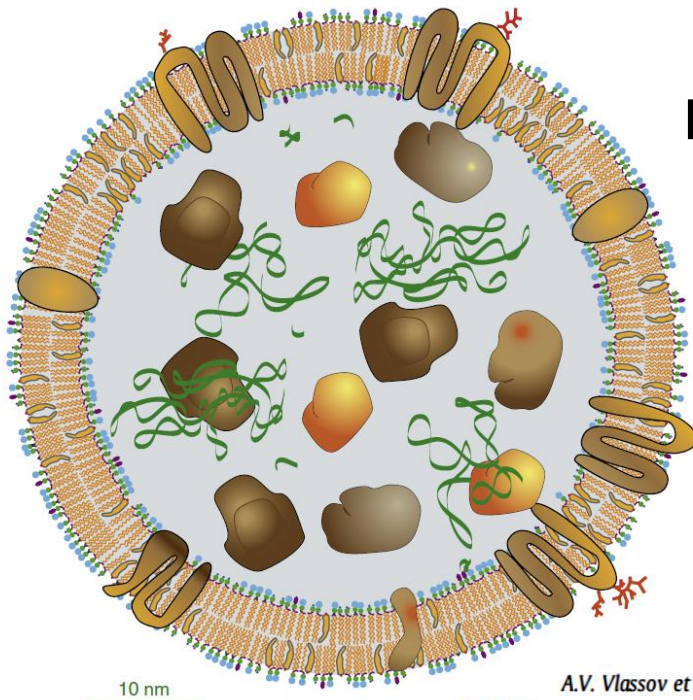
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Direct Biologics is a Late-stage biotechnology company focused on directing the next paradigm shift in medicine with its platform of therapeutics called extracellular vesicles

ExoFlo™

- ExoFlo is a natural extracellular vesicle product isolated from human bone marrow MSCs that contains growth factors and extracellular vesicles including exosomes.
- Extracellular vesicles are 30-150 nm in size and are involved in direct cell to cell communication.
- The extracellular vesicles are manufactured and purified using proprietary cGMP processing and are sterile per USP<71>.

Anatomy of an Extracellular Vesicle



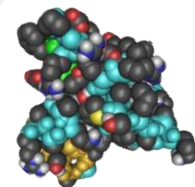
A.V. Vlassov et al. / *Biochimica et Biophysica Acta* 1820 (2012) 940–948

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Mesenchymal Stem Cell EV and Exosome Signals

- **Chemotaxis & Migration** (e.g., MCSF, PDGF, SDF-1 ...)
- **Angiogenesis** (e.g., Angiogenin, PIGF, VEGF...)
- **Extracellular Matrix Development & Repair** (e.g., ICAMs, TIMPs...)
- **Inflammation & Cell Survival Support** (e.g., TGFβs, MIF, Interleukins...)
- **Tissue & Wound Repair** (e.g., bFGF, Activin, HGF...)
- **Tumor Suppressor** (e.g., DAN, OPN, IGFBPs..)

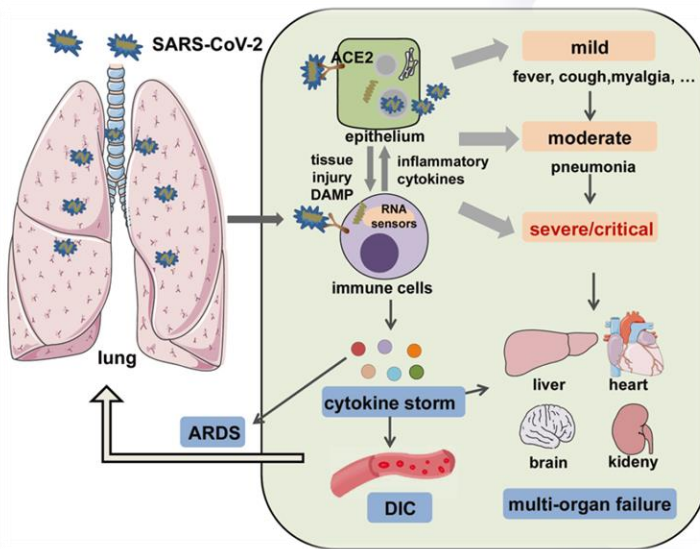


Direct Biologics EV Drug Pipeline

Therapeutic Area	Preclinical Studies	IND-enabling Clinical Studies	Phase I	Phase II	Phase III
COVID-19 ARDS (Moderate to Severe) <i>RMAT Designation</i>	Completed	Completed	Completed	Completed	In Progress
	Completed	Completed	Open-Label Expanded Access - Granted		
	Completed	Completed	eIND - Emergency Approval for Single Patients		
Post-Acute COVID	Completed	Completed	In Progress	TBD	TBD
Mild-Moderate COVID	Completed	Completed	In Progress	TBD	TBD
ARDS (<i>non-COVID-19</i>)	Completed	Completed	In Progress		TBD
UC / Crohn's	Completed	Completed	In Progress		TBD
Organ Transplant GvHD	Completed	Completed	In Progress		TBD
Osteoarthritis	Completed	Completed	TBD	TBD	TBD

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COVID-19 & Acute Respiratory Distress Syndrome



SARS-CoV-2 infects via binding to ACE2 receptors, causing tissue damage and release of inflammatory cytokines by epithelial cells and immune cells.

Then, the crosstalk between epithelial cells and immune cells leads to a wide range of clinical manifestations:

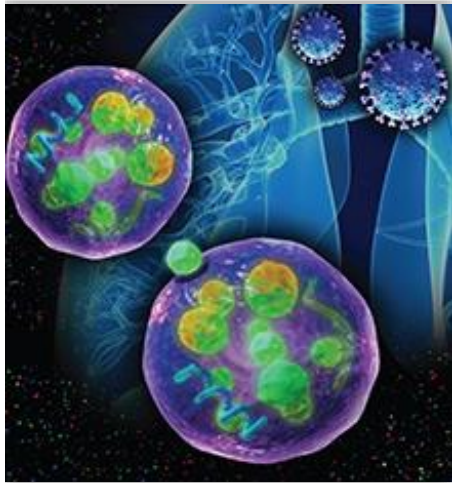
- **Mild forms** (e.g., fever, cough, and myalgia)
- **Moderate forms** requiring hospitalization (pneumonia and localized inflammation)
- **Severe/Critical forms** with often fatal outcomes that are manifested as pneumonia, ARDS, DIC, and multiorgan failure.

ARDS usually leads to formation of gel in the lungs and patients require mechanical ventilation that has an approximate 50% mortality rate.

Yang L, Xie X, Tu Z, et al. The signal pathways and treatment of cytokine storm in COVID-19, *Nature-Signal Transduction and Targeted Therapy* (2021) 6:255

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ExoFlo™ to Treat Severe ARDS from COVID-19



Investigator Initiated Trial (April 2020):

N=24 Severe ARDS patients with COVID-19 treated with 15mL ExoFlo under hospital IRB and physician oversight

Acute phase reactants (CRP, ferritin, & D-dimer)

Before Treatment vs. 5 days post ExoFlo

- **C-Reactive Protein (CRP) = 77% reduction** ($p < 0.001$)
- Ferritin = **43% reduction** ($p < 0.001$)
- D-Dimer = **42% reduction** ($p < 0.05$)
- Absolute Neutrophil Count (ANP) = **32% reduction** ($p < 0.001$)

Immune cell populations

- **Total Lymphocyte Count = 36% increase** ($P < 0.05$)
- **CD3+ T Lymphocytes = 46% increase** ($p < 0.05$)
- **CD4+ T Lymphocytes = 45% increase** ($p < 0.05$)
- **CD8+ T Lymphocytes = 46% increase** ($p < 0.001$)

Sengupta V, Sengupta S, Lazo A, Woods P, Nolan A, Bremer N. Exosomes Derived from Bone Marrow Mesenchymal Stem Cells as Treatment for Severe COVID-19. *Stem Cells & Dev.* 2020;29(12):747-754. doi:10.1089/scd.2020.0080

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ExoFlo™ to Treat Severe ARDS from COVID-19

Phase II (Dosing Study) - Completed

- Prospective, Double-Blind, Placebo Controlled, Randomized, Multi-Center Study
- 10mL or 15mL on Day 1 and Day 4 (Phase I was single 15mL Tx)
- Primary outcome 60-day mortality
- Completed successfully
- Submitted for publication (expect to be In-Press soon)

Expanded Access (Safety & Efficacy Study) - Completed

- Prospective, Open-label Trial, multi-center
- 50 patients per center

Phase III (Efficacy Study)

- Prospective, Double-Blind, Placebo Controlled, Randomized, Multi-Center Study
- Currently enrolling patients



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IIT/IRB Clinical Study – Osteoarthritis Pain

A Study to Evaluate the Safety of a Bone Marrow Derived Mesenchymal Stem Cell Extracellular Vesicle Isolate Product for the Treatment of Osteoarthritis in Combat Injured Joints



- Retired US Navy SEALs with joint pain (n=33)
 - Prospective, Open Label, Non-Randomized
 - Treat Grade 2-4 Kellgren-Lawrence OA Joints
 - 2mL EVs per painful joint (n=132 joints)
- Primary Outcome = Safety **Completed! Zero Adverse Events – Safety**
 - Secondary Outcome = Detailed joint specific pain questionnaires:
Pre-injection (baseline); 6 weeks; 3 mo; 6 mo; 12 mo

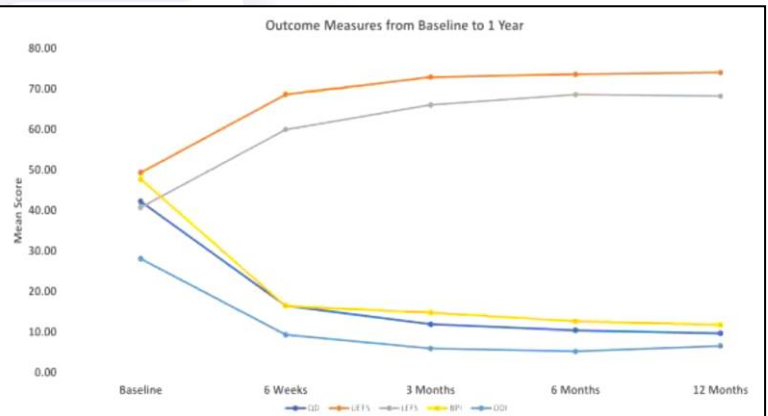
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IIT/IRB Clinical Study – Osteoarthritis Pain

Patient Progress vs. Time after ExoFlo injection into Joints (n=132)

Percent Improvement at 12-Months

- **Lower Extremity Functional (LEFS) = 67.45%**
(measure function - higher scores are better)
- **Upper Extremity Functional (UEFS) = 49.97%**
(measure function - higher scores are better)
- **Brief Pain Inventory (BPI) = 81.82%**
(Lower Scores are less pain)
- **Oswestry Disability Index (ODI) = 76.55%**
(measure of function - lower scores are better)
- **QuickDASH (QD) = 77.11%**
(measure of function - lower scores are better)



p < 0.001 for all timepoints versus pre-treatment baseline.

East, J., and Dordevic, M., *Journal of Stem Cell Research* 2021;2(2)-21.

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Thank you



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Blood brain Barrier: Exosome Capabilities and Opportunities

Dr. Steve Stice
Chief Scientific Officer
Professor, University of Georgia

March 9th, 2023

Proprietary In-house Manufacturing and Production

THE Challenges

- >> • Limited knowledge exists in manufacturing exosomes for therapeutic use in humans
- Cells are cultured and release exosomes into culture media
 - Exosomes are fragile: isolating, purifying and concentrating from media is difficult process

THE Opportunity

- >> • Aruna has strong expertise in purifying and concentrating exosomes
 - Highly valuable know-how and trade secrets
- In-house cGMP facility; currently scaling-up for production of clinical material
- Ability to manufacture clinical grade batches, ultimately scale to Phase 3 and potentially commercial batches



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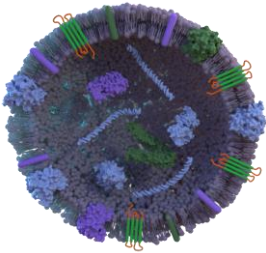
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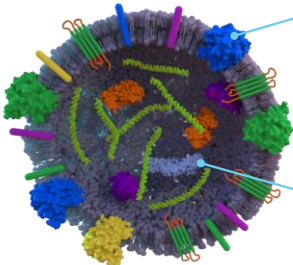
AB126: Specialized Exosome from Proprietary Neural Stem Cell Line

AB126 is an unmodified exosome derived from neural stem cells with ability to cross the BBB and contain therapeutic activity in its native form

Non neural exosomes do not have inherent CNS specificity



AB126 has natural affinity for CNS



Crossing the Blood Brain Barrier

- Markers on the surface of AB126 result in unique properties specific to neural cells

Therapeutic Capabilities

- Cargo contained in AB126 has footprint unique to neural stem cells
- Provides therapeutic benefit for neurodegenerative diseases and reducing neural inflammation

Exosome fingerprint is unique to Aruna's proprietary neural stem cells

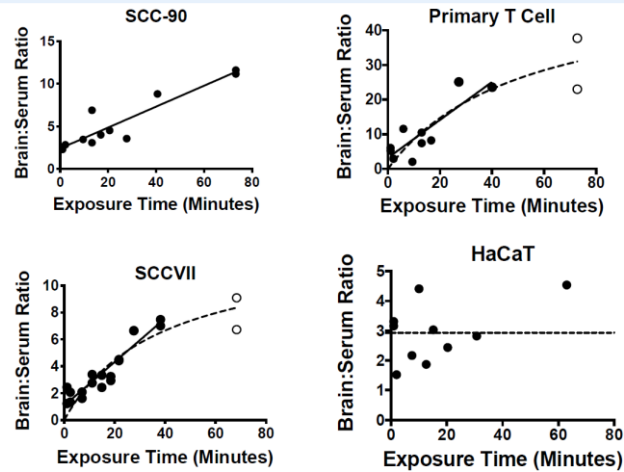
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Exosomes Regardless of Species and Type Cross BBB

- Used 10 different lines, all but one crossed
- Levels of crossing differed by 10 fold
- Rapid lineal, plateau or in one case no uptake



Banks et al., 2020

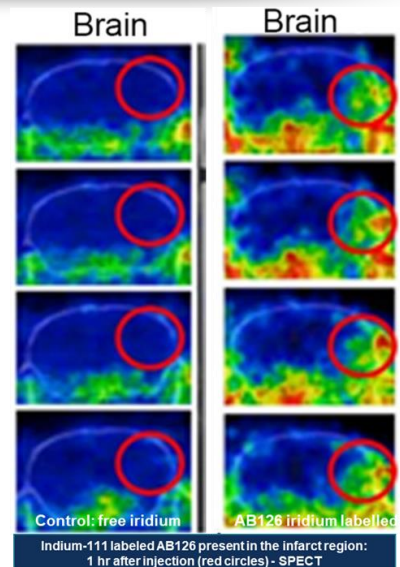
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Confirming AB126 Distribution in the Disrupted and Inflamed Brain

- Accomplished by labelling AB126 with indium-111 vs free I-111
- Mice were injected 1 hr. post stroke and imaged 1 hr. after injection by single photon emission computed tomography (SPECT)
- AB126 was present in the infarcted hemisphere and preferentially accumulates in the penumbra of the injury



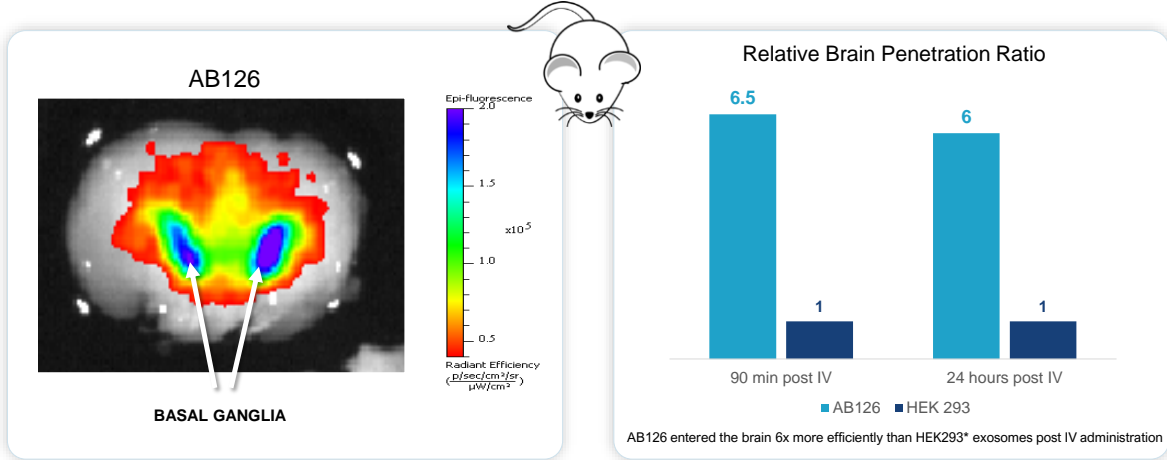
ARUNABIO * Translational Stroke Research (2018) 9:530-539

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Preclinical Data – AB126 Has High BBB Permeability

AB126 Demonstrates Greater Brain Uptake, Distribution and Durability vs. Non-Neural Exosomes



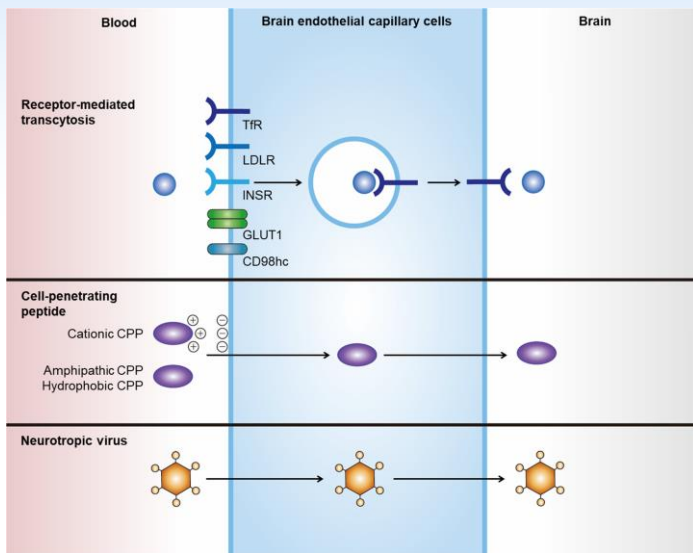
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*HEK293 is a widely available commercial cell line

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Strategies for Enhancing Exosome Brain Delivery



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- RVG-exosome; Lamp2ba ligand-decorating combined with rabies virus glycoprotein (RVG), a small peptide that specifically binds to an acetylcholine receptor expressed by neuronal cells.
- TfR1 presence in some not all EVs, can they be further enhanced
- Kim et al. used a T7 peptide, a TfR-binding peptide, for the delivery of exosomes (J. Control. Release 2020, 317, 273–281)

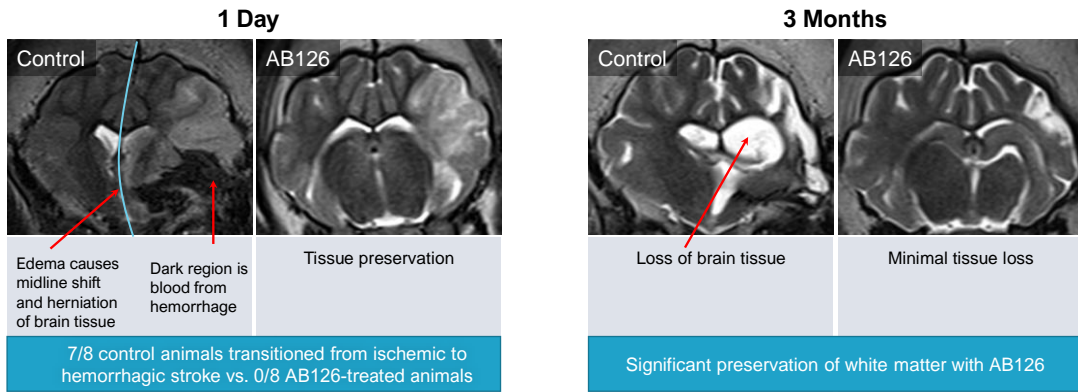
Choi et al., (review)
2023 Pharmaceutics

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AB126 Facilitates Tissue Repair Post Ischemic Stroke

Proprietary Porcine Stroke Model (West Lab)

- Ischemic stroke results in massive neuronal cell death, leading to severe neurological damage
- AB126 preserved cells, evident after only 24 hours, and continues to prevent tissue damage 3 months post-dosing



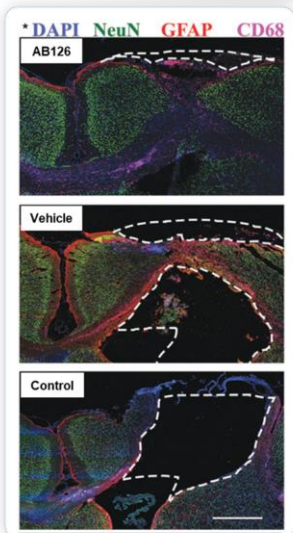
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Source: Webb, et al. Human Neural Stem Cell Extracellular Vesicles Improve Recovery in a Porcine Model of Ischemic Stroke. Stroke, 2018.

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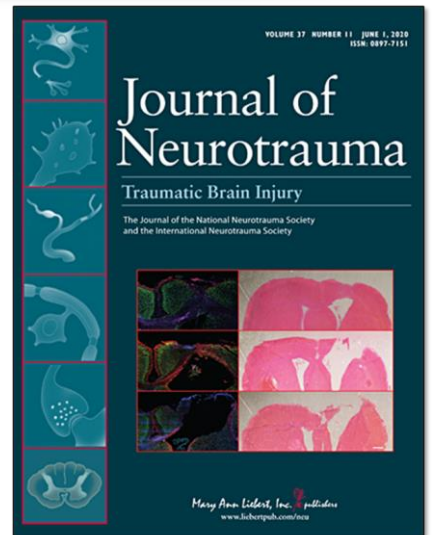
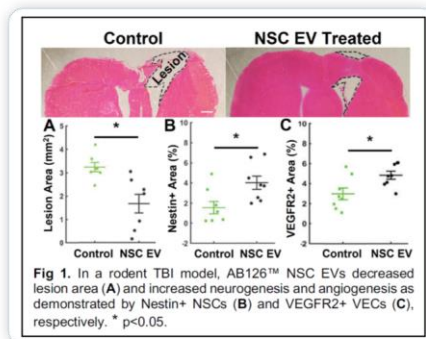
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AB126 Decreases Lesion Size: neurogenic and vasculogenic



2. AB126 demonstrated decreased lesion size vs control: 1.675 vs 3.237mm² (p=0.011)

- AB126 exhibited maintenance of the cortical structure whereas vehicle and control mostly exhibited tissue cavitation



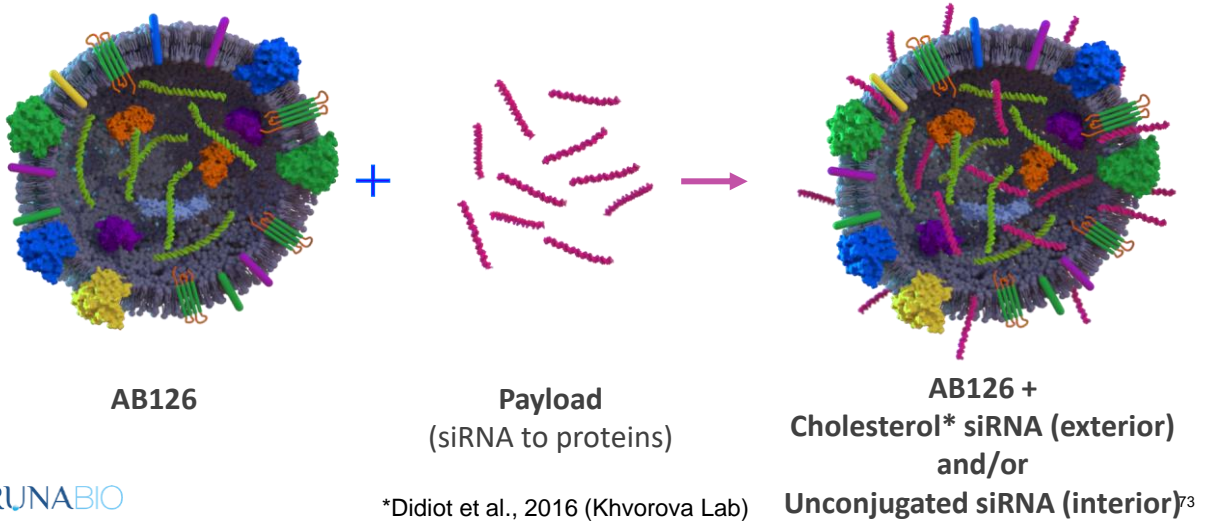
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* neurons (NeuN; green), reactive astrocytes (glial fibrillary acidic protein; red), macrophages and microglia (CD68; magenta) and 4',6-diamidino-2-phenylindole counterstain (blue)

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AB126 Can Carry Large Quantities of Payloads

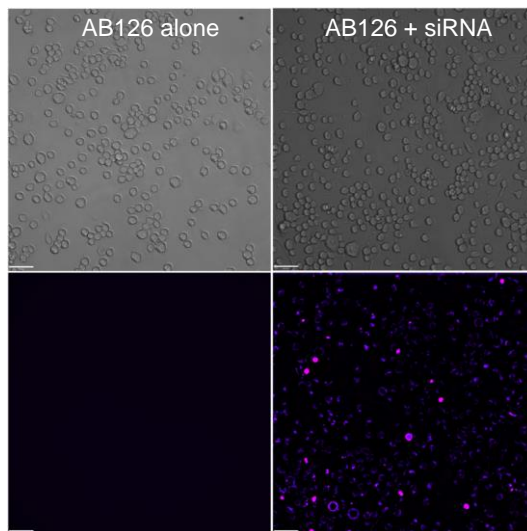


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AB126 Transports Fluorescent Tagged siRNA Payload into Neural Cell Line (N2a)

N2a are a neural cell line



Visible and measurable high levels of fluorescent (pink/purple) tagged siRNA cargo in AB126 (lower right)

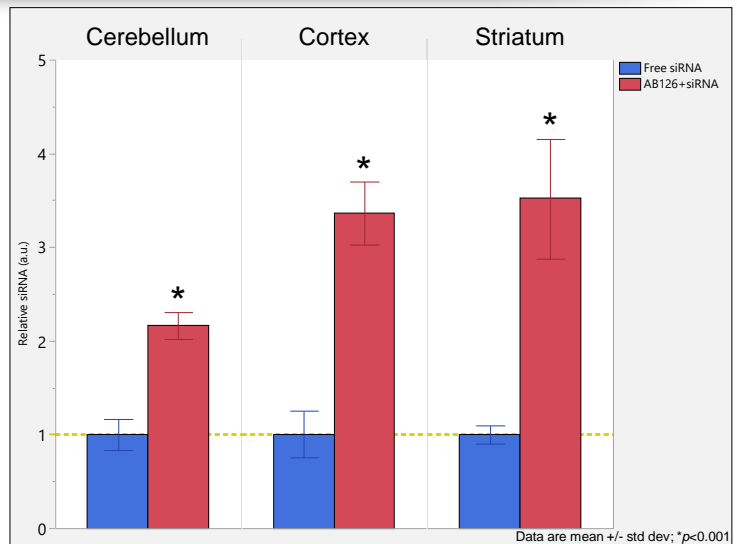
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AB126 Facilitates Delivery of siRNA to the Rodent Brain

- Healthy mice were dosed systemically with matching amounts of cholesterol siRNA or AB126 + cholesterol siRNA
- 72 hours post-administration, perfused brain dissected and assayed for siRNA via qPCR
- **AB126 delivers 2.1x (cerebellum), 3.4x (cortex) and 3.5x (striatum) more siRNA to the mouse brain compared to siRNA alone**



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Conclusion Limitations

- No two exosomes are alike in their ability to cross the BBB, much of the mechanism is still unknown
- Neural exosomes (AB126) have unique and important qualities for neural applications for regeneration and protection
- Exosomes can be loaded with various cargos and delivered to the CNS
- Further understanding of the mechanisms underlying the BBB crossing will enhance EV utility
- Clinically approved exosome delivery in brain will benefit from better quantitative and qualitative methods for monitoring delivery and **function** in vivo

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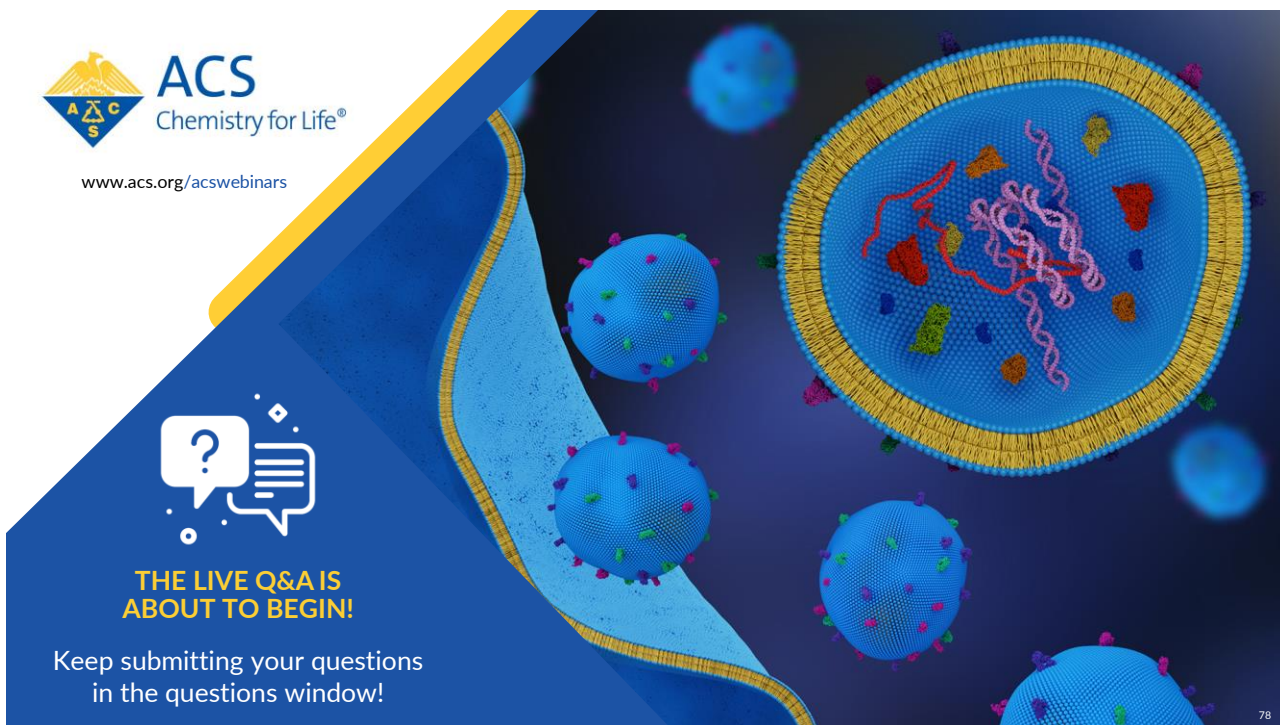
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LEADER IN THE DEVELOPMENT OF NEURAL EXOSOMES FOR THE TREATMENT OF NEURODEGENERATIVE DISEASES

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Co-produced with the ACS Younger Chemists Committee and the ACS Committee on Ethics



Thurs., March 16, 2023 | 2:00-3:00pm ET

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