

# Move over Stem Cells - Exosomes are Here!

## What are Exosomes & their Role in Regenerative Medicine?

**Author/Presenter: Amartej Singh Deol MD4 & Advisor: Shivinder S. Deol MD**

### WHAT ARE EXOSOMES (EX) & EXTRACELLULAR VESICLES (EV)?

#### INTRODUCTION

All human cells release chemicals or tiny nano-particles or Extracellular Vesicles (EV) in all bodily fluids. These secretions were initially thought to be waste products or cell debris. It has now been established that these excreted bioactive chemicals are crucial for cell-to-cell communications & numerous other cell functions.

#### TYPES OF EXTRACELLULAR VESICLES (EV):

- Apoptotic bodies or blebs (ABs). Large cell fragments from cells undergoing apoptosis
- Intramural Vesicles (ILVs). Early endosomes (tiny vesicles) invaginate within cells
- Multivesicular Body (MVB). Derived when endosomes invaginate to ILVs
- Microvesicles or Ectosomes. Large particles measuring 50-300 µm
- Exosomes (EX). Biological vesicles originate as ILVs in MVBs & released outside cells when MVBs fuse with plasma membrane

#### AVERAGE SIZES:

- Distal Capillaries (DC): 5-10 microns (µm: one millionth of a meter)
- Mesenchymal Stem Cells (MSC): 8-12 µm. Can get caught in DC.
- Exosomes: 30-150 nanometer (nm: one billionth of a meter)

#### WHAT FLUIDS ARE EXOSOMES FOUND IN? ALL FLUIDS:

- Blood, Milk, Mucus, Saliva, Semen, Sweat, Tears, Vaginal Fluids

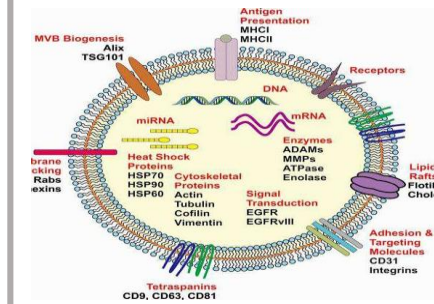
#### WHAT BIOACTIVE CHEMICALS ARE CARRIED BY EXOSOMES?

- Lipids, Proteins & Enzymes
- MicroRNA (miRNA) & Messenger RNA (mRNA)

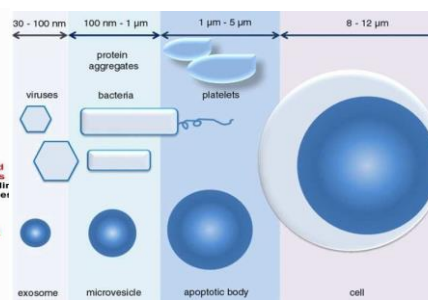
#### MAJOR ACTIONS OF EXOSOMES:

- Physiological: Based on different chemicals, factors, miRNA, mRNA secreted & carried to target cells for normal functions.
- Pathological: Older damaged or cancer cells secrete chemicals which cause cell death, and expansion or progression of diseases esp. neurodegenerative diseases.

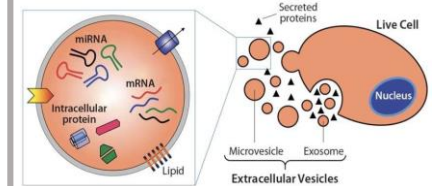
### INSIDE AN EXOSOME



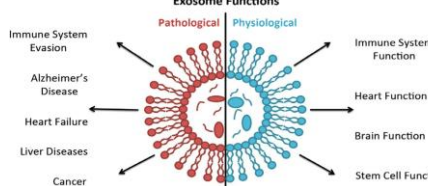
### AVERAGE SIZES



### MSC RELEASE EV & EX



### PHYSIOLOGICAL & PATHOLOGICAL ACTIONS



### EXOSOMES MAY HELP IN:

Exosomes can be given IV, Intranasal, Intra-articular, Intrathecal or Locally	Several conditions may require repeat Exosome injections for optimal results
Neurodegenerative conditions: MS, ALS, Alzheimer's Parkinson's, Huntington, Ataxia	Musculoskeletal: Joints, Discs, Muscles, Bones, Ligaments, Tendons, Injuries, Surgery
CNS Injury: CVA, Stroke, Brain & Spinal Cord Injury, Traumatic Encephalopathy, Myelitis	Heart: CAD, Myocardial Infarction, Angina, Congestive Heart Failure, Cardiomyopathy
Lungs: COPD, Pulmonary Fibrosis, Interstitial	Liver & Kidney Diseases, Autoimmune Diseases
Inflammatory Bowel: Crohn's, Ulcerative Colitis	Erectile Dysfunction, Urinary Incontinence
Diabetes Mellitus & Complications, Retinopathy	Peripheral Vascular Disease, Infertility, Alopecia
Neuropathy: Inflammatory, Demyelinating, DM	Cerebral Palsy, Seizures, Autism, Bipolar Illness
Burns, Scars, Wounds, Injuries, Wrinkles	Reverse Aging, Wellness, Preventive Health

### WHAT ARE STEM CELLS (SC)?

#### INTRODUCTION

Stem Cells (SC) are responsible for ongoing repair, replacement & regeneration of all parts of the body and are unique in their ability to:

1. Renew themselves &
2. Differentiate into multiple different cell types.

**Mesenchymal Stem Cells (MSC)** are derived from mesoderm, are multipotent & found in all tissues. MSC have been studied extensively for many conditions. Even though the clinical efficacy of MSC has not been yet proven, these are used frequently off-label to treat many cell-based Regenerative conditions esp. Cardiac, Orthopedic & Neurological Conditions.

#### CLASSIFICATION & TYPES OF STEM CELLS:

- Embryonic (risk of Teratomas) or Non-Embryonic (Placental, Cord, Amniotic, or Adult {all SC after Fetal 3 Germ Layer Division})
- Autologous (self or own) or Allogeneic (donor)
- Potency: Totipotent (Embryo & Placenta), Pluripotent (can develop all tissues except placenta), Multipotent (develop many tissues depending on origin: Ectoderm, Endoderm or Mesoderm origin)
- Differentiation: Hematopoietic (HSC), Neural (NSC), Mesenchymal (MSC), Induced Pluripotent (iPS: skin cells programmed like embryonic cells)

#### STEM CELLS ARE FOUND IN:

- All Tissues: Blood, Adipose, Skin, Dental, Neural, Organs, Joints, etc.
- Fetal: Embryo, Placenta, Amniotic Fluid, Umbilical Cord

### MSC EXOSOMES CHARACTERISTICS

- Pure Exosomes with no Preservatives, Additives
- Do not contain DNA, Mitochondria or Golgi Apparatus
- More than 200 Signaling Proteins & Growth Factors identified in high doses like: BMP5, GDF15, OPG, G-CSF, SCF, TGFβ3, VEGF, ICAM-1, IL-1RA, IL-6,
- IL-10, MCP-1, MIP-1, PDGF-BB, TIMP1, TIMP2, HGF, GDNF, BDNF, FGF, TNFR1, Anti-Inflammatory Cytokines, Angiogenic Growth Factors
- Anti-Tumor, Regenerative & Healing Signals
- Direct Cell-to-Cell Communications
- Messenger RNA (mRNA) - ON Switch for Healing & Repair Processes
- Micro RNA (miRNA) - OFF Switch for reducing Inflammation