

**Innovations in Medical Technology:**

**Therapeutic Potential of Human Umbilical  
Vascular Endothelial Cells (HUVECs) in the  
Treatment of Rheumatoid Arthritis**



**INVITrx**

# Rethink and Evolve...

- INVITRX product platform was developed in order to address a variety of pathologies with its cellular and acellular technologies.
- All platform technologies are classified under CFR361-17, minimally manipulated tissue guidelines per FDA.
- Stem cell fluid is a placental-derived cellular product. The premise of this technology is to identify specific cell morphologies in order to address therapeutic uses of stem cells and to quantify cell viability pre and post thaw.
- Bone products are specifically designed to accept cellular attachment attributes while simultaneously increasing the proteomic composition of cytokines and growth factors that are critical in building bone

We are a scientifically driven company and we view the discovery of allograft attributes differently than our industry competitors.

# Cell Therapy Types: Allogeneic Vs Autologous

## Allogeneic

- ▶ Cells come from a related or unrelated donor
- ▶ Blood taken from the placenta and umbilical cord of newborns is a newer source of stem cells for allogeneic transplant
- ▶ Introduction of new cells into your system may improve autoimmune disorders by providing an anti-inflammatory response
- ▶ Allogeneic cell types:
  - ▶ HUVEC
  - ▶ Embryonic Stem Cell
  - ▶ Mesenchymal fat
  - ▶ Amniotic fluid

## Autologous

- ▶ Cells come from your own body
- ▶ Offers smaller chance of immune reaction such as graft versus host (GVH) than with allogeneic transplant
- ▶ Can only collect adult stem cells
  - ▶ Autologous cell types:
    - ▶ Hematopoietic stem cell
    - ▶ Natural killer cells
    - ▶ PRP
    - ▶ Bone marrow
    - ▶ Adipose Fat
    - ▶ Cardiomyocytes
    - ▶ Split skin graft
    - ▶ Cornea

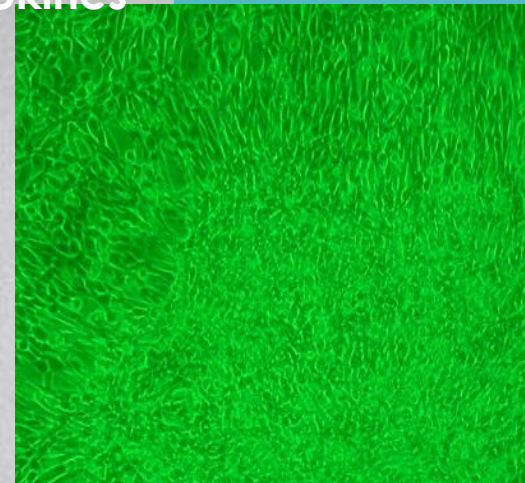


# Stem Cells in Cell Therapy

- Stem cells can be harvested from blood, fat tissue, and skin
- Various types of stem cells
  - Mesenchymal Stem Cells
  - Fibroblast Stem Cells
  - Adipose-Derived Stem Cells
  - Amniotic Stem Cells
- Stem cell transplants can be allogenic or autologous

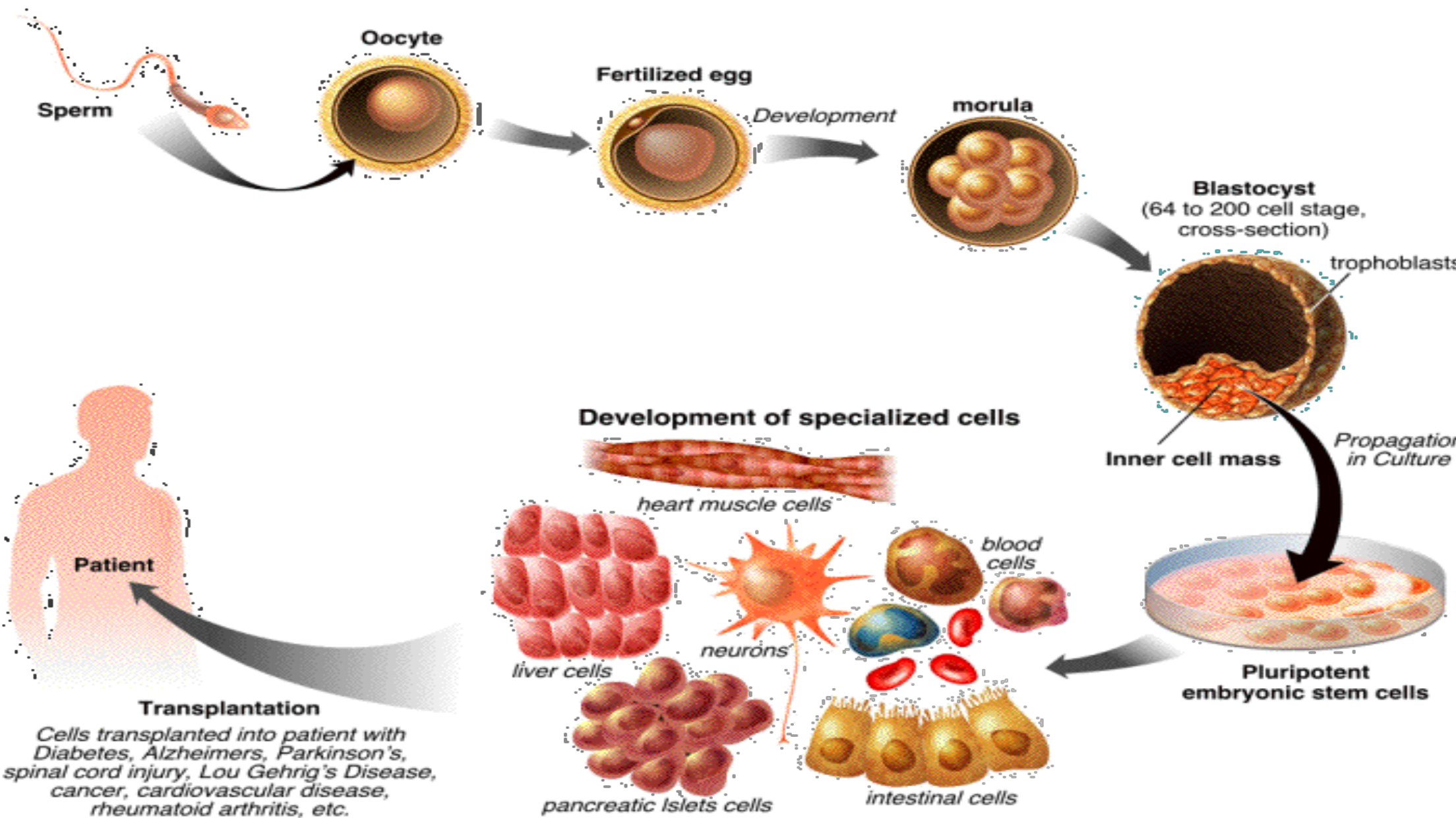
## Stem Cell Characteristics

- Self renewal
- Ability to decaffeinate
- homing ability
- Anti-inflammatory response
- Pluripotent
- Release growth factors and cytokines



(iPS) induced Pluripotent stem cell colony in culture

# Stem Cell Therapy



# Clinical Injections

- Amniotic fluid contains multiple excellent properties for pain relief and for promoting tissue regeneration and repair.
- Like steroid injections, the fluid has important anti-inflammatory properties including progesterone cytokines that naturally relieve the fluid also contains many types of growth factors which interact with native stem cells to help promote new tissue growth.
- Amniotic fluid works to relieve pain and heal the damaged pain
- Stem Cell counts as we age: When we are born 1 in 10,000 cells are MSC's, at age 50 there is 1 in 400,000 are MSC's and by age 80 they have decrease to only 1 in 2 million.



# Why is cellular viability important?

In order to quantify a statistical benefit derived from a cellular based allograft, it is critical to understand the cellular component as it relates to total cell count, post thaw cell count and the chemical component of related cytokines, proteins and growth factors.

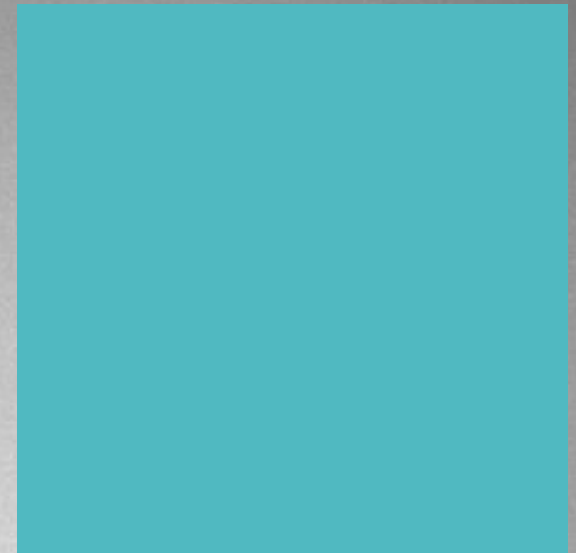
Studies conducted by physicians have shown that there is a direct correlation between the number of cells used in various therapies and the corresponding therapeutic benefit.

What Sets invitrx Apart?

INVITRX is the only company to evaluate the cellular component on every lot and donor and we have this documentation on file in the event we need to provide it to our physicians.

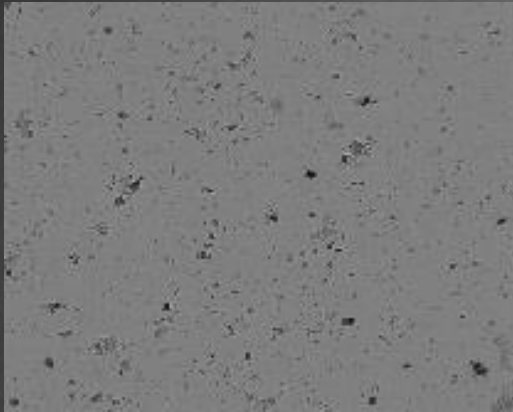
We are the only company to document histological data related to the morphology of cells in our tissue.

We are the only company to document the proteomic, growth factor and cytokine content of our tissue.



# The Difference

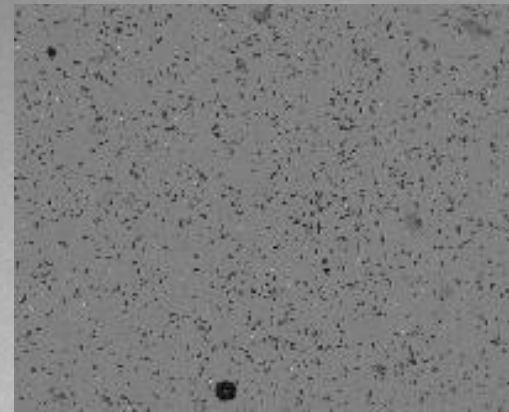
## OTHERS



Sample Count: Competitor Factor  
Sample Dilution Factor: 1:1  
Total cell count:  $5.14 \times 10^6$  cells/ml  
Live cell count:  $2.27 \times 10^6$  cells/ml **2.27M**  
Live cells: 44%

Comments:  
Non-Diluted, Heavy Debris

## INVITRX



Sample Count: INVITrx Fluid  
Sample Dilution Factor: 1:10  
Total cell count:  $8.39 \times 10^7$  cells/ml  
Live cell count:  $6.41 \times 10^7$  cells/ml  
**64.1M**  
Live cells: 76%

Comments:  
Dilution Required, Heavy Cellularity



# Conditions Used

## Hand

- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries
- neuroma/other nerve pain
- tendinitis

## Wrist

- tendinitis
- carpal tunnel syndrome
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries

## Elbow

- tennis elbow (lateral epicondylitis)
- golfer's elbow (medial epicondylitis)
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease  
(ex: injured joint from gout, old fracture)
- old fractures/breaks/injuries

## Shoulder

- bursitis
- bicipital tendinitis
- acromioclavicular joint injury
- rotator cuff injury
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries

## Muscular Pain

- chronic myofascial pain syndromes
- pinched nerves
- whiplash (cervical myofascial syndrome)
- old muscular/soft tissue injuries wound, burn

## Foot/Toes

- tendinitis
- heel spur (plantar fasciitis)
- neuroma/other nerve pain
- pain/inflammation of ball of foot (metatarsalgia)
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries

# Conditions Used Cont.

## Knee

- patellar tendinitis
- knee pain from unresolved ligament injury
- bursitis
- shin splints (Osgood-Schlatter disease)
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries

## Hip

- tendinitis
- knee pain from unresolved ligament injury
- trochanteric bursitis
- osteoarthritis
- rheumatoid arthritis
- joint pain from other systemic disease
- old fractures/breaks/injuries


## Misc. Systemic Conditions

- Rheumatoid Arthritis
- Reactive Arthritis
- COPD
- Osteoarthritis

# Cell Therapies for Bone Injuries and Diseases

- ▶ Cell therapy involves the transplantation of cells from your own body or a donor
- ▶ Cells can be transplanted into joints to treat and relieve symptoms from orthopedic conditions
- ▶ Studies have shown that interactions between healthy transplanted cells and damaged cells in the affected area can provide rejuvenating effects for the patient
- ▶ Cell type plays a key role in the effectiveness of the treatment process

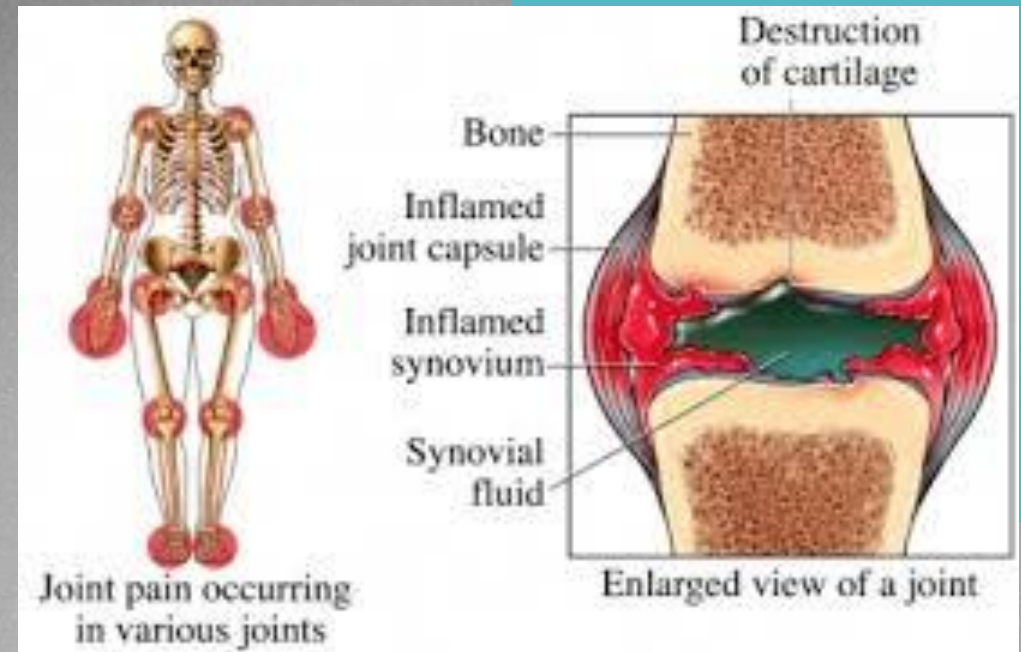




# Case study: Rheumatoid Arthritis and HUVEC Therapy

# Rheumatoid Arthritis

- ▶ Rheumatoid Arthritis is a chronic inflammatory disorder that can affect multiple joints within the body.
- ▶ It causes swelling in the lining of the joints causing tissue damage and possible deformations of the bone.



# Human Umbilical Vascular Endothelial Cells for Cell Therapy

Human Umbilical Vascular Endothelial Cells (HUVECs) transplants are considered Allogenic.

The HUVECs are derived from umbilical cord blood and provides cell growth

- Organic compounds & structural properties in addition to being a rich source
- Growth factors that facilitate nutrients
- Hyaluronic acids
- Amino acids

The main function of stem cells is to provide patients with surgery alternatives. The

presence of these cells may provide ancillary clinical benefits by enhancing the body's natural regenerative process.



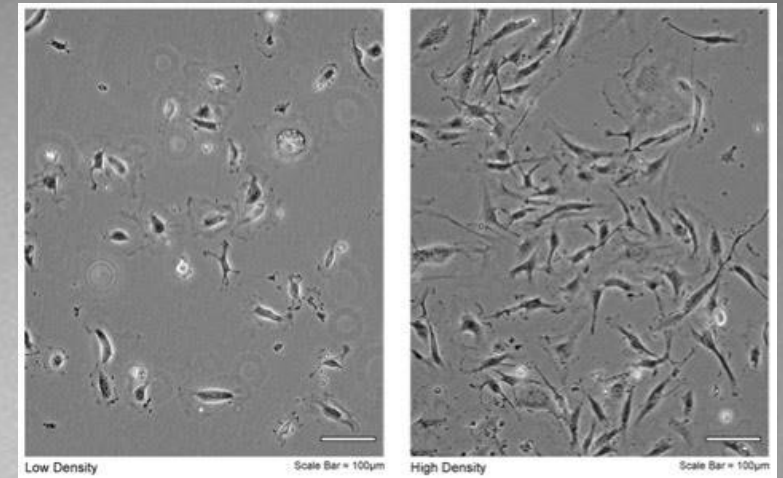
# HUVEC Therapy Approach

Patient Suffered from Rheumatoid Arthritis and Sclerosis.

HUVECs were extracted from cord blood and injected into the problem area of a patient

The patient received a dose of HUVECs at specific intervals over a 2 year time period

The patient showed improvement in physical health and reduction in symptoms that he suffered from for 4 years



**HUVECs under light microscope**

# Before and After HUVEC Therapy



- Pt presented with severe (R.A.) Rheumatoid Arthritis that was non responsive to traditional therapies.
- Pt. began having severe plaque cerreuses ulcerations. As a result traditional therapies where suspended.
- Pt then received a series of infusions with stem cells fluid and 250-500cc's lactated saline.
- Timeline to follow-up was 8 months.



# Before and After HUVEC Therapy



- Eight (8) month follow-up revealed that all ulcerations were healed, symptoms resided.
- Arthritic conditions and range of motion improved.
- PT is no longer on R.A. Medication.





# Advantages of Cell Therapy

- Some cell therapies are not as harsh on the patient as some drug treatments
- Potentially expedite the amount of recovery time patients need
- Possible to maintain higher quality of life and physical health

# Treatment Complications with Drugs

Rheumatoid Arthritis is conventionally treated with steroids and other injectable drugs

Treatment with HUMIRA can worsen symptoms such as osteoporosis and stress in patient

Ineffective treatments cataloged in the case study demonstrate why alternative solutions such as stem cell therapies are becoming important in patient recovery.