What is Rheumatoid Arthritis?

Joint Inflammation and Pain

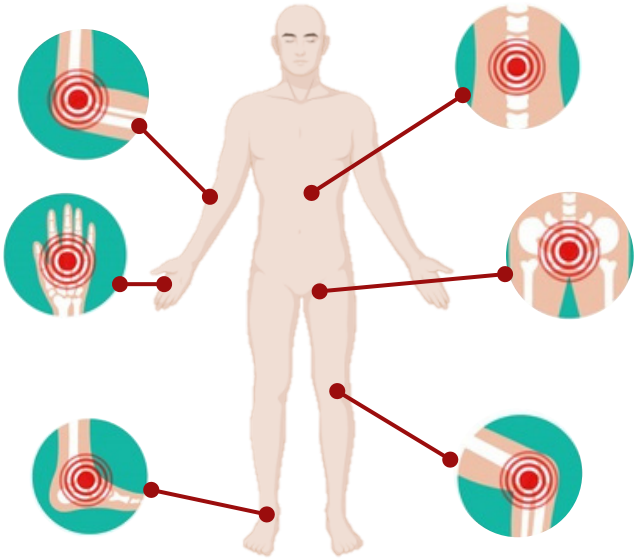
CYTO+

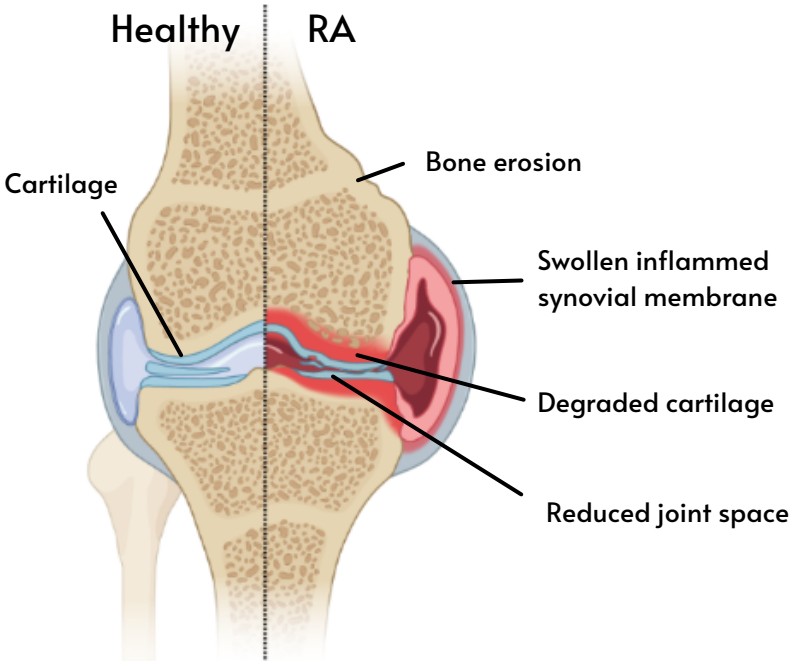
Joints

JOINT: The place where 2 or more bones meet

The movable joint is surrounded by the SYNOVIAL MEMBRANE. The membrane has cells to produce fluid that lubricate & nourish joint tissues such as cartilage.

CARTILAGE: a tough slippery covering on the ends of the bones which allows smooth joint movement.





Rheumatoid Arthritis (RA)

RA is an autoimmune disease.

The IMMUNE SYSTEM mistakes the body's cells for foreign invaders and releases inflammatory chemicals that attack the synovial membrane.

RA mainly attacks the joints, e.g. joints in the hands, wrists, and knees. In a joint with RA, the lining of the joint (synovial membrane) becomes inflamed, causing damage to joint tissue.

Risk Factors

The factors that increase the risks of getting RA:

GENETIC FACTORS

People born with specific genes, HLA-DR1 & HLA-DR4, might develop RA after exposed to something in the environment

ENVIRONMENTAL FACTORS

Smoking

Pathogens
(e.g. Gut bacteria)

These environmental factors can cause modification of our own antigens, increase the chance of develop autoimmune diseases.

Symptoms

- RA can affect multiple joints (>5)
- Symmetrically inflammation

IN THE EARLY STAGE:

- Small joints (wrists, certain joints in the hands and feet) are affected.

AS DISEASE WORSENS:

- Large joints (e.g. shoulders, elbows, knees, ankles) are inflammed.

RA in hands

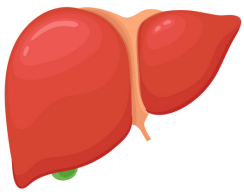
Hand deformity resulted from RA

People with RA experiences FLARES (sudden worsening):

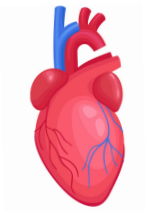
- Joint pain
- Tenderness
- Swelling
- Morning stiffness

Multiple Organs: Systemic Inflammation

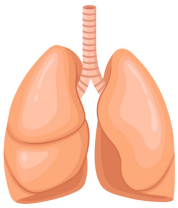
Inflammatory cytokines that cause inflammation & damage of joint tissues may flow through blood vessels into multiple organ systems and affect the organs.



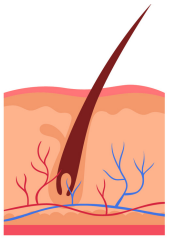
Liver



Heart



Lungs



Skin

Treatment

The goals of RA treatment are to stop or reduce inflammation, and prevent joint and organ damages.

DMARD: a medicine that interferes with signs and symptoms of RA, improves physical function, and inhibits progression of joint damage.

- Synthetic DMARD (small chemical molecules; given orally)
- Biologic DMARD (proteins; administered non-orally)

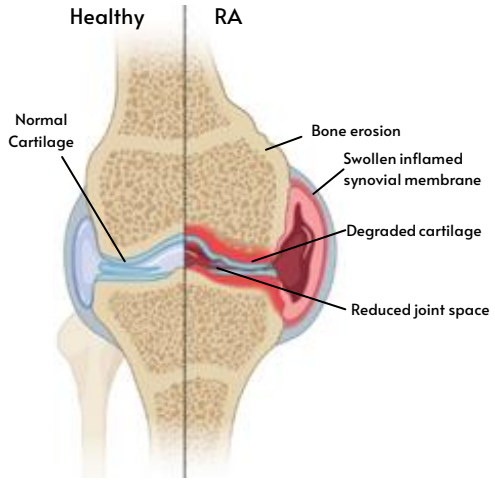
REFERENCE

1.Centers for Disease Control and Prevention (2020). Rheumatoid arthritis (RA). Retrieved from https://www.cdc.gov/arthritis/basics/rheumatoid-arthritis.html, at 26th August 2021. 2. Cojocaru, M., Cojocaru, I. M., Silosi, I., Vrabie, C. D., & Tanasescu, R. (2010). Extra-articular manifestations in rheumatoid arthritis. Maedica, 5(4), 286. 3. McInnes, I. B., & Schett, G. (2011). The pathogenesis of rheumatoid arthritis. New England Journal of Medicine, 365(23), 2205-2219. 4. Aletaha, D., & Smolen, J. S. (2018). Diagnosis and management of rheumatoid arthritis: a review. Jama, 320(13), 1360-1372.

BROUGHT TO YOU BY

*This poster is for educational purposes only.

Potential Therapeutic Effects of Mesenchymal Stem Cells On Rheumatoid Arthritis



Rheumatoid arthritis (RA)

RA is an **AUTOIMMUNE** disease, in which the immune system mistakes the cells at synovial membrane (a layer of tissues surrounded joints) as foreign invaders and attack them.

A series of **inflammatory responses** happened leads to degraded cartilage & bone erosion & swollen synovial membrane. Severe RA can cause extra-articular problem (symptoms that found at tissues other than joint).

Mesenchymal stem cells (MSCs)

MSCs are stem cells that can replicate and differentiate into a variety of specialized cells such as bone cells, liver cells, skin cells, nerves, etc..

Can help in →

- Anti-inflammation
- Immunomodulation
- Homing & Regeneration

Safety & Efficacy of MSC treatment for RA

SAFETY

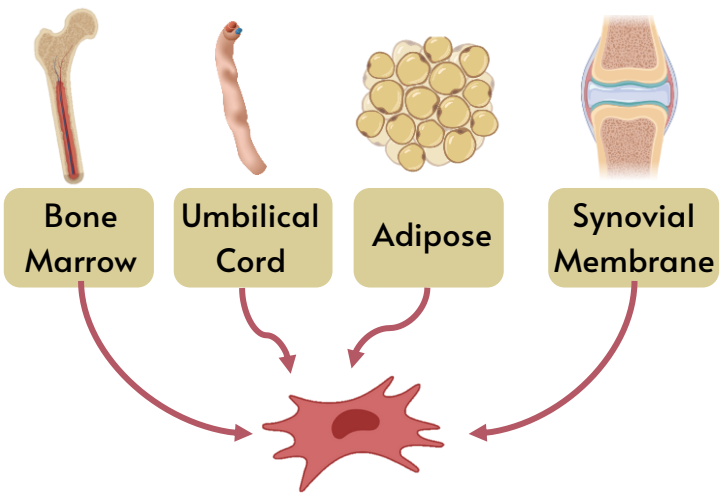
No serious adverse effects observed during or after treatment

EFFICACY

The therapeutic effects of MSCs maintained for 3-6 months without continuous administration, correlating with the increased percentage of Treg cells of peripheral blood

Different sources of MSCs: Will these affect the therapeutic effects?

MSCs can be isolated from different sources: bone marrow, umbilical cord, adipose, synovial membrane, etc.



MSCs show a potency of how to develop and differentiate are depending on where they found. For example, Synovial membrane-derived MSCs have a higher potential in repairing damaged cartilage when compared to MSCs from other sources.

While MSCs isolated from the umbilical cord show low immunogenicity, this means they will not stimulate immune system to attack during administration.

Potential therapeutic effects of MSCs

1 IMMUNOMODULATORY EFFECT

Treg cell ↑↑↑
-act to suppress immune response & maintain self-tolerance

Th17 cells ↓↓↓
-a type of T cells that activate the macrophages and recruit more immune cells to attack (will trigger more immune responses)

MSCs upregulate Treg cells & downregulate the expression of Th17 cells, to **restore the immune function (not to attack body's own cells)** by removing overreactive immune response.

MSCs also secrete **cytokines and growth factors with immunosuppressive properties**, which inhibit B & T cell (immune cell) proliferation.

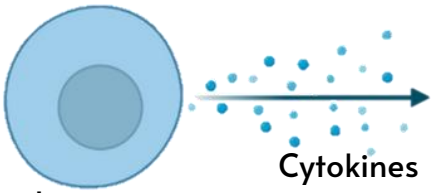
2 ANTI-INFLAMMATORY EFFECT

MSCs inhibit the proliferation and expression of proinflammatory cytokines, such as:

Interferon-γ

TNF-α

which are involved in the inflammatory response within the synovial membrane. The anti-inflammation effect delivered by MSCs greatly reduces tissue damage & relieves pain in joint areas.



Immune cell

Cytokines

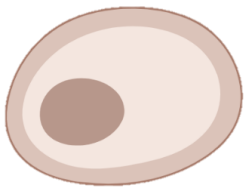
(A group of molecules released by immune cell that functions for cell signaling.)

3 PROTECTIVE AND REGENERATIVE EFFECT

MSCs can **inhibit the formation of osteoclasts** that cause joint damage. Studies also show that the MSC administration can prevent the occurrence of severe and irreversible damage to bone and cartilage caused by chronic arthritis.

Osteoclast ↓↓↓
-the key player in leading to RA
-osteoclast is a bone-resorbing cell, that can cause the erosion & inflammation of joint tissues that leads to the destruction of joints.

MSCs can be induced and differentiate into specialized cells, such as osteoblasts (bone cells) & chondrocytes (cells that are involved in the formation of cartilage) for self-renewal or self-repair of damaged tissue.



Osteoblast

Chondrocyte

REFERENCES

1) Tanaka, Y. (2015). Human mesenchymal stem cells as a tool for joint repair in rheumatoid arthritis. Clin Exp Rheumatol, 33(4 Suppl 92), S58-62. 2) Wang, L., Wang, L., Cong, X., Liu, G., Zhou, J., Bai, B., ... & Liu, Y. (2013). Human umbilical cord mesenchymal stem cell therapy for patients with active rheumatoid arthritis: safety and efficacy. Stem cells and development, 22(24), 3192-3202. 3) Ansboro, S., Roelofs, A. J., & De Bari, C. (2017). Mesenchymal stem cells for the management of rheumatoid arthritis: immune modulation, repair or both?. Current opinion in rheumatology, 29(2), 201-207.

*This poster is for educational purposes only.

BROUGHT TO YOU BY