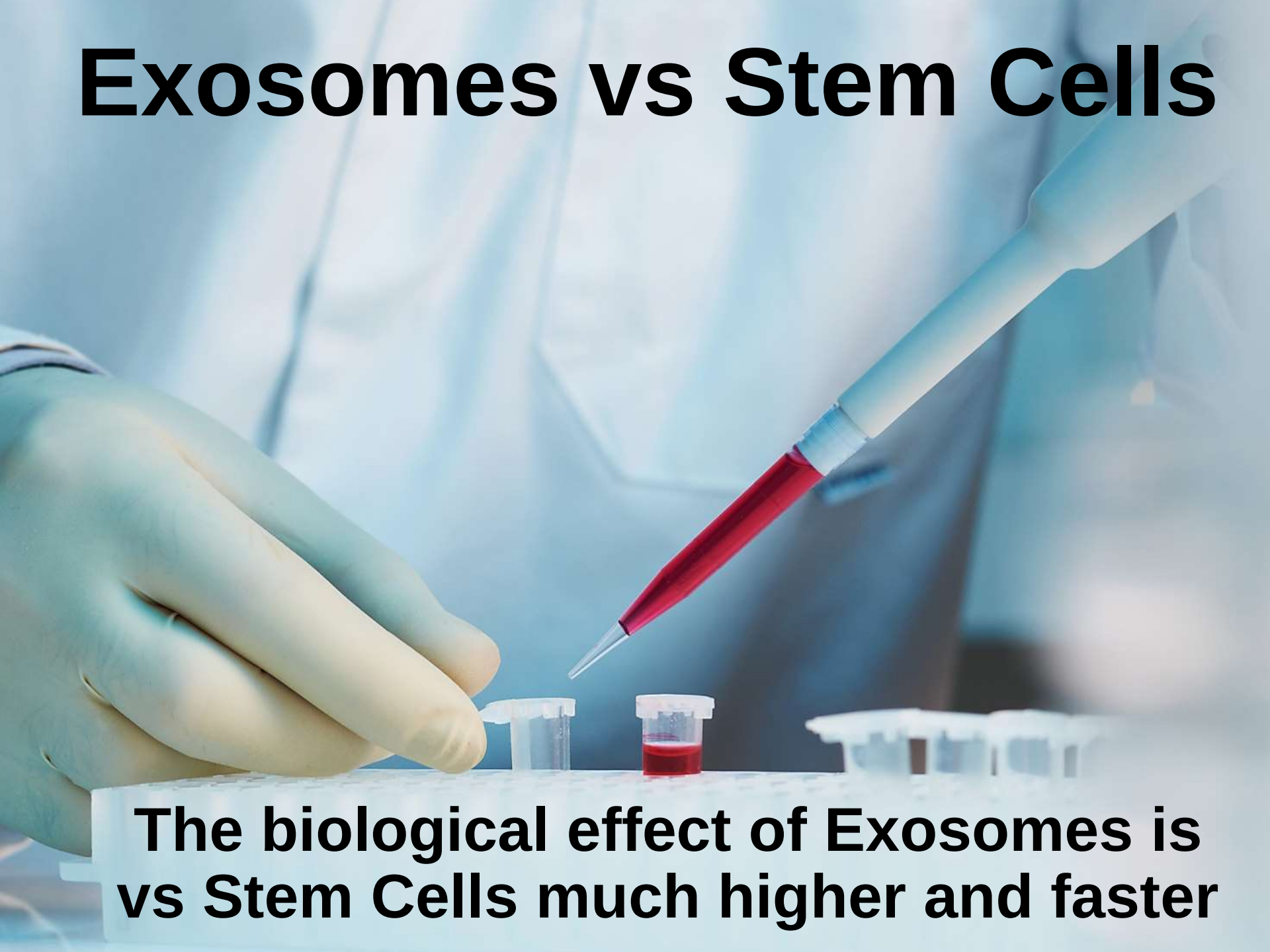
Exosomes – The new Generation of Stem Cell Therapy

BioMed Lab Bangkok

Exosomes vs Stem Cells



The biological effect of Exosomes is vs Stem Cells much higher and faster

- An **Exosome** is a term that applies to a tiny extracellular vesicle. They are acellular vesicles that are produced by most cells throughout the body.
- They are present in all body fluids such as breast milk, urine, lung fluid, semen, saliva.
- Exosomes are produced by cells, but are not cells themselves.

Exosomes are part of the heterogenous Extracellular vesicles which include:

- Microvesicles - larger vesicles
- Apoptotic Bodies – sometimes the same size as exosomes.

Exosomes are 30-150nm in in size, which is 1000 times smaller than stem cells. They were discovered in 1983 and found to carry proteins, small RNA, cytokines, and growth factors within them.
Exosomes are formed by what is called an endosomal route.
Think of a soap bubble, with a lot of "information" contained within it. Exosomes are released from cells by the soap bubble fusing to the cell membrane and then being released into the extracellular space.
The regulation of this process is not well understood. There has been a huge amount of interest in exosomes due to the following:

- They are extremely small and acellular. About 1000 times smaller than stem cells. So providers don’t have to worry about damaging a cellular component.
- Cost effective – lower cost than most other tissue products.
- Less restrictive storage requirements – if lyophilized they can be stored at room temp for months. If not, they can be put into a regular refrigerator temp for 1 month or a freezer for a year.
- Great topical results.
- •The best exosomes are those made from umbilical cord mesenchymal stem cells. The MSCs are cultured, and the byproduct is exosomes.

Which is a BETTER THERAPY? Stem cell vs exosome

Stem cell therapy

Using Live Stem Cells

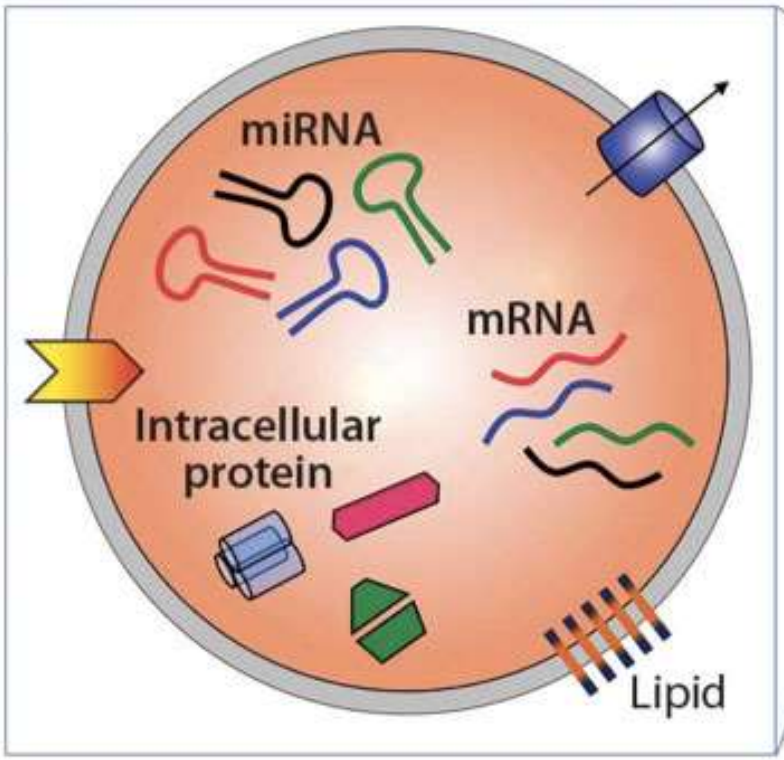
Can replicate in body for long-lasting cell repair & cell renewal effect

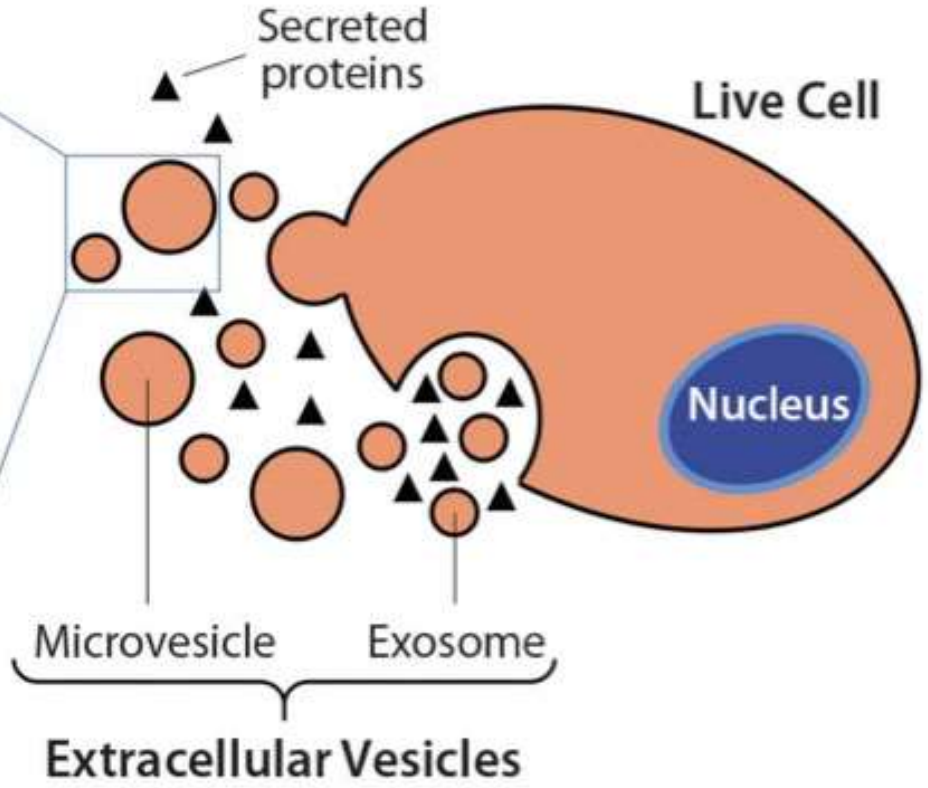
VS

Exosome therapy

Exosomes are used to send "repair message" to damaged organs

Short term (4-6 months) repair effect as exosomes "message" will wear off





“STEM CELLS” In Clinics Around The World

Mesenchymal Stem Cell in the culture dish

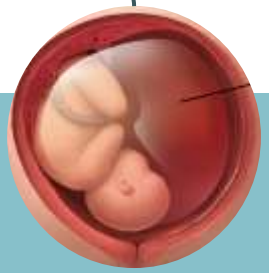
Adult stem cells

are

Multipotent Stem cell

Umbilical cord

Placenta



Amniotic fluid

Bone marrow

Adult Stem cells normally found in the body tissues and at embryonic tissues

Limitations of using MSC

Limited Number of Cells

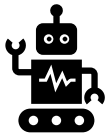
Tissue donation can produce only a limited number of MSC doses, For e.g. Bone marrow donation typically yields fewer than 20,000 MSCs

Loss in Potency

MSCs start to change as culture expansion progresses. This results loss in potency and cells goes to senescence

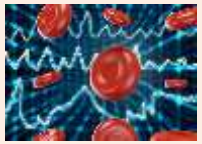
Screening Cost

Significant logistical challenges and costs involved with collection of tissue, for example, screening and testing multiple donors, followed by collecting and testing the donated material, is both time consuming and expensive.



Sample variation

Quality of MSC that isolated from different donations varies substantially.



Rejection

There is always the risk of immune defense (rejection) of cells that are not the body's own; also with cell banking of babies born within the family.

Risk for side effect

Exosomes

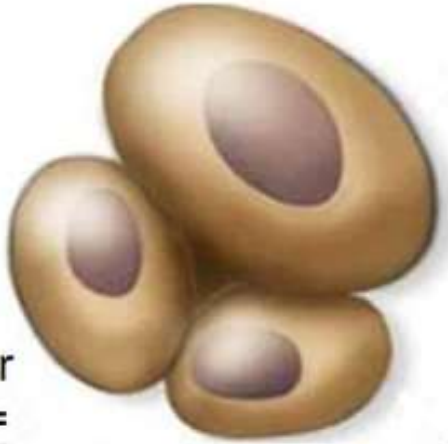
The new generation of Stem Cell Therapy

Unlimited Exosomes

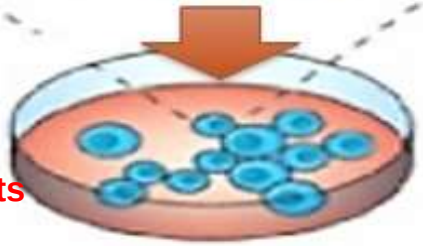
For example, squeeze a lemon

juice extract

It's a similar procedure in the lab. Reprograming means to create the extract of your own Stem Cells =



Exosomes



better to say: iExosomes (which come from patients own iPSC/iMSC)

You can make Exosomes from any kinds of human cells, also from animal cells. At the end you can call it Exosomes.
Most exosomes on the market are made from normal MSC or other cells; Cells from donors or cells from the patient.

Our Exosomes are derived from the patient's own stem cells; not only from their own stem cells, but from their own "embryonic stem cells".
How does it work; the patient is not an embryo? We transfer the skin cells obtained by biopsy to these patient-own embryonic stem cells, the so-called iPSC (= introduced pluripotent stem cells). After that, these cells are transformed into normal stem cells and then the exosomes are extracted.
The effect of these exosomes cannot be compared to other exosomes.

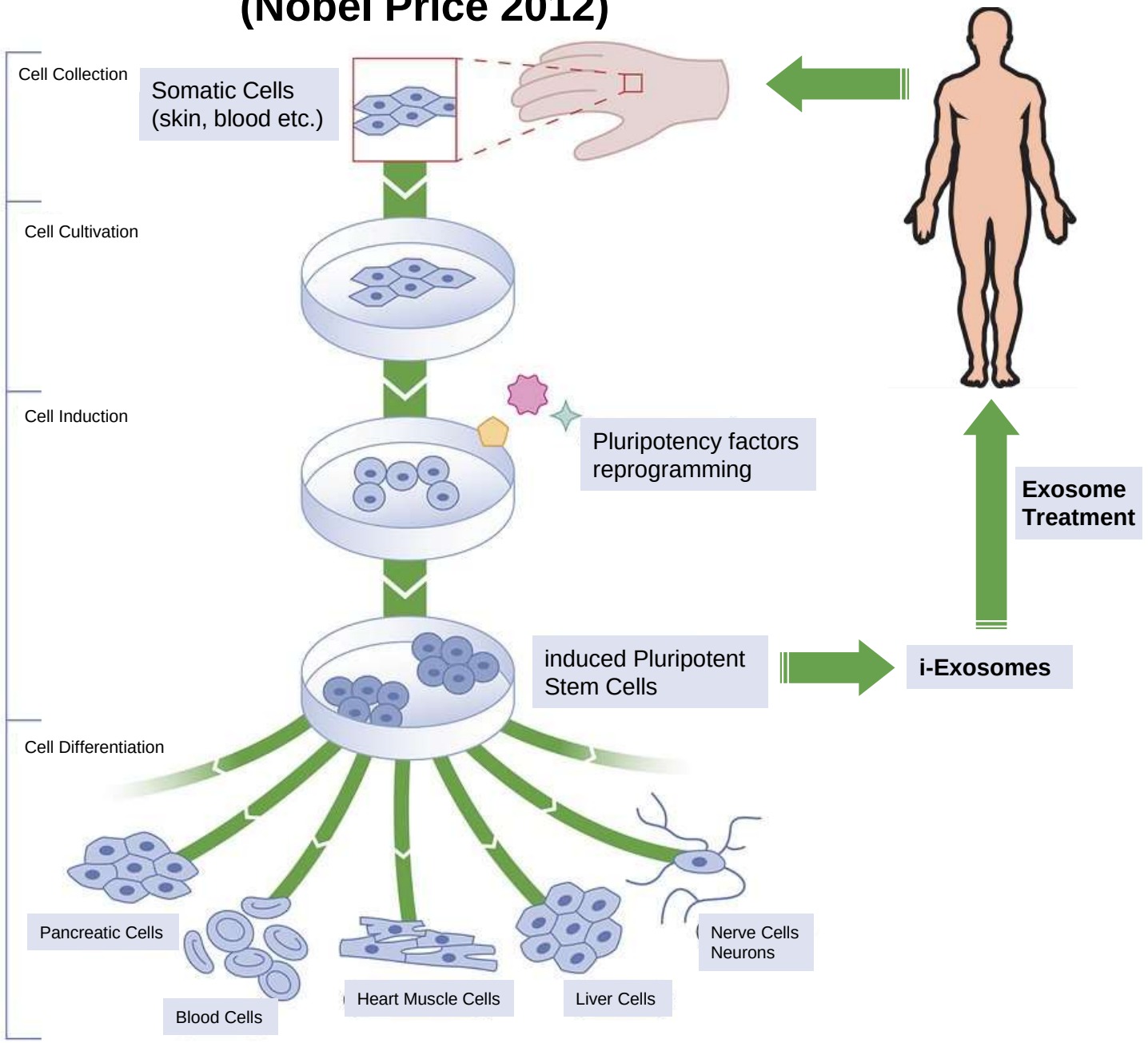
Embryonic and Pluripotent Stem Cells

A very exciting alternative to embryonic stem cells that holds great promise for clinical use are induced pluripotent stem cells (iPSC).

They are obtained by “reprogramming” ethically harmless adult cells, such as connective tissue cells of the skin, by introducing some genes that are very active during early embryonic development. The activity of these “embryonic genes” turns back the developmental clock in the differentiated cells almost completely, so that the reprogrammed cells are returned to a state that is almost identical to that of embryonic stem cells. Therefore, induced pluripotent stem cells are currently attracting enormous interest in biomedical research.

There is great hope that iPSCs can soon be used successfully in the treatment of, for example, Parkinson's disease, ALZHEIMER's disease and other diseases that are associated with the loss of a certain cell type or tissue. This is why research with pluripotent stem cells is of great medical importance.

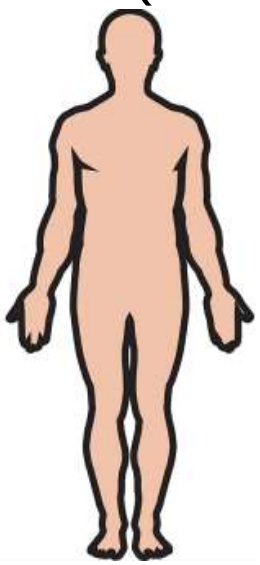
Our procedure for cell reprograming according Prof. Yamanaka, Japan (Nobel Price 2012)



Standard Exosome Production

D-Exosomes from MSC Donor Stem Cells = DMSC

(stem cell donation from **umbilical cord/placenta tissue**)



iv or local injection

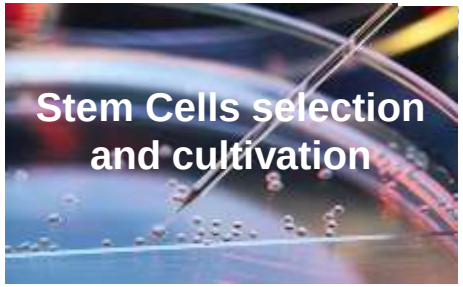
Implementation back to the patient

Step 4

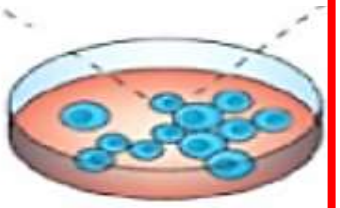
Blood Collection form Umbilical Cord and/or Placenta

Step 1

Step 2



Step 3



Extraction of the D-Exosome

… from the normal MSC straight to Exosome

Or...

Standard Exosome Production

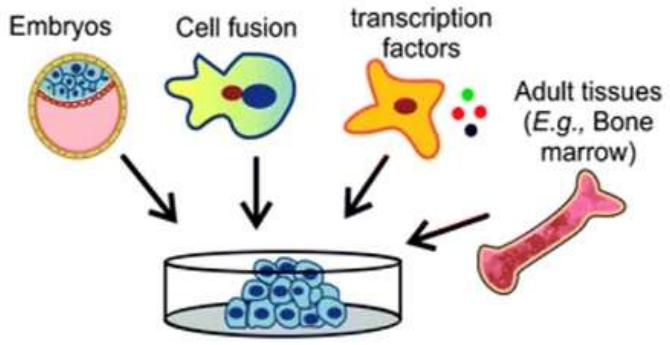
D-Exosomes from MSC Donor Stem Cells = DMSC

from other sources of stem cell

iv or local injection

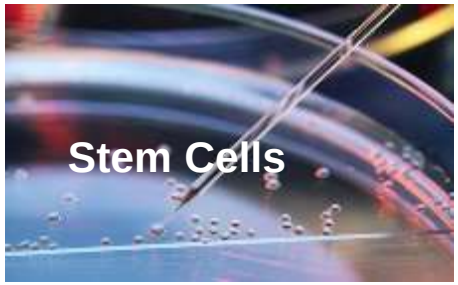
Implementation back to the patient

Step 4

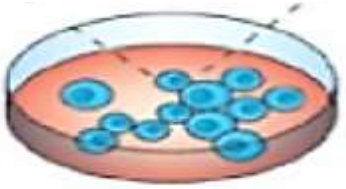


other sources of Stem Cells

Step 1



Step 2



Extraction of the Exosome

Step 3

… from the normal stem cells straight to Exosome

Or from…

i-Exosomes

iPSC-iMSC & i-EXOSOME Program

A Nobel Prize Technology

presented by:
Prof. Dr. Shinya Yamanaka, Japan
Dr. Rajneesh Verma, Australia

Biomed Clinic & Lab Bangkok, Thailand

Production of i-Exosomes

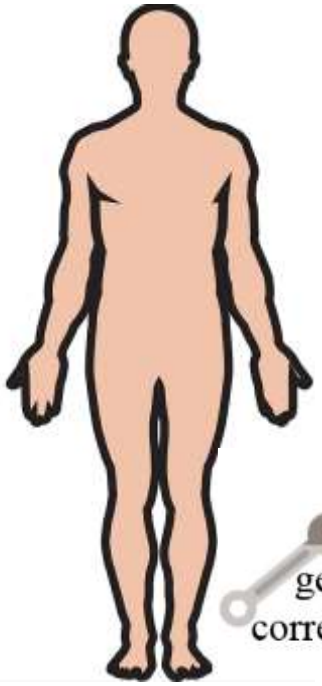
from your own somatic cells (blood cells or skin cells)

According to our therapeutic experience in field of cell therapy, BioMed suggests to all our patients the new generation of stem cell therapy

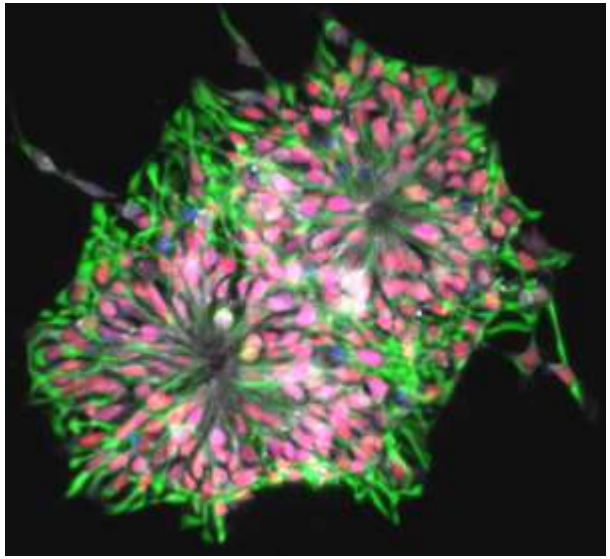
Exosomes

obtained from the patient's own stem cells

What it means:
"patient's own stem cells?



Reprograming
to iPSC



Prof. Dr. Shinya Yamanaka, Japan
Kyoto University, Kyoto, Japan;
Gladstone Institutes, San Francisco, CA, USA
Nobel Prize in Physiology and Medicine 2012 "for the discovery that mature cells can be reprogrammed to become pluripotent"

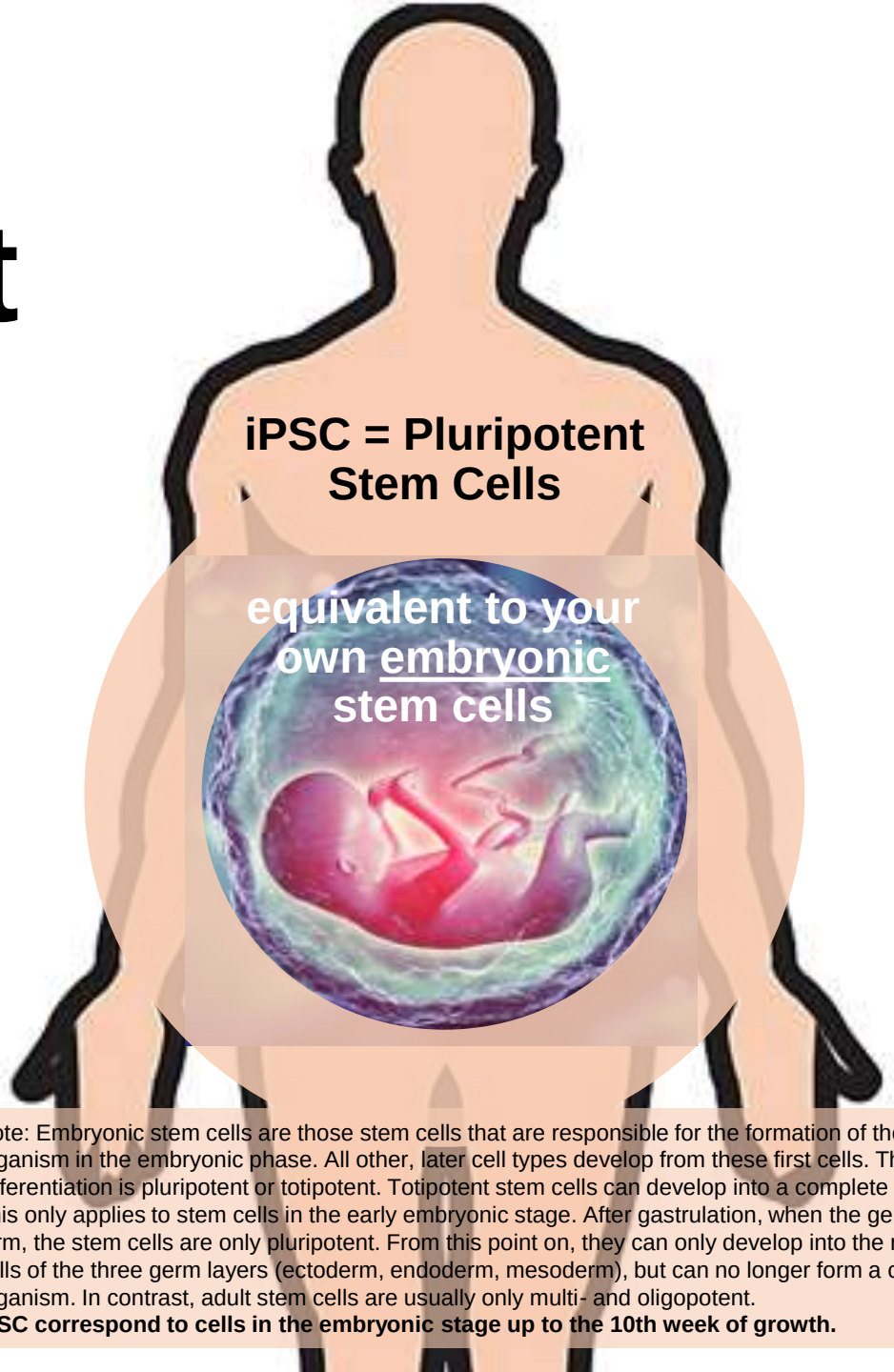
We have found a way to transform normal human (somatic) cells into stem cells that correspond and are equivalent to Patient's own Embryonic Stem Cells. These stem cells therefore have the highest possible effect as pluripotent stem cells.

Note: iPSC are derived from skin or blood cells that have been reprogrammed back into an embryonic-like pluripotent state that enables the development of an unlimited source of any type of human cell needed for therapeutic purposes. For example, iPSC can be prodded into becoming beta islet cells to treat diabetes, blood cells to create new blood free of cancer cells for a leukemia patient, or neurons to treat neurological disorders.

iPSC = Pluripotent Stem Cells

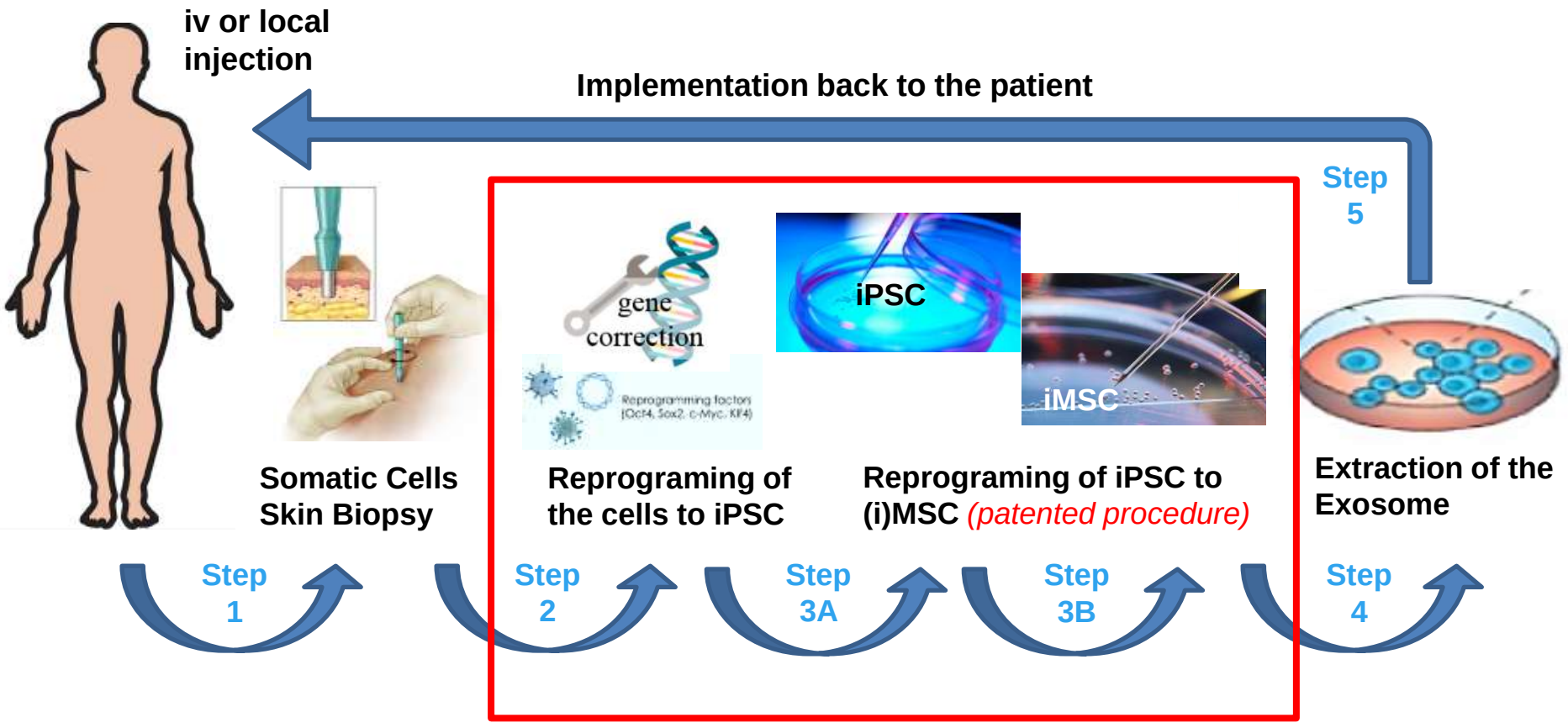
iPSC-Exosomes (i-Exosomes) means Exosomes from patient's own (induced) Pluripotent Stem Cells

Pluripotent stem cells can differentiate into almost all body cells – like embryonic stem cells from



Note: Embryonic stem cells are those stem cells that are responsible for the formation of the entire organism in the embryonic phase. All other, later cell types develop from these first cells. Their degree of differentiation is pluripotent or totipotent. Totipotent stem cells can develop into a complete organism. This only applies to stem cells in the early embryonic stage. After gastrulation, when the germ layers form, the stem cells are only pluripotent. From this point on, they can only develop into the respective cells of the three germ layers (ectoderm, endoderm, mesoderm), but can no longer form a complete organism. In contrast, adult stem cells are usually only multi- and oligopotent.
iPSC correspond to cells in the embryonic stage up to the 10th week of growth.

Exosome Production from patient's own iPSC-iMSC



BioMed's iPSC-Exosomes

Offer for international partners

Exosome-Offer for *BioMed's Clinic Partnership*

A) Exosomes from patient's <u>own stem cells</u>

<u>Source:</u> somatic cells (fibroblasts) ➔ iPSC ➔ iMSC ➔ i-Exosome

B) Exosomes from BioMed's <u>Donor Stem Cell Banking</u>

<u>Source:</u> BioMed's own SC Donor Bank Umbilical Cord and Placenta

C) Exosome from Patient's <u>Family's Stem Cell Banking</u>

<u>Source:</u> Patients own Banking Lab (Umbilical Cord and Placenta etc.)