



โรงพยาบาล
ราชวิถี
www.rajavithi.go.th

Stem cells in Breast milk- From Theory to Reality ?

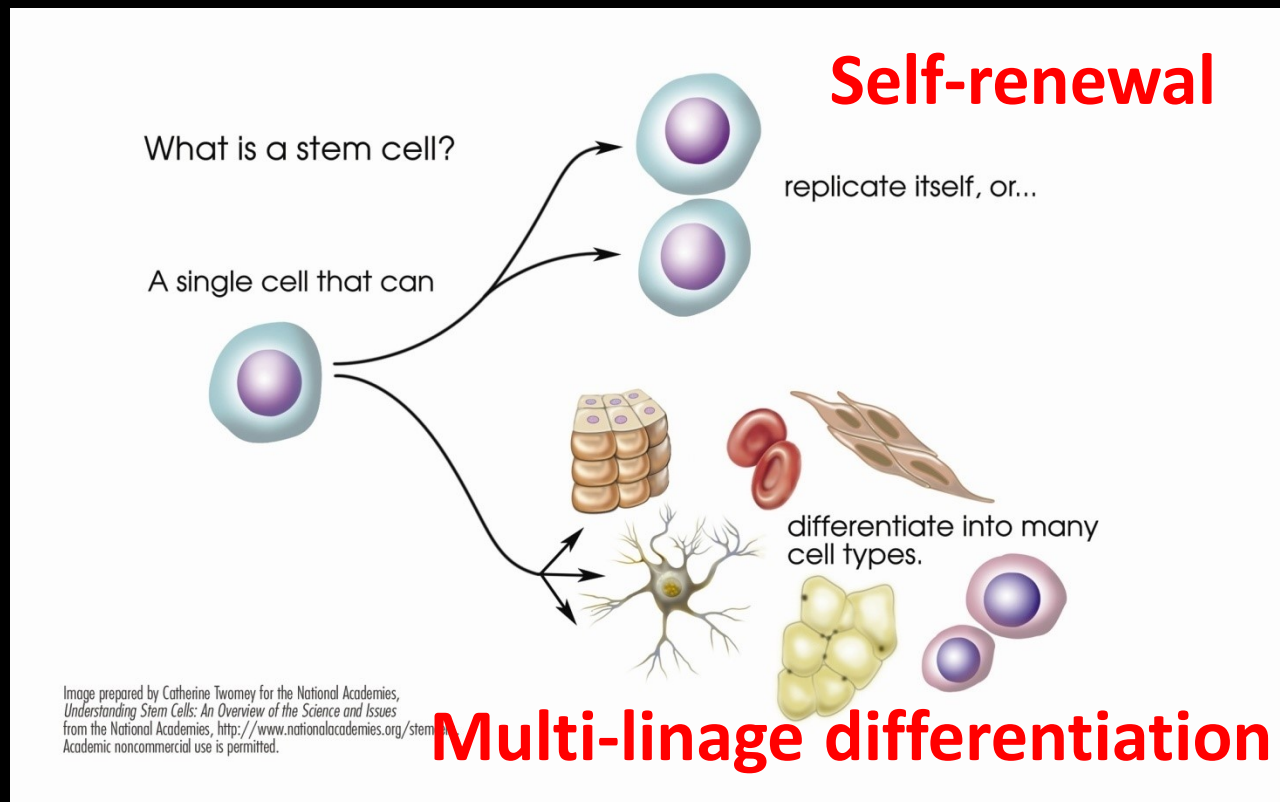
พญ. ยุรี ยานาเซะ

งานเวชศาสตร์มารดาและทารกในครรภ์

กลุ่มงานสูตินรีเวชศาสตร์ โรงพยาบาลราชวิถี

What are stem cells ?

- Undifferentiated cells that are able to differentiate into specialized cell



Sources of stem cells

- Embryonic stem cells
 - Inner cells mass of blastocysts
- Adult stem cells
 - Various organs : brain, bone marrow, blood, skeletal muscles, skin, GI tract, endometrium , bladder, liver and mammary gland
 - Repair system
 - Stem cells and progenitor cells

Stem cells VS Progenitor cells

	Stem cells	Progenitor cells
Self-renewal in vivo	Unlimited	Limited
Self-renewal in vitro	Unlimited	Limited
Potentiality	Multipotent	Unipotent , Oligopotent
Maintenance of self-renewal	Yes	No

Potency

- **Totipotent** - all possible cell types
 - Zygote formed at egg fertilization
- **Pluripotent** - almost all cell types
 - Embryonic stem cells
- **Multipotent** - closely related family of cells
 - Hematopoietic (adult) stem cells
 - Red and white blood cells or platelets
- **Oligopotent** - differentiate into a few cells
 - Adult lymphoid or myeloid stem cells
- **Unipotent** - cells of their own type, but have the property of self-renewal
 - Adult muscle stem cells

I DIED WAITING FOR
EMBRYONIC STEM CELL
RESEARCH TO FIND A CURE.
WHAT ABOUT YOU?

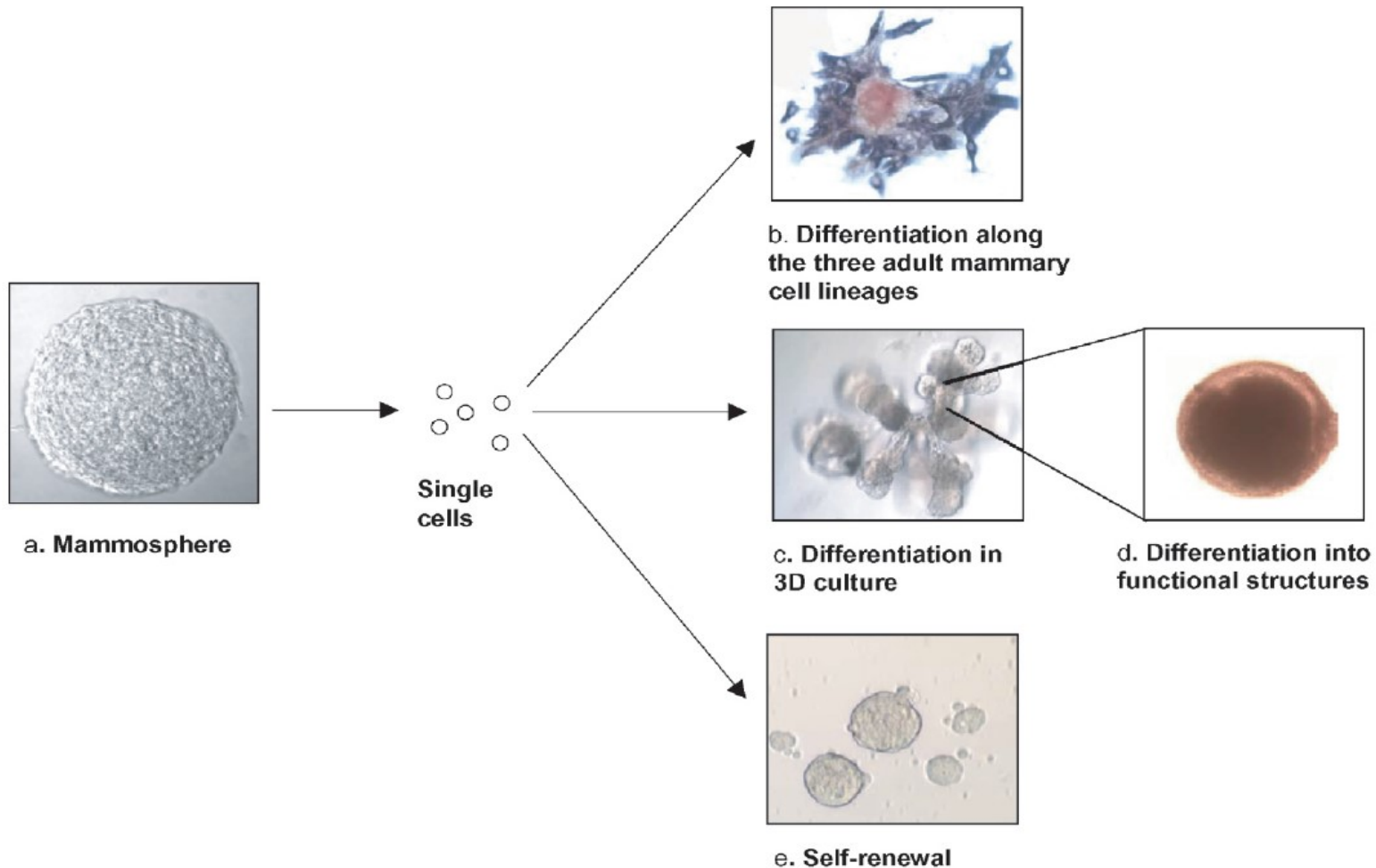
I WAS THE
EMBRYO



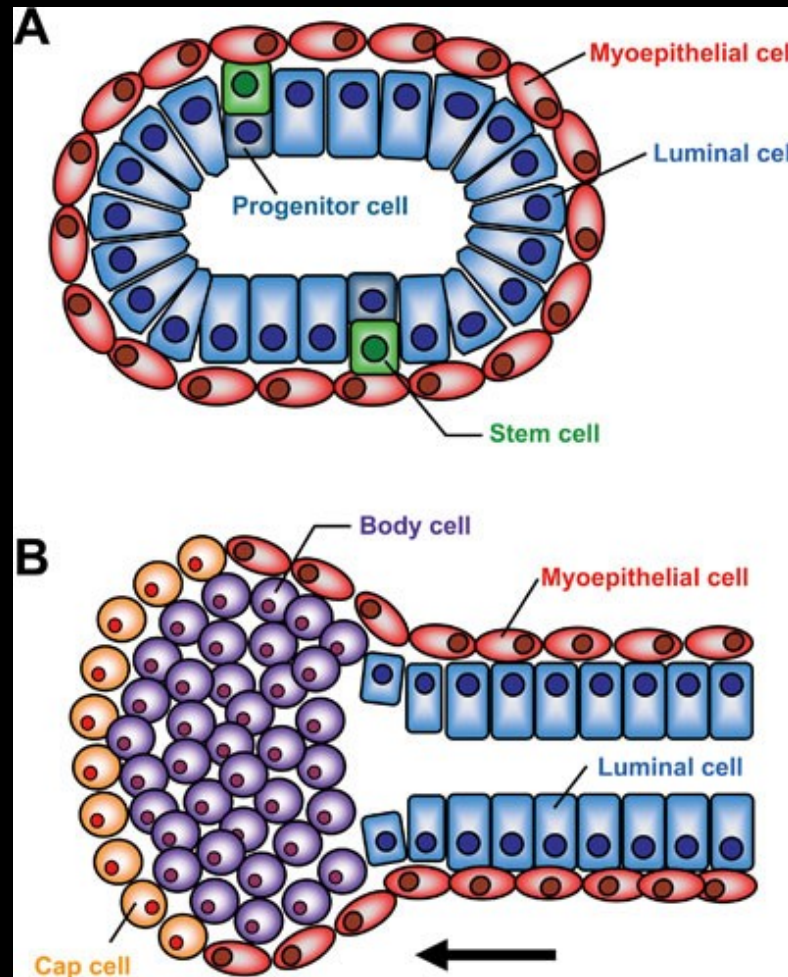
Stem cells collection

- Hematologic stem cells
 - Bone marrow
 - Peripheral blood
 - Umbilical cord blood
- Mesenchymal stem cells
 - Bone marrow
 - Peripheral blood
 - Adipose tissue
 - Wharton's jelly
 - Placenta and umbilical cord
- **Breast milk ???**

Mammosphere (Cultured mammary epithelial cells)



Stem cells in mammary gland

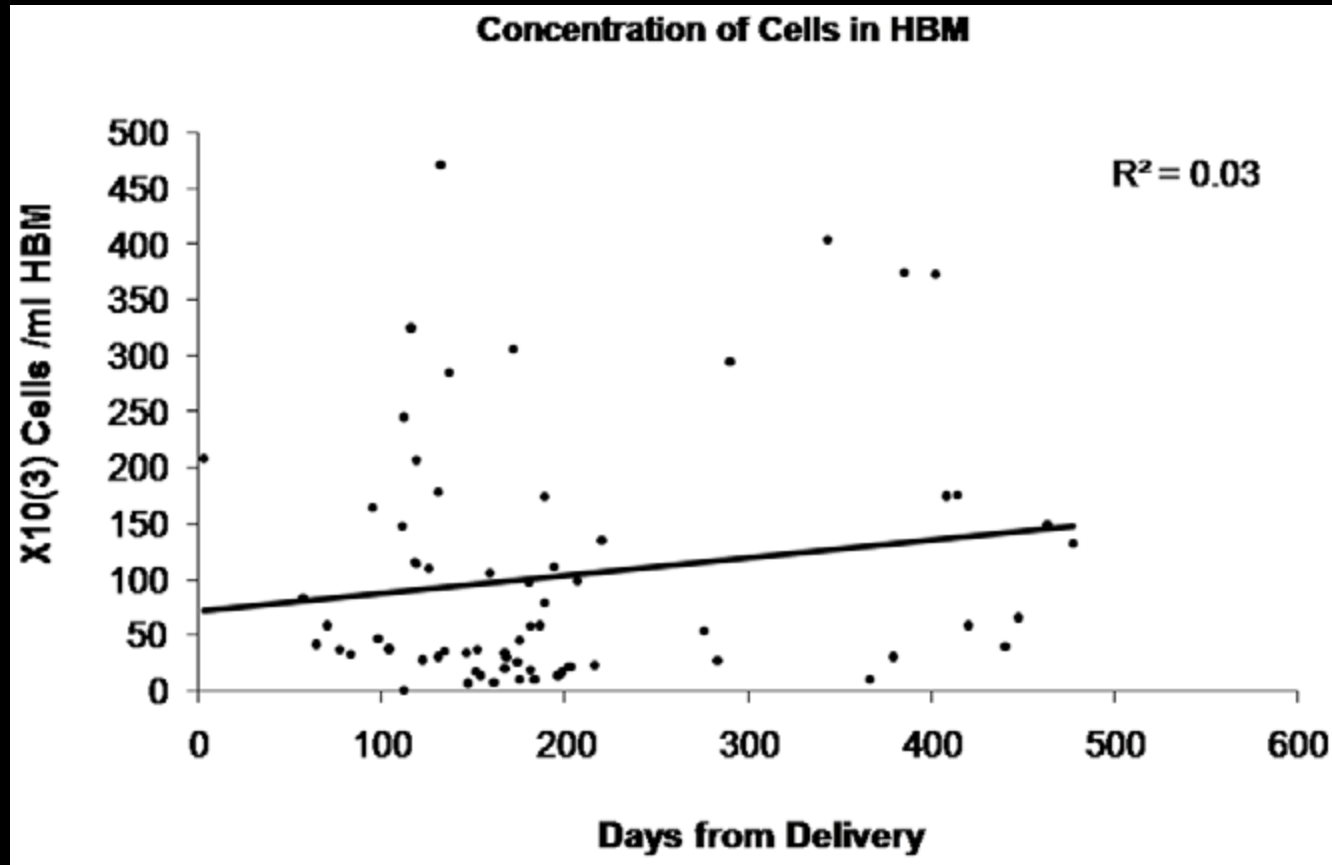


Adapted from Tiede et al., 2011

Functions of stem cells in mammary gland

- Give rise to tissue of mammary gland during development
- Tissue expansion and remodeling during pregnancy , lactation and involution
- Reserve for repairing tissue damage

Cells concentration in HBM



- Not vary in relation to the duration of breastfeeding

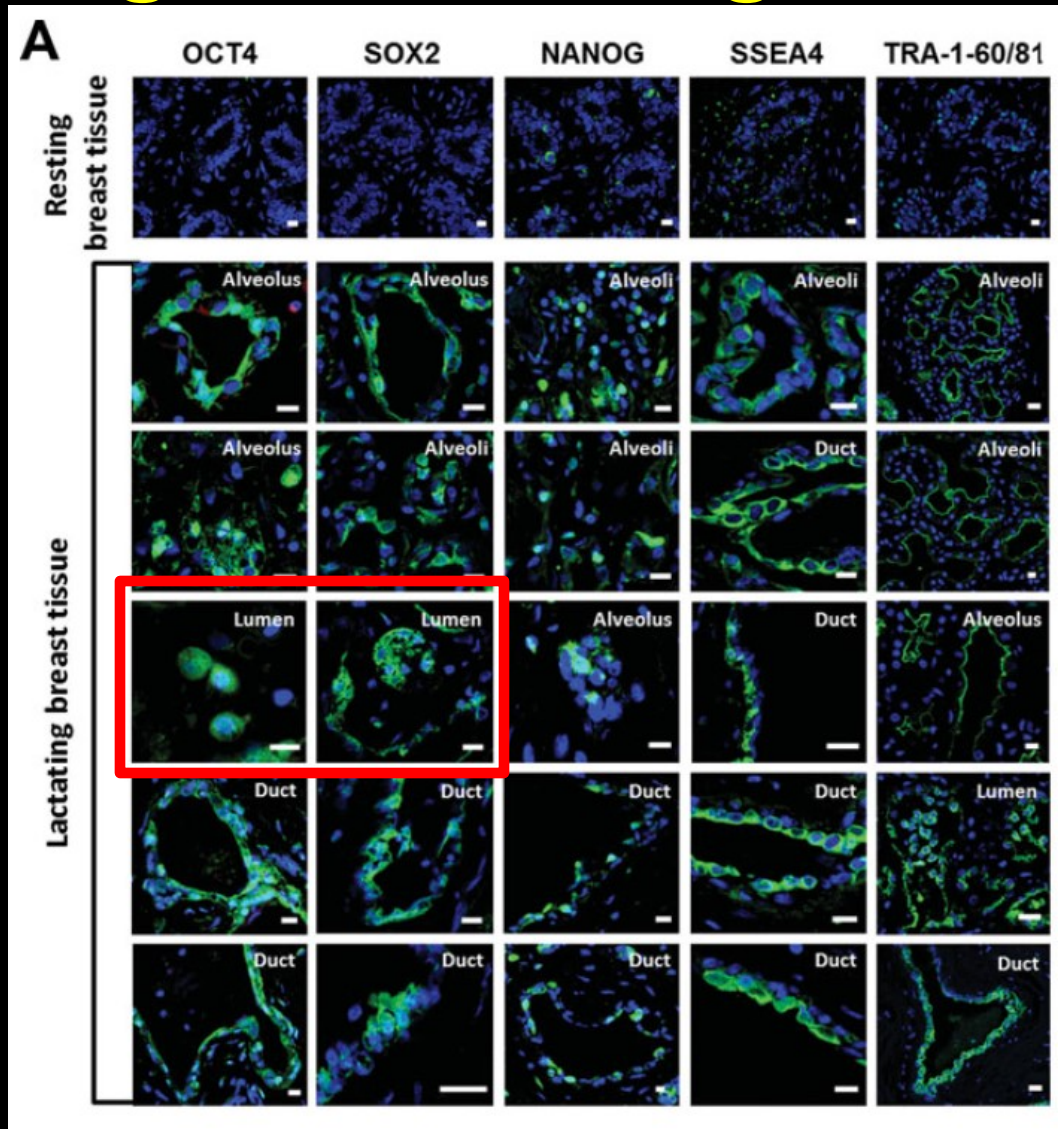
Cells in breast milk

- Epithelial cells
- Colostral corpuscles
- Polymorphonuclear leukocytes
- Mononuclear phagocytes
- Lymphocytes
- Stem cells / Progenitor cells

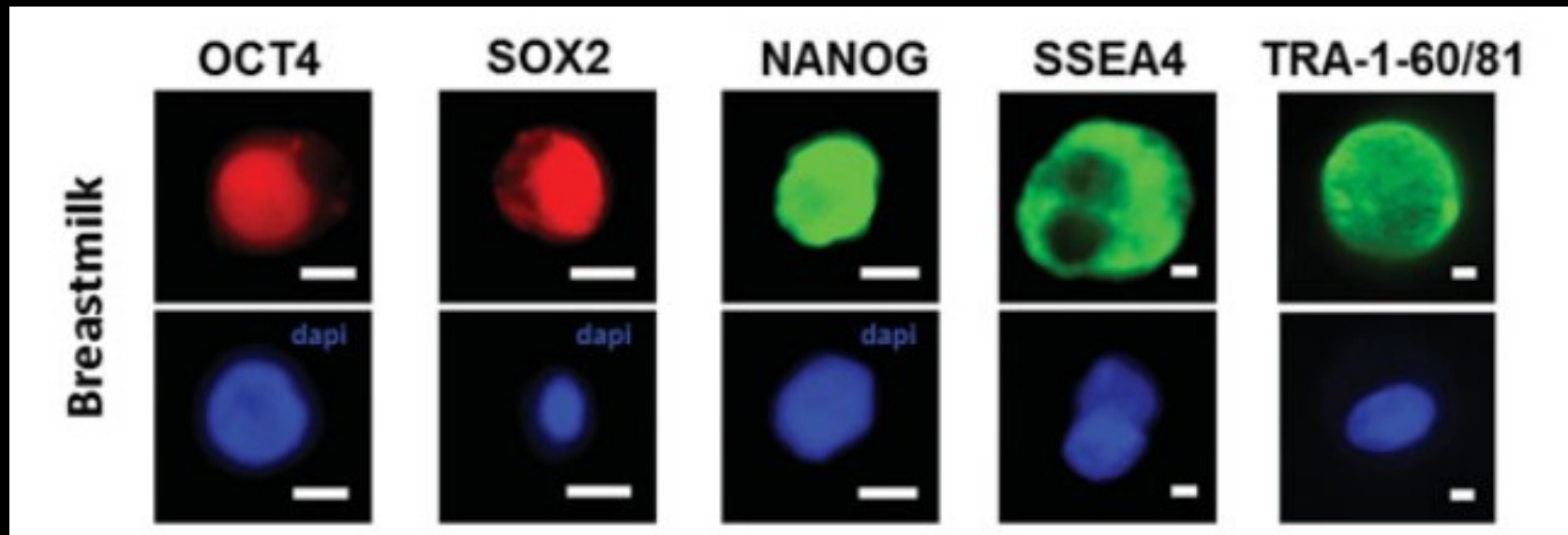
Cells shedding from ductal and luminal epithelial layer

- Heightened turnover of secretory tissue
- Mechanical shear force associated with the continued filling and emptying cycle of breast milk synthesis and lactation

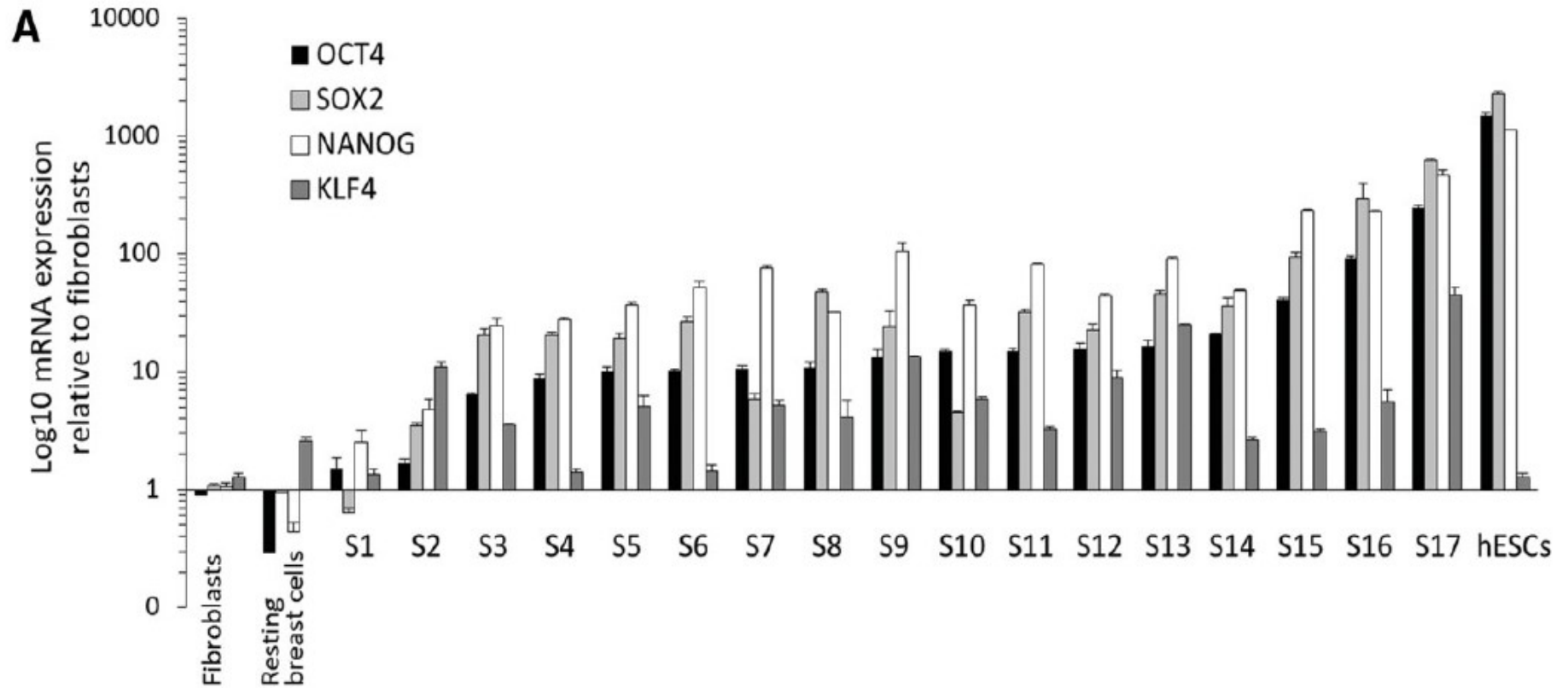
Resting VS Lactating breast tissue



Immunostaining of fresh breastmilk

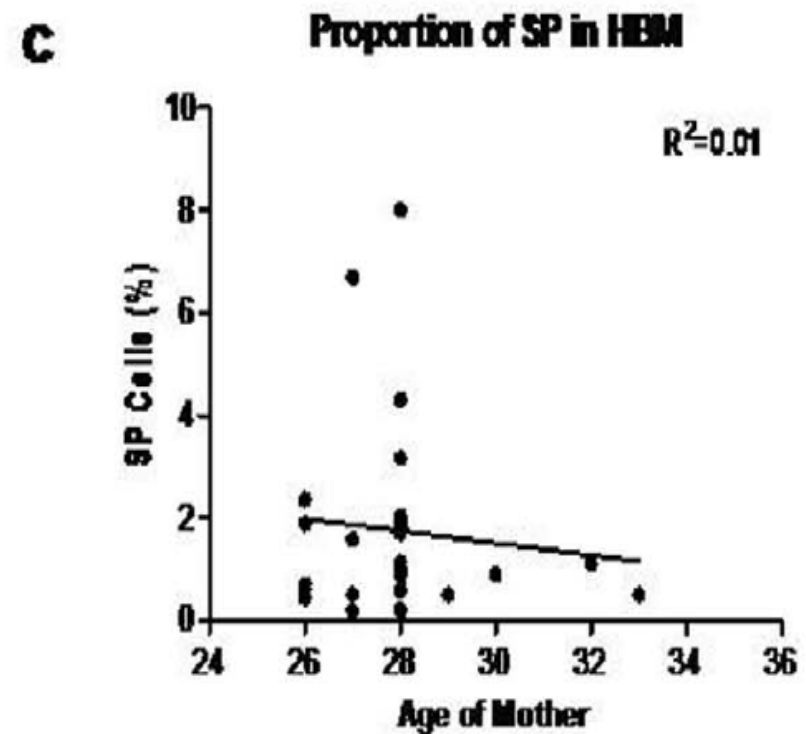
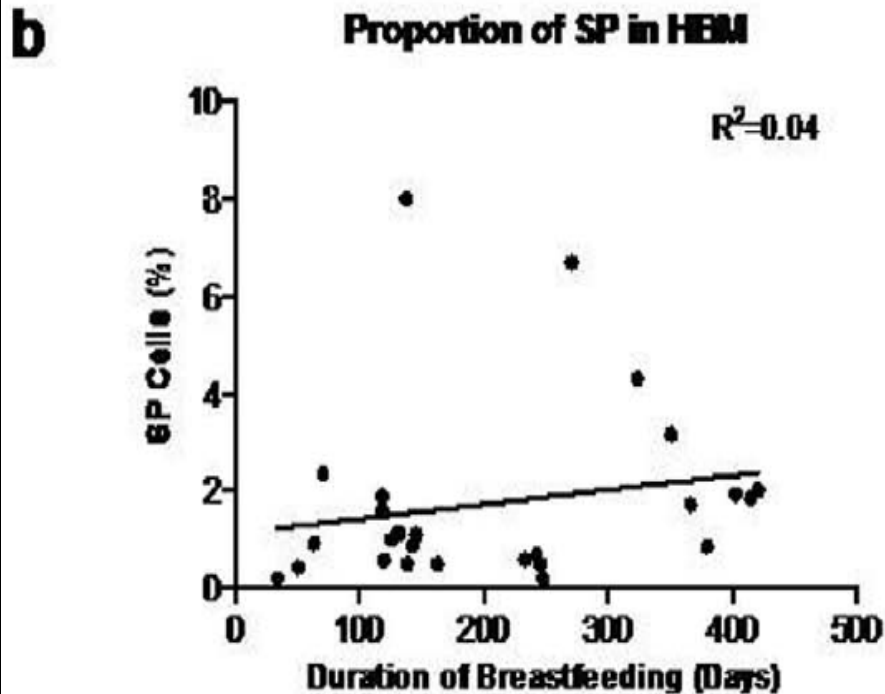


Quantitative-real time PCR



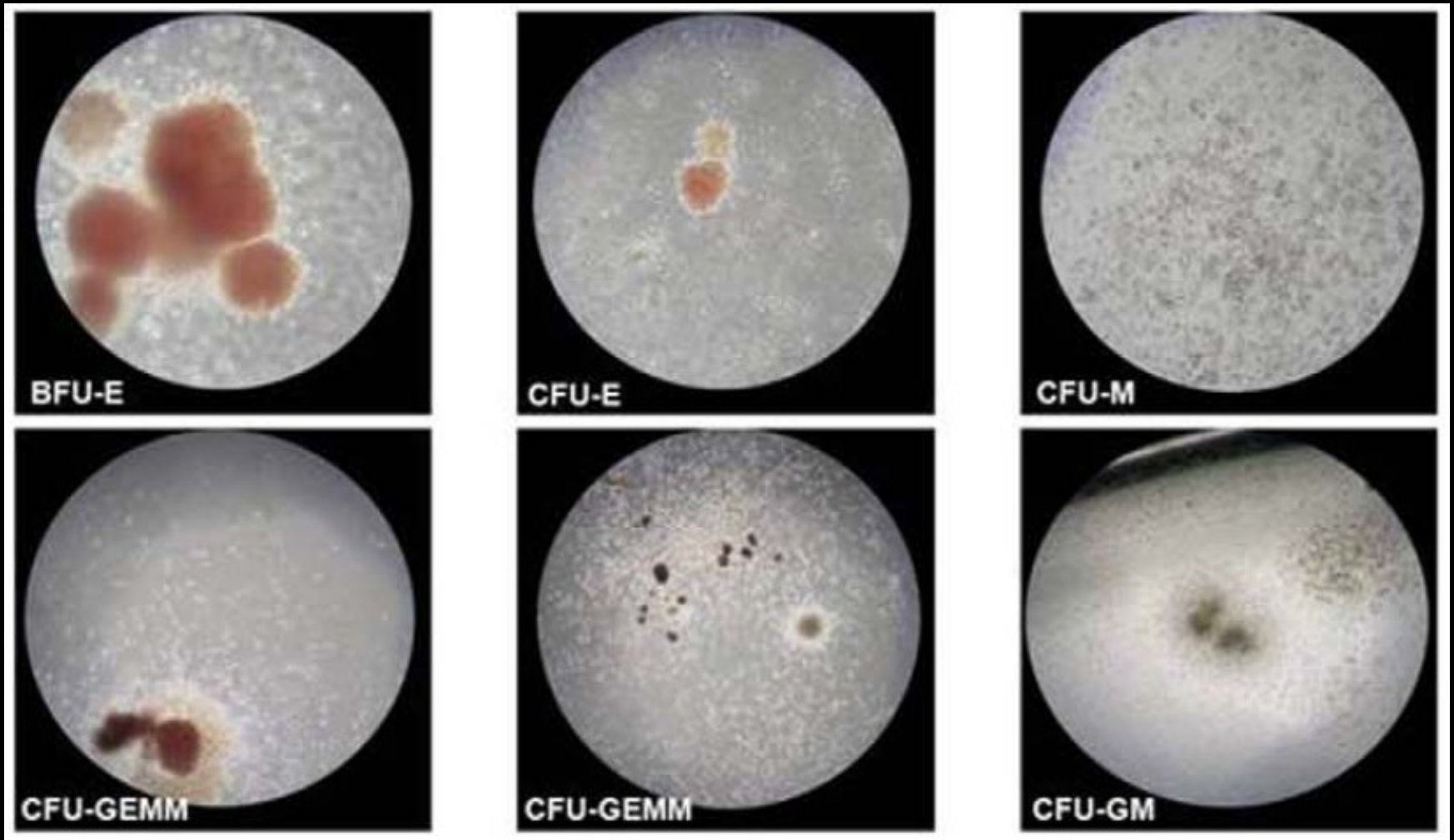
- Wide variation was observed in mRNA expression levels among samples from different women

Scatter plots

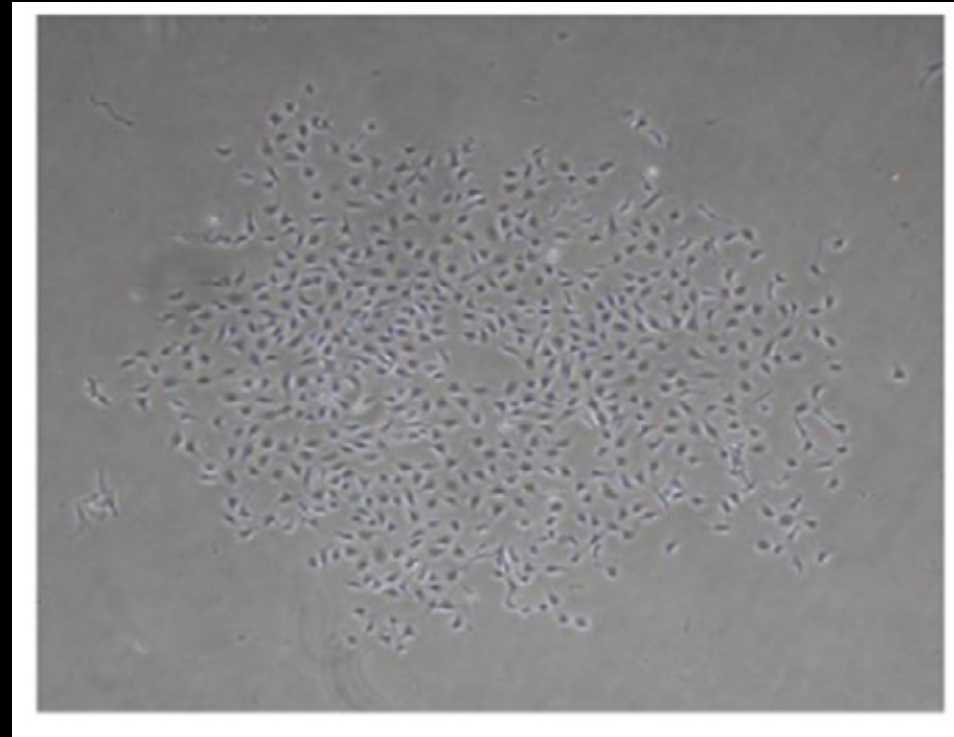
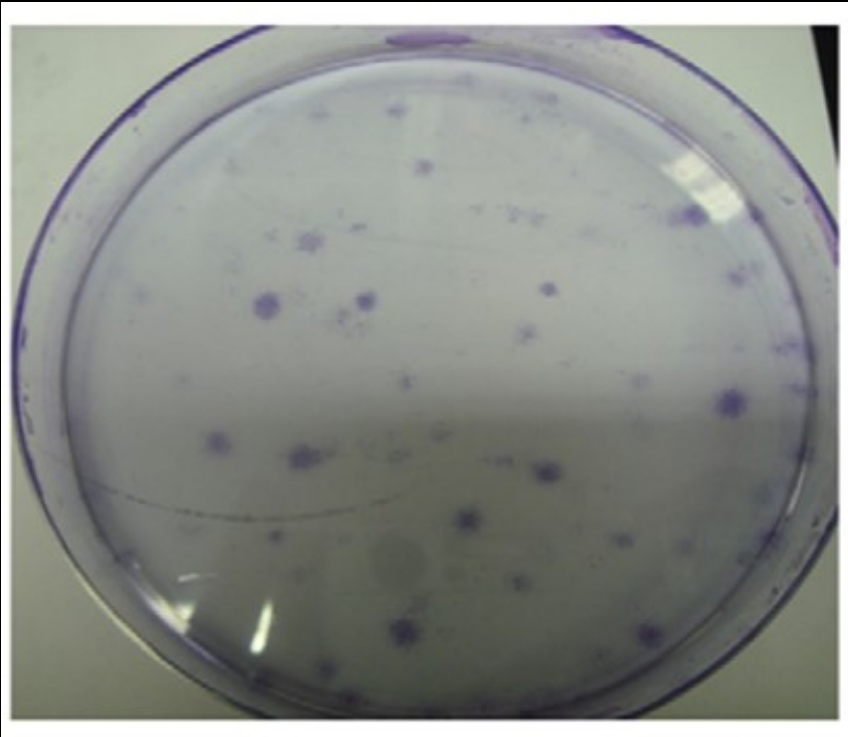


- No relationship between the percentage of SP and duration of breastfeeding and age of mother

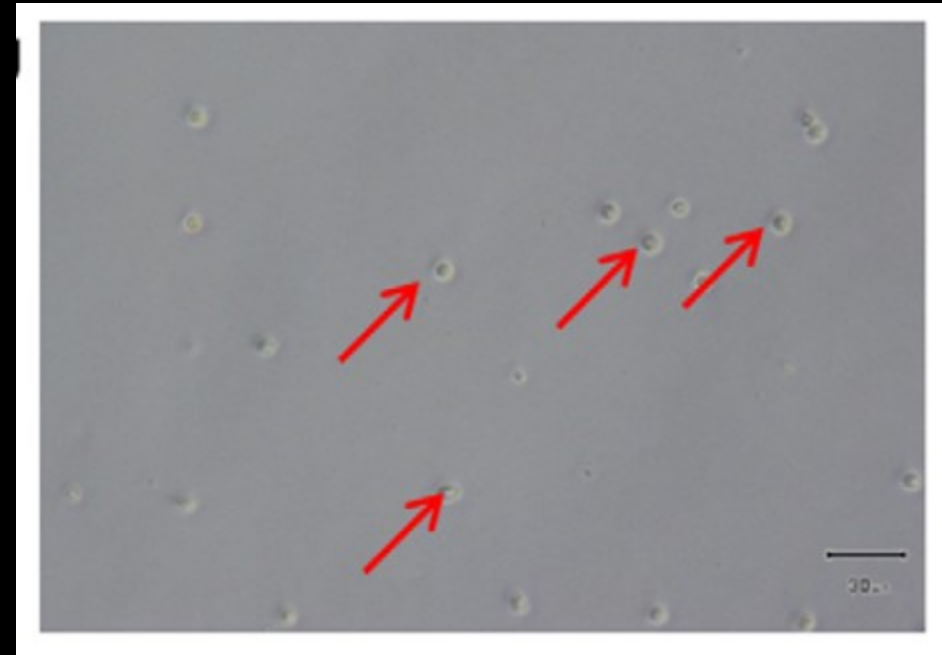
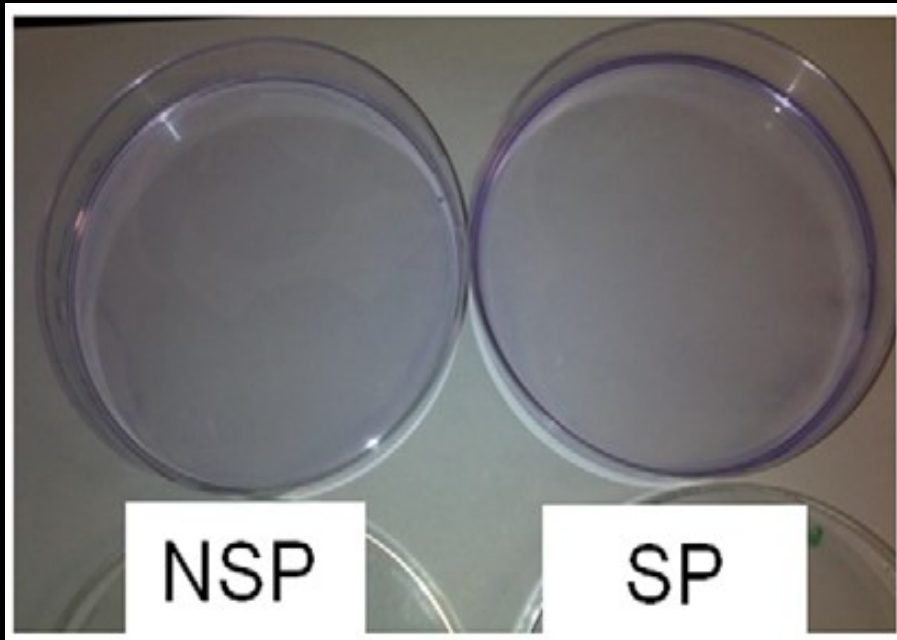
Colony forming unit in cord blood



Colonies of fetal mesenchymal stem cells



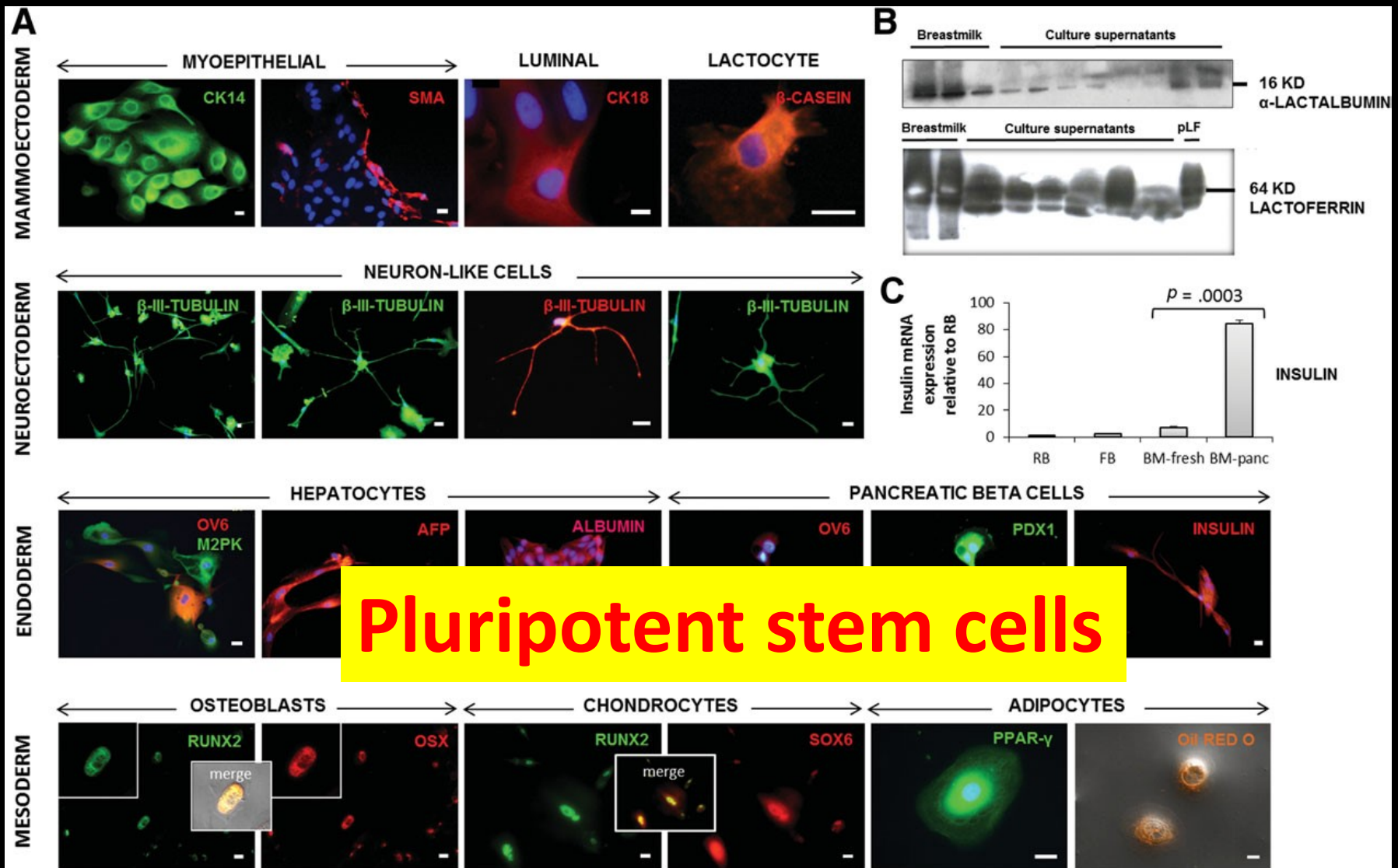
Mesenchymal culture of cells in HBM



OMG!!!



Breast milk stem cells differentiate into cells of three germ layer



From Breast Milk to Brains: The Potential of Stem Cells in Human Milk

Journal of Human Lactation
29(2) 136–139
© The Author(s) 2013
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/0890334413475528
jhl.sagepub.com



Alecia-Jane Twigger, BSc (Hons)¹, Stuart Hodgetts, PhD¹, Luis Filgueira, MD²,
Peter E. Hartmann, PhD³, and Foteini Hassiotou, PhD³

Keywords

brain, breastfeeding, breast milk, breast milk stem cells, cell replacement therapy, central nervous system, infant development, lactation, regenerative medicine

The breast is a unique organ in that it fully matures during pregnancy and lactation, when it undergoes complete remodeling of its epithelium and stroma to support the synthesis and secretion of milk and its delivery to the infant.¹ Mammary stem cells are responsible for the changes that occur in the breast during this period, which can be repeated many times during the life of a female. What is less well known is that these stem cells, together with other cell types from the breast, filter down into breast milk and are ingested by the breastfeeding child. Interestingly, stem cells in human breast milk have been recently shown to have pluripotent features. This means that they are able to differentiate into not only breast-specific cells but also many other cell types, including neural-like cells.² This provides new grounds to support the

to be bipotent stem cells, can create a full gland. Since then, this has been repeated with transplantation of single MaSCs, which were able to reconstitute a full functional mammary gland in mice.⁶ In vitro spheroid assays confirmed the presence and assisted characterization of bipotent MaSCs.⁷ Most studies, however, have been conducted in the mouse mammary gland, which is now known to contain MaSCs with the signature of CD49f^{high}/CD29⁺/CD24^{low}/Sca-1⁺.^{4,8} Human MaSCs have been less characterized, particularly in the fully mature organ, due to the scarcity of human lactating breast tissue.^{1,9} It has been proposed that MaSCs in the human resting (in non-pregnant, non-lactating females) breast have the phenotype CD49f^{high}/CD29⁺/CD24^{low}/EPCAM^{low/-} and also express cytokeratin 5.^{1,10} Marker profiles for more differen-

Cell replacement therapies

- Inj the
- are
- Stem Multilineage tumors (teratoma)
 - **not formed** by human breast milk stem cells.
 -
 -

All associated with multilineage tumors (Teratoma)!

What stem cells do in the baby ?

- Is it possible that stem cells pass through the intestinal layer of the neonate into systemic circulation ?
- Is stem cells from the mother can contribute to organ development in the newborn ?

Future Prospects

- Cells replacement therapies (CRTs) for brain and spinal cord injuries
- Survival of hBSCs in neonate gut and transportation to distant sites
- Integration of hBSCs into infant's tissues

Take home message

- Positive expression of pluripotent stem cells in human breast milk
- Benefit of breast milk stem cells
 - Ethical
 - Noninvasive
 - Plentiful nature
- Clinical applications need further studies



โรงพยาบาล
ราชวิถี
www.rajavithi.go.th



Thank You

