Breast Milk: the Gold Standard

พญ. รัชดา เกษมทรัพย์
สถาบันสุขภาพเด็กแห่งชาติมหาราชินี

Top 7 Components of Human Milk

1. Oligosaccharides
2. Antibodies
3. Anti-oxidants
4. Lactoferrin
5. Osteopontin
6. White blood cells
7. Stem cells.

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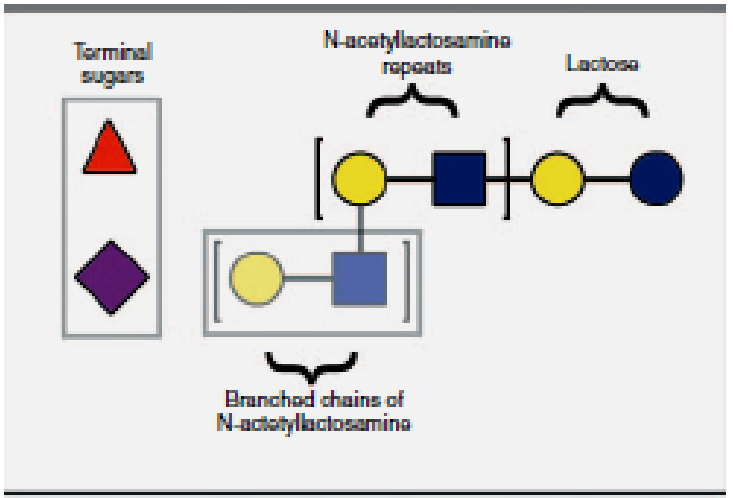
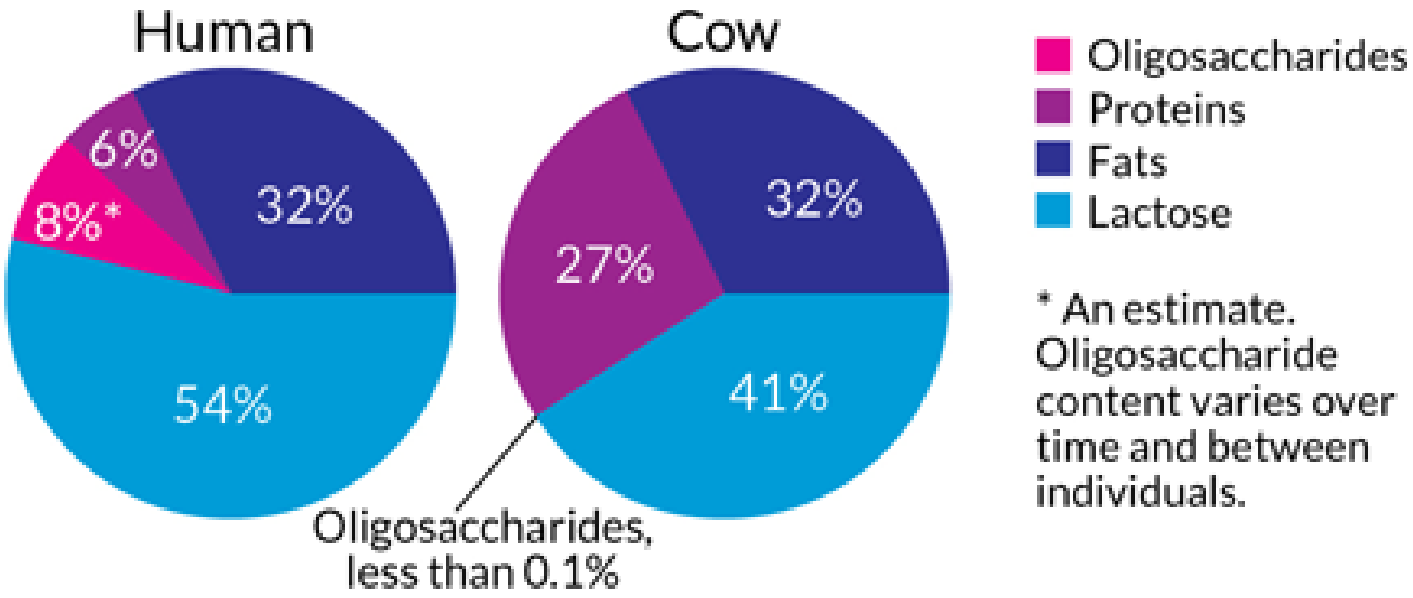
Human Milk Oligosaccharides (HMOs)

- Indigestable complex carbohydrates
- Synthesized in the mammary glands
- Oligosaccharides are highly resistant to hydrolysis in the gastrointestinal tract.
- Most HMOs will enter colon. A few is absorbed in the neonatal small intestine.



Human Milk Oligosaccharides (HMOs)



HMOs are the third most predominant component in human milk.

Human Milk Oligosaccharides (HMOs)

Table 1 **Total and sialylated oligosaccharides in human milk, bovine milk, and infant formulas based on cow's milk.**

Oligosaccharides	Human colostrum (<7 days)	Mature human milk (30–120 days)	Bovine colostrum	Mature bovine milk	Infant formulas
Total oligosaccharides[27–31]	13,300–23,000 mg/L	3,500–14,000 mg/L	~1,000 mg/L	300–500 mg/L	400–8,000 mg/L[a]
Sialylated (acidic) oligosaccharides[5,9,14,18,30,32–39]	1,000–3,300 mg/L	135–2,150 mg/L	230–1,500 mg/L	10–195 mg/L	14–288 mg/L
6′-sialyllactose[18,32,39–43]	250–1,300 mg/L	170–500 mg/L	30–243 mg/L	17–88 mg/L	3.8–4.6 mg/L
3′-sialyllactose[18,20,32,39–45]	90–350 mg/L	76–300 mg/L	354–1,250 mg/L	30–119 mg/L	17–19 mg/L

[a] Products include formulas supplemented with galacto-oligosaccharides and/or fructo-oligosaccharides.

Nutrition Reviews; 72(6): 377-389

Human Milk Oligosaccharides

- > 100 different HMOs in breast milk
- **Neutral HMOs:**

  galacto-oligosaccharides, fructo-oligosaccharides
- **Acidic HMOs:**

  sialyllactose, other sialylated milk oligosaccharides

HMOs: potential effects

1 - Development of microbiota:
- Stimulation of outgrowth of specific bifidobacteria and bacteroides

2 - Gut maturation:
- Regulation of EGF-receptor activation → epithelial differentiation
- Adhesion of maternal IgG to infant intestinal epithelium

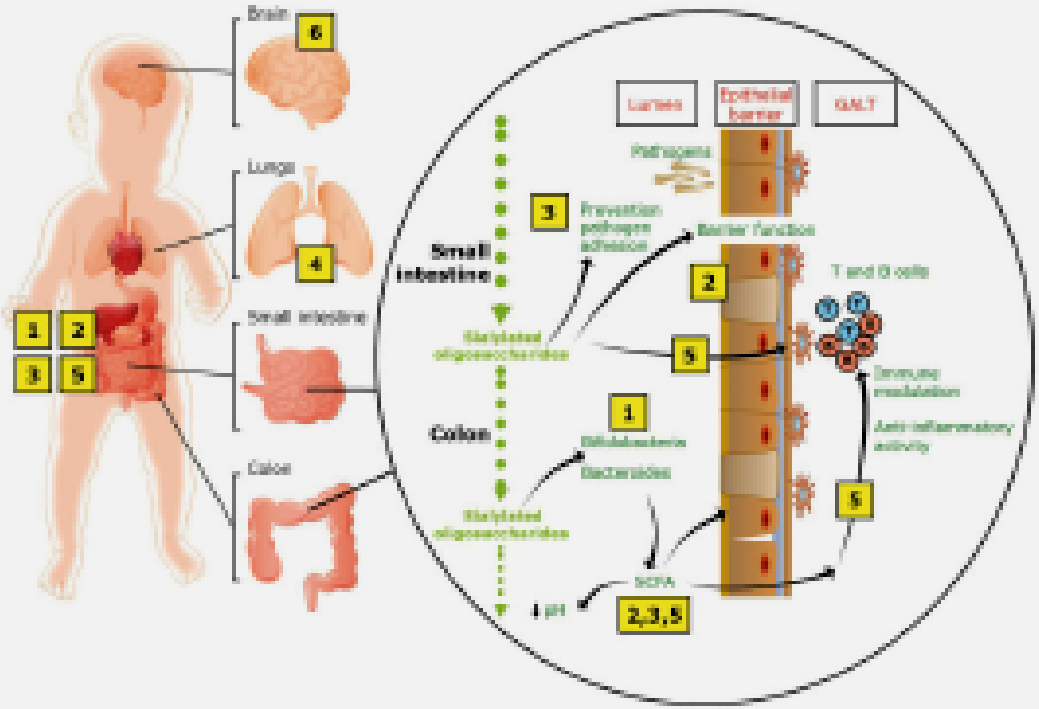
3 - Resistance to gut pathogens:
- Competition for pathogen binding sites on epithelium (decoy activity/prevention of adhesion)
- Reduction of pH in lumen of colon
- Mucin composition

4 - Resistance to respiratory tract pathogens:
- Increase of pathogen phagocytosis
- Mucin composition

5 - Immune function and inflammation:
- Enhancement of endocytosis by DCs
- Induction of immune regulation by SA-receptors on immune cells
- Reduction of leucocyte adhesion to endothelium
- Induction of T cell skewing
- Reduction of inflammation in IBD
- Involvement in reduction of NEC

6 - Brain and cognitive development:
- Incorporation of SA in brain gangliosides (learning ability)

Potential effects of SL and sialylated oligosaccharides



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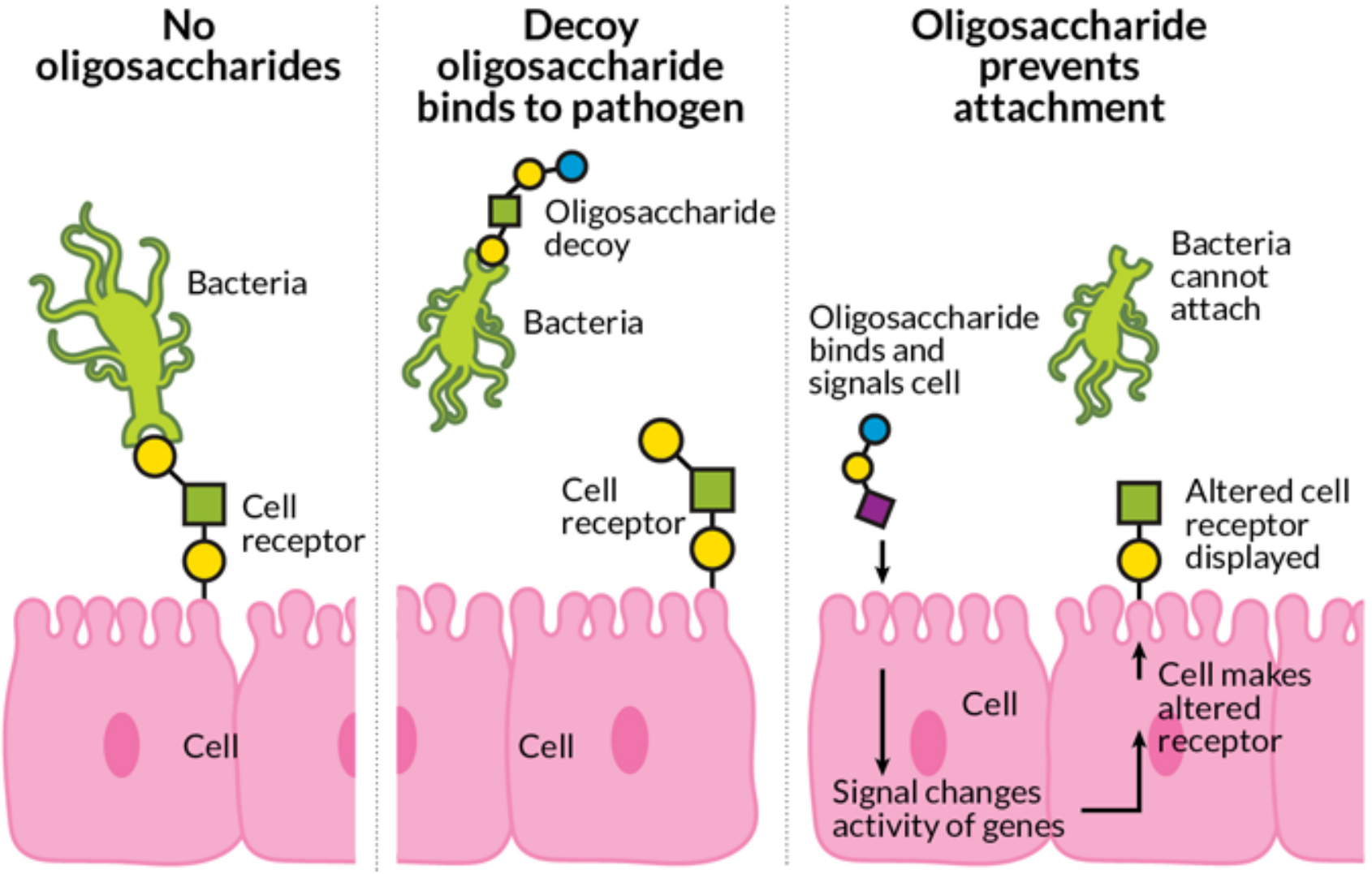
HMOs: potential effects

1. Development of microbiota & Resistance to gut pathogens

- Limit pathogenic microbes (e.g. E. coli) by blocking the binding of microbe to infant's mucosal receptors.
- Oligosaccharide-mucosal receptor complex allows specific attachment of B. bifidum to the intestinal mucosa, competitively inhibiting the attachment of pathogenic organisms.
- ↑ Growth on non-pathogenic commensal microbe (Bifidobacterium bifidus)

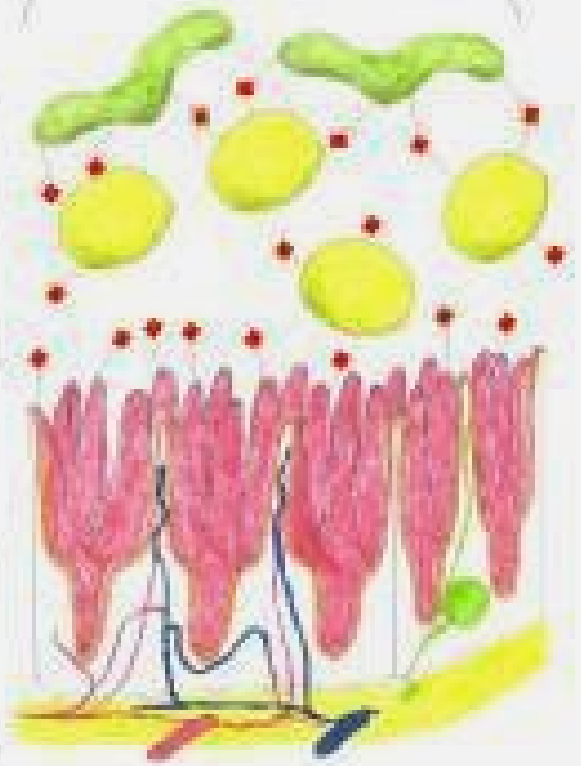

No oligosaccharides
Bacteria
Cell receptor
Cell
Decoy oligosaccharide binds to pathogen
Oligosaccharide decoy
Bacteria
Cell receptor
Cell
Oligosaccharide prevents attachment
Bacteria cannot attach
Oligosaccharide binds and signals cell
Altered cell receptor displayed
Cell
Cell makes altered receptor
Signal changes activity of genes

Intestine of Breast Fed Infant

Bacteria Adhering to Milk Fat Globules Preventing Infection

Human Breast Milk Fat Globules with Carbohydrate Decoys

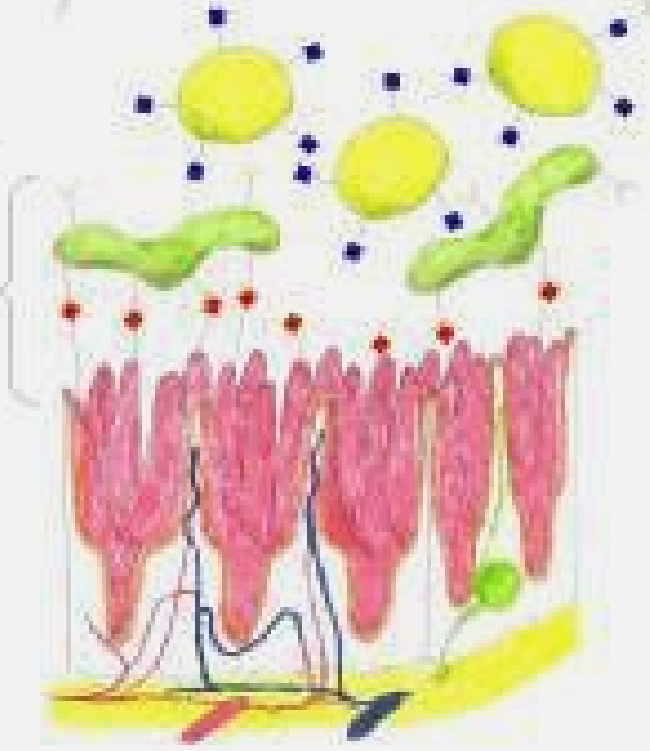
Infant Intestinal Mucosa Covered with Specific Protein Carbohydrates



Intestine of Bovine Milk Fed Infant

Bovine Milk Fat Globules without Human Type Intestinal Carbohydrate Decoys

Bacteria Adhering Directly to Infant Mucosa Initiating Infection



HMOs: potential effects

1. Development of microbiota & Resistance to gut pathogens

- Gut microbiota produce SCFA (short chain fatty acids).
- SCFA
  - Barrier against pathogens
  - Antidiarrheal agents (↑ sodium and water absorption)
  - Nutrient absorption
  - Immune development

HMOs: potential effects

2. Gut maturation

- Regulation of EGF (epidermal growth factor) – receptor activation → epithelial differentiation
- Adhesion of maternal IgG to infant epithelium

HMOs: potential effects

3. Resistance to respiratory tract pathogens:

- ↑ pathogen phagocytosis
- Mucin composition (sialic acid)

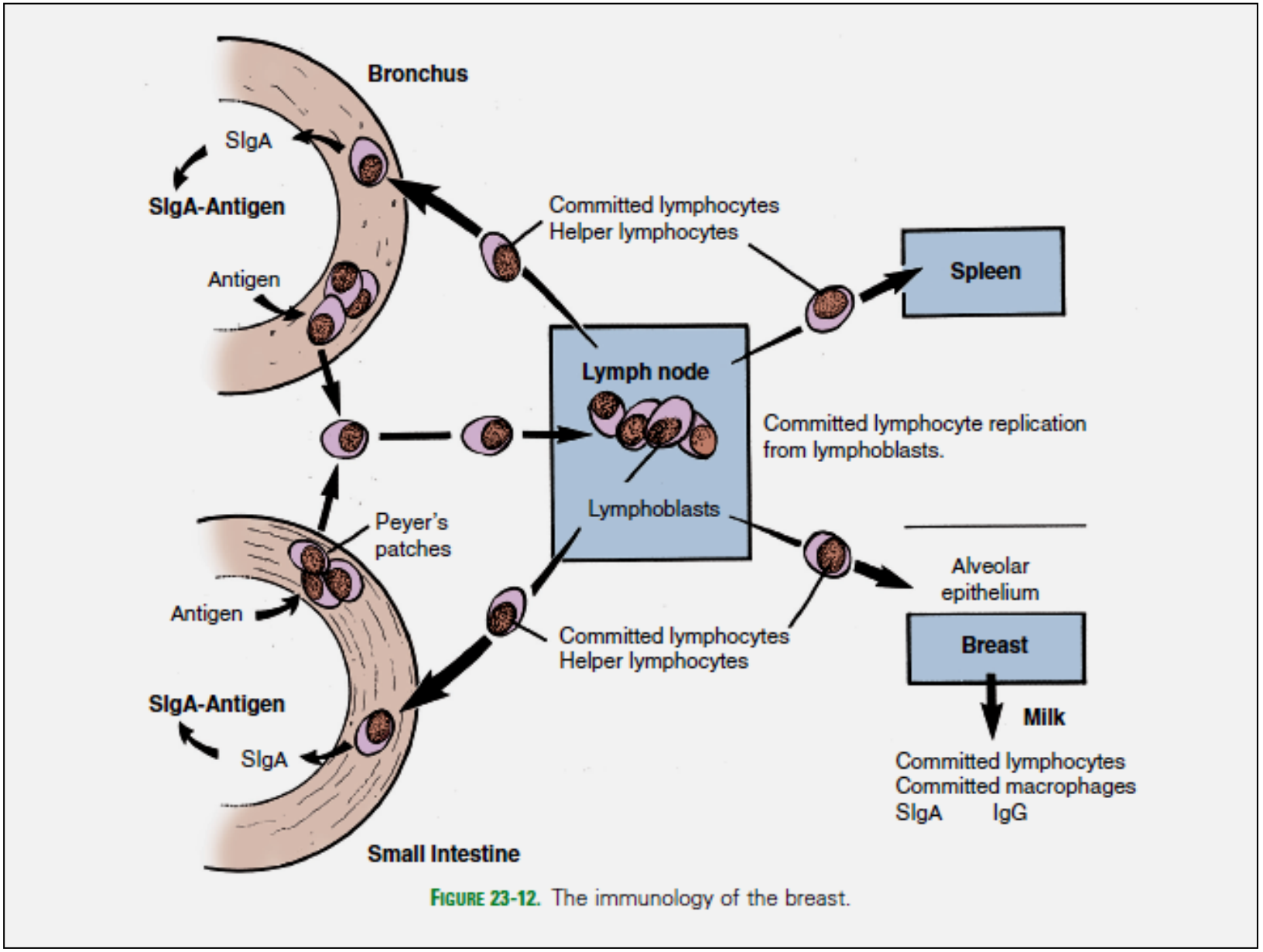


FIGURE 23-12. The immunology of the breast.

Newton ER. Lactation and Breastfeeding in Obstetrics: Normal and Problem Pregnancies

HMOs: potential effects

4. Immune function and inflammation

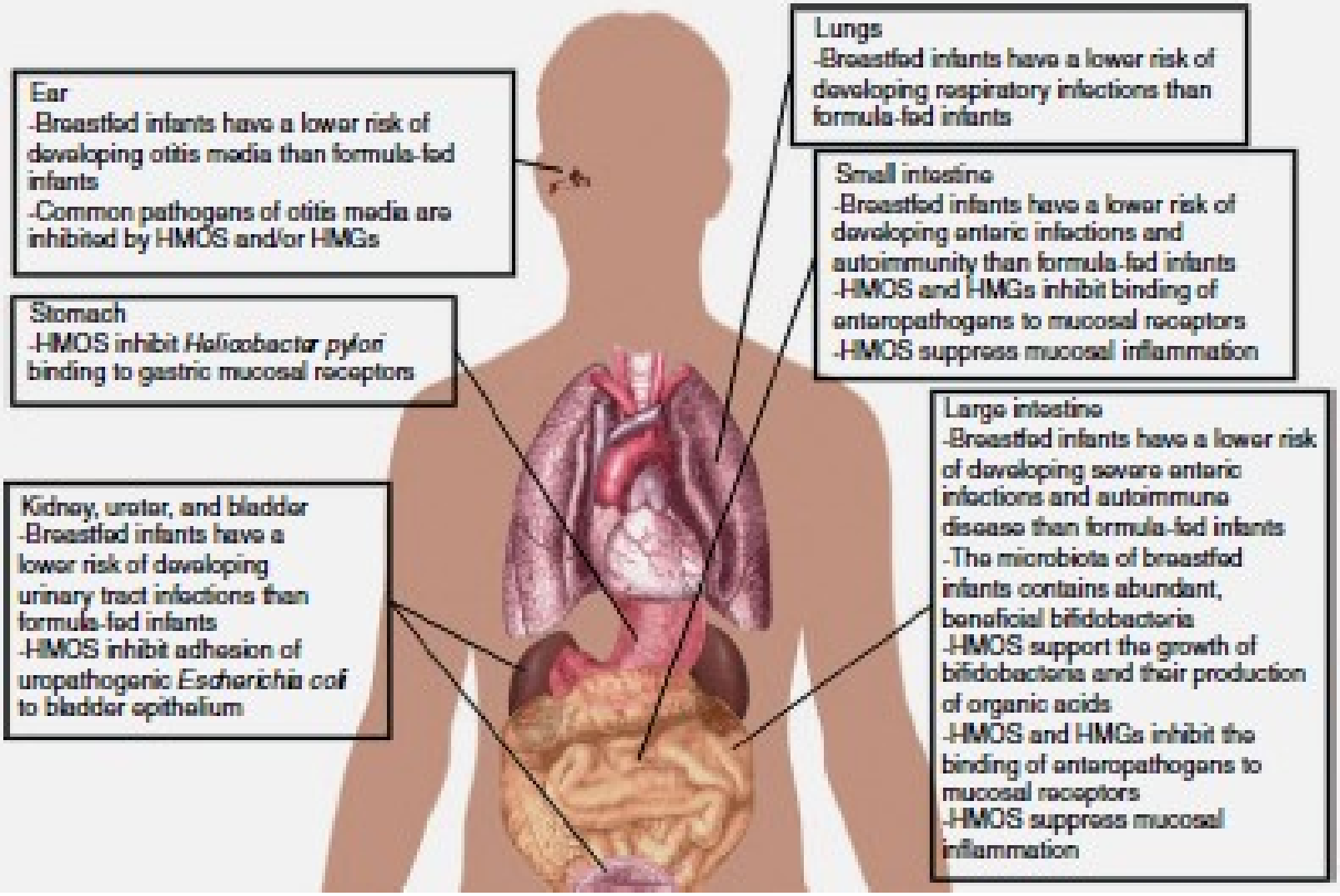
- Anti-inflmmatory properties by ↓ proinfalmmatory cytokines (IL-8, TNF-a, etc.)
- ↓ risk of NEC (necrotizing enterocolitis) in preterms
- May prevent inflammatory bowel disease in adulthood.

HMOs: potential effects

5. Brain and cognitive development

- Sialic acid is mostly found in brain's grey matter (gangliosides, glycoproteins) → cell-to-cell communication
- Breastfed babies have 32% more protein-bound SA in brain tissue.
- Brain disorders e.g. retardation, psychosis, alzheimer's disease associated with lower SA content of the brain.

HMOs: potential effects



Pediatric Research 2014;75:675-679

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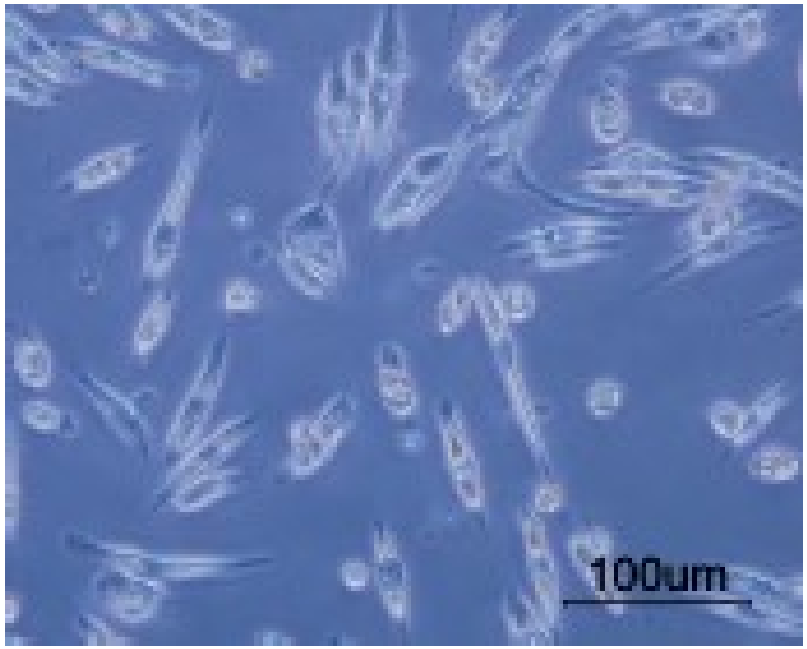
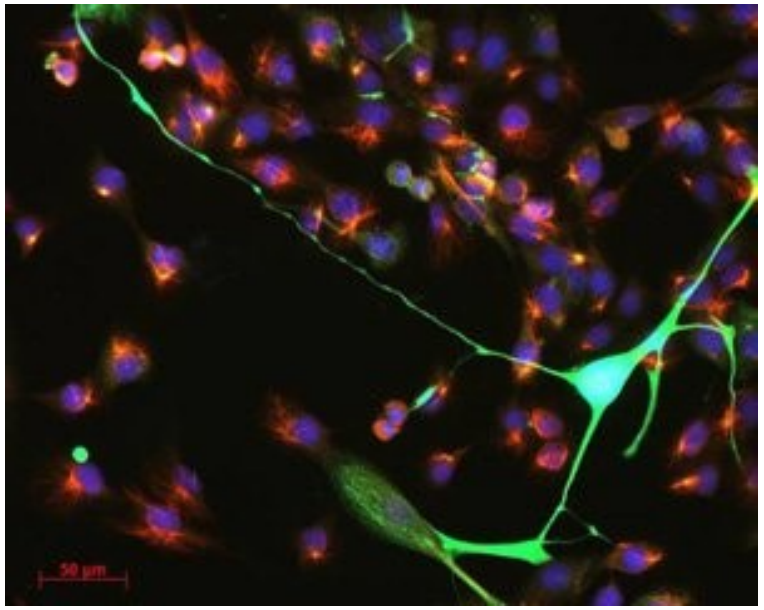
Stem cells in breastmilk: theory becomes reality



Breast milk-derived cells
Neuro Res Int 2014



Mammary stem cells (red/blue) and differentiated adult mammary cells (green) isolated from breast milk.
Stem Cells 2012;30:2164-2174

Stem Cells 2012;30:2164-2174

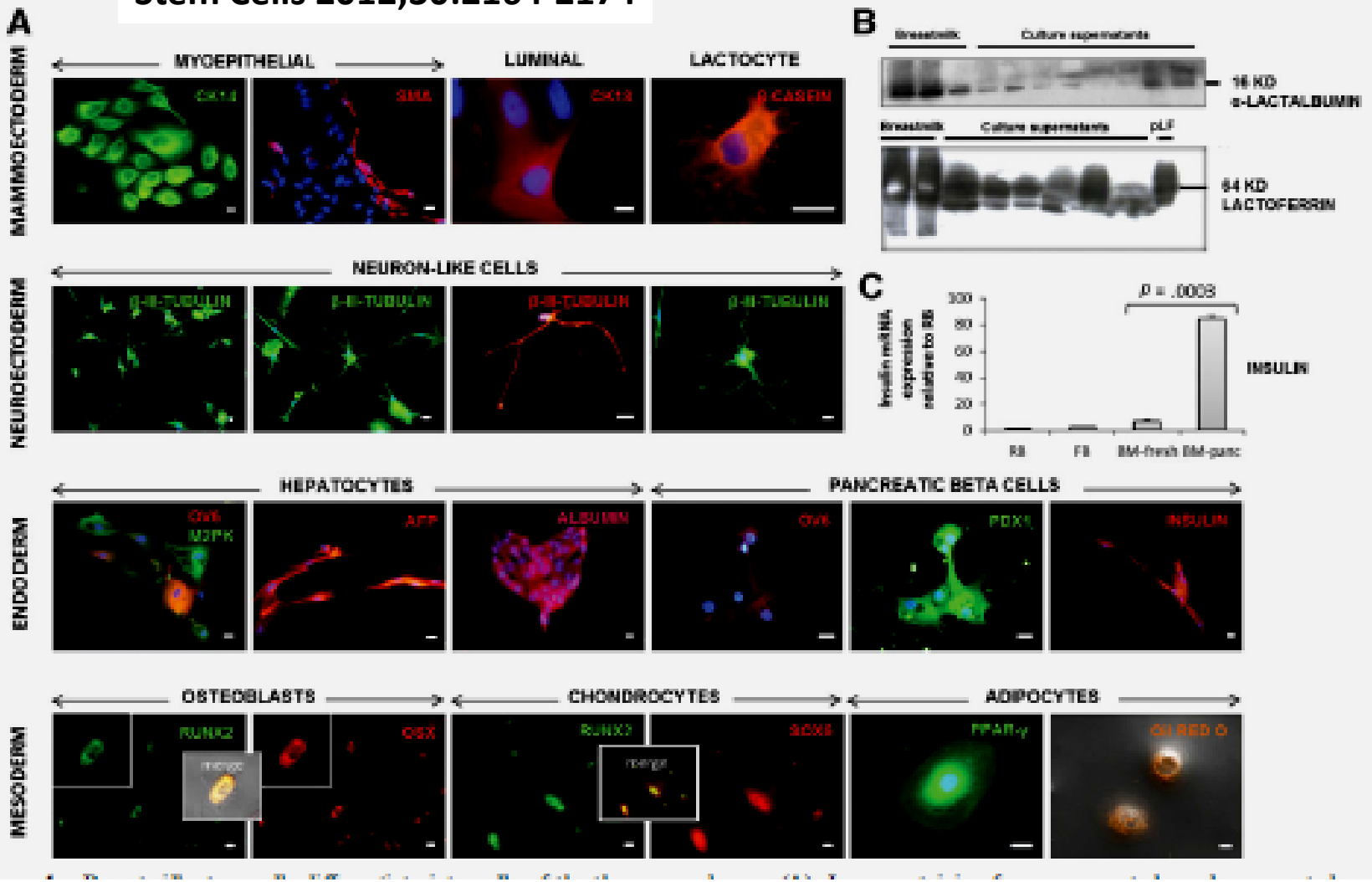
Human milk stem cells

" Internal Repair System"

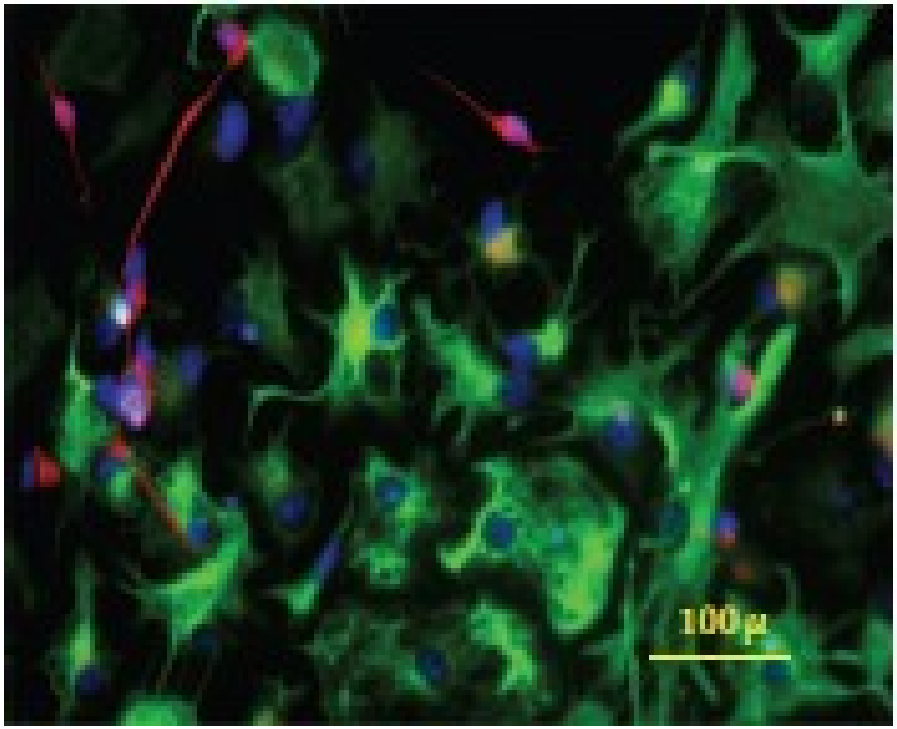
- Develop into many different cell types in the body during early life and growth.
- Hassiotou et al. studied on cell culture of pump-expressed mature breastmilk.

Human milk stem cells

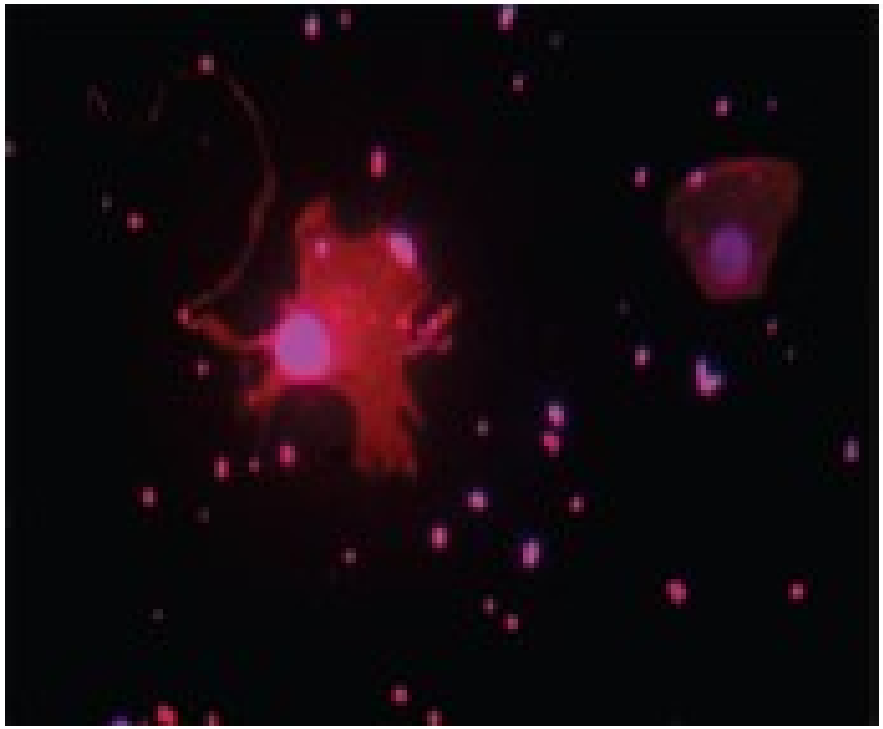
Stem Cells 2012;30:2164-2174



Human milk stem cells-derived neural stem cells



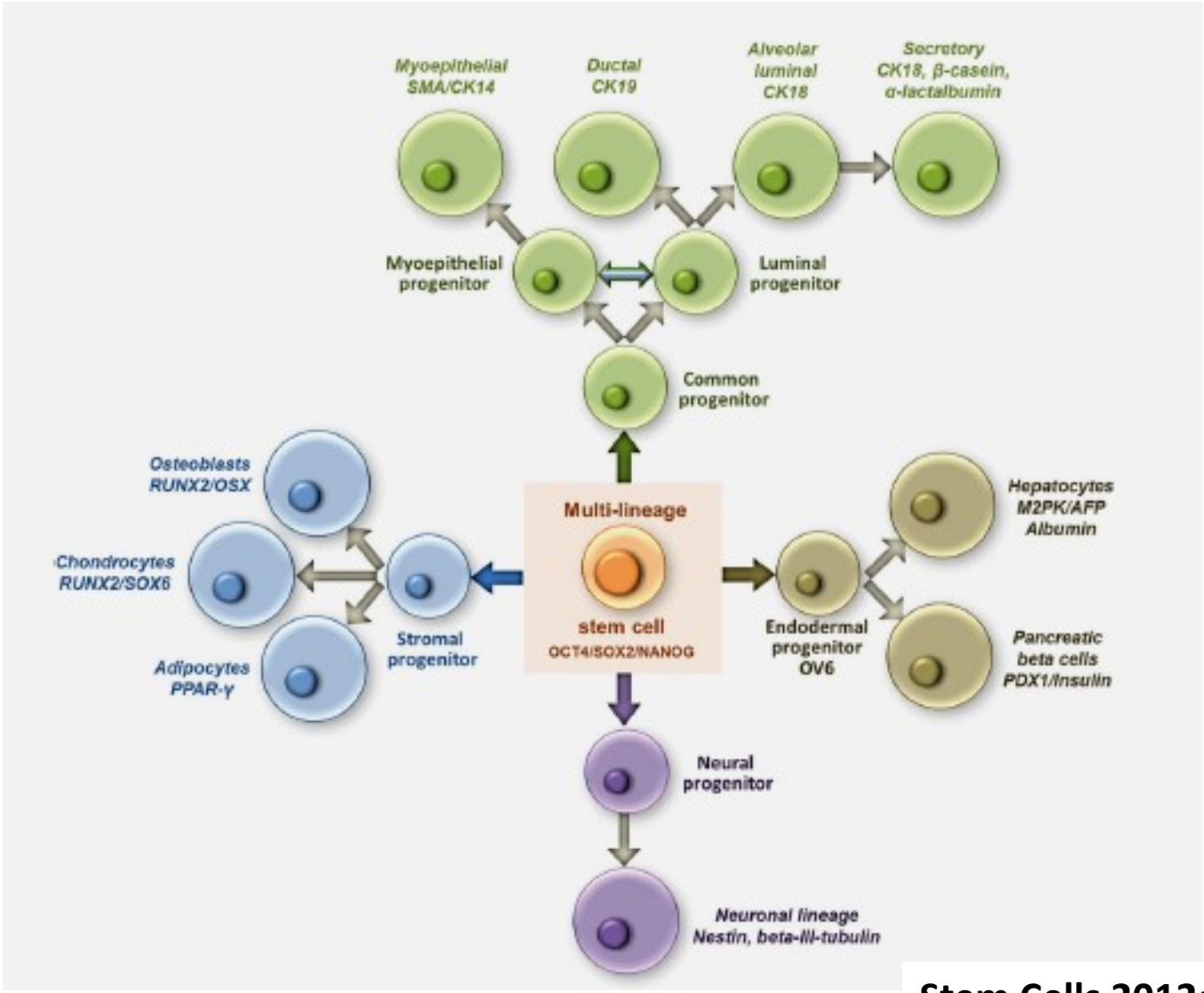
Neurons and astrocytes



Oligodendrocytes

Neurology Research International 2014

Human milk stem cells



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