Full Name:	Civics group: 21S	Index no.:	Date:

Core Idea 1: Cells and Biomolecules of Life

Stem Cells
Tutorial 12

MCQ

1	2	3	4	5	6	7
D	A	C	D	B	A	D

1 Which of the following shows the correct developmental potency of the following stem cells.

	Zygotic stem cells ➔ can differentiate into all types of cells to form a whole organism i.e. totipotent	**Embryonic stem cells** ➔ can differentiate into most types of cells except extra-embryonic tissues i.e. pluripotent	**Myeloid stem cells** ➔ can differentiate into specific lineage of cells found in the blood eg. RBCs, neutrophils, basophils i.e. multipotent	**Neural stem cells**➔ can differentiate into specific lineage of cells that make the nervous system eg. neurons, oligodendrocytes, astrocytes i.e. multipotent
A	Pluripotent	Totipotent	Multipotent	Unipotent
B	Totipotent	Pluripotent	Multipotent	Unipotent
C	Pluripotent	Totipotent	Pluripotent	Multipotent
D	Totipotent	Pluripotent	Multipotent	Multipotent

2 Which of the following best illustrates totipotency?

A A somatic cell isolated from a root tip develops into a normal adult plant. ➔ only totipotent cells can divide and differentiate into any cell type to form a whole organism.

B Stem cells are able to divide indefinitely. ➔ This is characteristic of all stem cells, not just totipotent stem cells.

C Mesenchymal stem cells can differentiate into an extensive range of cell types, including bone cells, cartilage cells, muscle cells and fat cells. ➔ This suggests that mesenchymal stem cells are multipotent as they can differentiate to form specific types of cells (albeit extensive)

D The replacement of the nucleus of an unfertilised egg with that of a pancreatic cell converts the egg into a pancreatic cell. ➔ This does not illustrate totipotency as a pancreatic cell is a specialised cell. A totipotent stem cell is unspecialised.

3 Which of the following statements is/are true regarding zygotic stem cells and cancer cells?

1 Both are able to move from one location to another. ➔ only cancer cells can undergo metastasis
2 Both are able to divide by mitotic division. ➔ True; both are eukaryotic cells capable of mitosis
3 Both are specialised cells and capable to differentiate further. ➔ False, both stem cells and cancer cells are not specialised (not playing a particular function) and are capable of differentiating further given the right environmental conditions
4 Both are capable of indefinite replication. ➔ True, telomerase gene is activated in both stem cells and cancer cells

A 2 only
B 1 and 3 only
C 2 and 4 only
D 1, 2 and 4 only

4 What is the role of stem cells with regard to the function of **adult** tissues and organs?

A Stem cells are fully differentiated cells that reside under the surface of epithelial tissue, in position to take over the function of the tissue when the overlying cells become damaged or worn out. ➔ False, stem cells are undifferentiated (not having any specific structures to play any function)
B Stem cells are embryonic stem cells that persist in the adult, and can give rise to all of the cell types in the body. ➔ False, stem cells that persist in adult are already called adult stem cells, which gives rise to limited cell types (e.g. rbc, wbc, platelets) of specific lineage e.g. blood cell line
C Stem cells are differentiated cells that have yet to express the genes and produce proteins characteristic of their differentiated state, and do so when needed for repair of tissues and organs.➔ False, stem cells are undifferentiated (not having any specific structures to play any function)
D Stem cells are undifferentiated cells that divide asymmetrically, giving rise to one daughter cell that remains a stem cell and one daughter that will differentiate to replace damaged and worn out cells in the adult tissue or organ.

5 [9648/2013/01/38] Stem cells are found in many tissues that require frequent cell replacement such as the skin, the intestine and the blood.

However, within their own environments, a bone marrow cell cannot be induced to produce a skin cell and a skin cell cannot be induced to produce a blood cell.

Which statement explains this?

A Different stem cells have only the genes required for their particular cell line. ➔ False. All stem cells of the same organism, should have the same genome

B Genes not required for the differentiation of a particular cell line are methylated. ➔ True, these genes are silenced in a long term.

C Binding of repressor molecules prevents the expression of genes not required for a particular cell line ➔ this mode of silencing is short term and is not used in stem cell's long term silencing, as the types of cells that each stem cell and its progenitors can eventually give rise to, are fixed, and a certain group of genes will not be needed to be expressed in the long run.

D Expression of genes not required for a particular cell line is controlled at translational level. ➔ Control is normally done at transcriptional level

Examiner's comments: Those selecting option C may have confused repression of genes in active cells with deactivation of genes not required by a particular cell line.

6 All the following statements about stem cells are **true except**

A Cord blood stem cells will only give rise to blood cells. ➔ False. Haematopoietic stem cells found in the cord blood are pluripotent. They have the ability to differentiate into any cell type except those found in extra-embryonic tissue.

B Cord blood from the newborn is a source of adult stem cells. ➔ True. Cord blood is rich in haematopoietic stem cells as well as other types of adult stem cells.

C Adult somatic cells can be reprogrammed to behave like embryonic stem cells. ➔ True. This is how induced pluripotent stem cells (iPSCs) are created.

D Cord blood stem cells are pluripotent. ➔ True. Haematopoietic stem cells found in the cord blood are pluripotent.

7 Which of the following is a valid **ethical concern** on the use of stem cells?

A Use of adult stem cells could result in the formation of new organism. ➔ adult stem cells are multipotent and cannot give rise to the entire new organism

B Totipotent stem cells should be recommended as they are in huge abundance. ➔ totipotent stem cells are not in huge abundance as they lasts for a short time only before differentiating into embryonic stem cells. Most research involves the usage of embryonic stem cells

C Skin stem cells usage should be prohibited as they are limited in quantities. ➔ not an ethical concern; skin stem cells are easily harvested.

D Embryonic stem cells retrieval results in the destruction of human embryos. ➔ human embryos might be regarded as alive.

STQ

QUESTION 1

(a) Describe the features of myeloid and lymphoid stem cells and discuss their use in the treatment of leukemia.

……[6]

Features (max 3)

General features

1 Self-renewal ability / divide continuously by mitosis to produce new stem cells;
2 Unspecialized and undifferentiated;

Specific features

3 Derived from **specialized tissues**.g. from the bone marrow / peripheral stem cells suspended in the blood / cord blood;
4 Multipotent as they are able to **differentiate into a limited range of cell type** by differential gene expression and produce only cells of a **specific lineage;**
[E.g. Myeloid stem cells can differentiate into red blood cells, platelets as well as various types of white blood cells (monocytes, neutrophils, basophils).
E.g. Lymphoid stem cells can differentiate into 3 types of white blood cells – B lymphocytes, T lymphocytes and natural killer cells.]

Use in the treatment of Leukemia (max 3)

1 Blood stem cells can be obtained from the patient or a donor and preserved.
2 Most of the cancerous cells in the patient are killed during chemotherapy/radiation therapy.
3 The stem cells are then re-injected after treatment is completed, wherein they are able to asymmetrically divide to form stem cells and progenitor cells which can differentiate into red blood cells, white blood cells and platelets to keep the body healthy and to help fight infections.

Enrichment:

Post mortem discussion:

Example 1: Skin grafting

- Skin stem cells are found in the basal layer of the epidermis and at the base of hair follicles.
- epidermal stem cells give rise to keratinocytes , which migrate to the surface of the skin and form a protective layers.
- Follicular stem cells give rise to both the hair follicle and the epidermis.
- Skin cells can be grown in large numbers, providing life-saving skin grafting treatment for burn victims.

Example 2: Type 1 Diabetes treatment

- Eliminate daily injections of insulin by generating insulin-producing pancreatic cells from stem cells obtained from a normal pancreas and transplanting them to the pancreas of a diabetes patient.

(b) Describe the differences between stem cells and cancer cells.

……[3]

1 Unlike stem cells, **cancer cells do not differentiate to form other cell types**;
2 Cancer cells do not show **density-dependence inhibition** while stem cells experience density-dependence/contact inhibition;
3 Cancel cells do not show anchorage-dependence for division / can divide while in suspension whereas stem cells show anchorage-dependence for division.
4 Cancer cells **metastasize** (dislodge from original tumour and form secondary tumours) while stem cells remain in tissue of origin;
5 Cancer cells have mutations in genes for eg. gain of function mutation in proto-oncogenes to form an oncogene / loss of function mutation in tumour suppressor genes *(give atleast 1 example of a mutation)* whereas stem cells do not have mutations in their genes.
6 Controlled vs uncontrolled cell division
7 **Dysregulation of cell cycle checkpoints** in cancer cells, but not in stem cells.

QUESTION 2 [Worked example]

Describe the features of zygotic and embryonic stem cells that distinguish them from each other.

……[4]

Feature	Zygotic stem cells	Embryonic stem cells
Source of cells	Derived from the cells of the morula	Derives from the inner cell mass of the blastocyst
Potency	Totipotent – they can divide and then their progenitor cells can differentiate into **any cell type**	Pluripotent – they can divide and then their progenitor cells can differentiate into **any cell** type except extra-embryonic tissues such placenta, chorion, amniotic sac etc.
Normal function	Divide via mitosis and differentiate to **form a blastocyst** that eventually forms the whole organism	Divide via mitosis and **differentiate into specialised tissues** to form specific organs of the organism
Use in therapy	Not used in therapy; **Difficult to harvest** due to the small number of cells in the morula (~16) and their rapid division to form a blastocyst (~2-3 days)	Use in therapy; **Easier to harvest** from the blastocyst and have approximately the same differentiation potential as zygotic stem cells.

QUESTION 3

The response of the human body to tissue damage depends on the types of tissues involved.

Epithelial tissue, liver tissue and cardiac muscle tissue each respond differently to damage.

- Epithelial tissue in the lungs contain stem cells.
- Liver tissue contains cells that can divide when stimulated.
- Cardiac muscle tissue contains cells that cannot divide at all. Damage is permanent and is associated with scar tissue formation.

Researchers hope to repair heart tissue damaged by heart attacks. Cellular therapy using stem cells offer ways to replace damaged cardiac muscle tissue.

Some fully differentiated cells from the patient can be reprogrammed into stem cells in tissue culture as seen in Fig. 3.1. Such cells are called induced pluripotent stem cells (iPSCs).

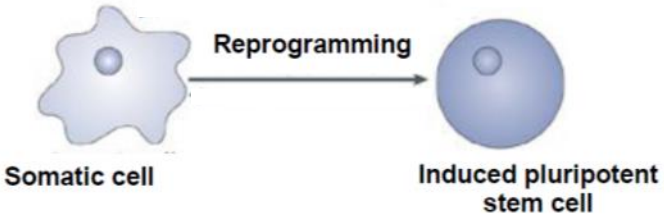

Fig. 3.1

(a) Outline two advantages of using induced pluripotent stem cells (iPSCs) in a patient suffering from a heart attack, to generate cardiac muscle for treatment.

……[2]

1 As iPSCs are derived from the patient, they <u>will not trigger immune</u> response/tissue rejection ;
2 As iPSCs are derived from the patient, there is no need for intake of immunosuppressant drugs to prevent tissue rejection that make the patient vulnerable to opportunistic infections
3 As iPSCs are derived from the patient, it overcomes problem of finding suitable donors who is a genetic match for the patient
4 There is no need to screen for eligible donors / there is no risk of infection from donor tissue
5 As use of iPSCs does not involve the destruction of embyros, they have lesser ethical issues associated with their use than embryonic stem cells.

[max 2]

In experiments with mice, it was discovered that the introduction of four specific genes that code for transcription factors would reprogramme fully differentiated cells to iPSCs.

(b) Suggest how the insertion of genes coding for transcription factors can cause a differentiated cell to become pluripotent.

……[2]

1 Ref. transcription and translation of inserted genes result in synthesis of transcription factors (proteins) ;
2 which will then activate / inhibit (idea of) expression of specific genes ; whose proteins enable cell to be pluripotent / ref. to divide continuously / ability to differentiate into almost any cell type;

There is evidence to suggest that the introduction of the four genes has caused an increase in the production of telomerase in the fully differentiated cells.

(c) Explain how telomerase may contribute to the re-programming of mouse skin cells into stem cells.

……[2]

1 Telomerase plays a part in increasing the length of the telomeres / Ref. mechanism involving telomerase extends chromosome ;
2 In doing so, **counteracts** (Reject: prevents) end-replication problem to allow indefinite cell divisions / DNA replication to continue over a longer period of time,

Scientists investigated the use of iPSCs to treat type I diabetes in mice. The scientists reprogrammed skin cells to form iPSCs. They inserted a normal copy of the insulin gene into the cells to correct the gene mutation. The scientists then stimulated the *in vitro* differentiation of iPSCs into pancreatic stem cells.

The scientists set up three experimental groups:

- Group **A** – 30 mice with type I diabetes received pancreatic stem cell transplants derived from iPSCs.
- Group **B** – 30 mice with type I diabetes were left untreated.
- Group **C** – 30 mice without diabetes were left untreated.

The scientists measured the fasting blood glucose concentration of all the mice on a weekly basis for 12 weeks.

The results the scientists obtained are shown in Fig. 3.2

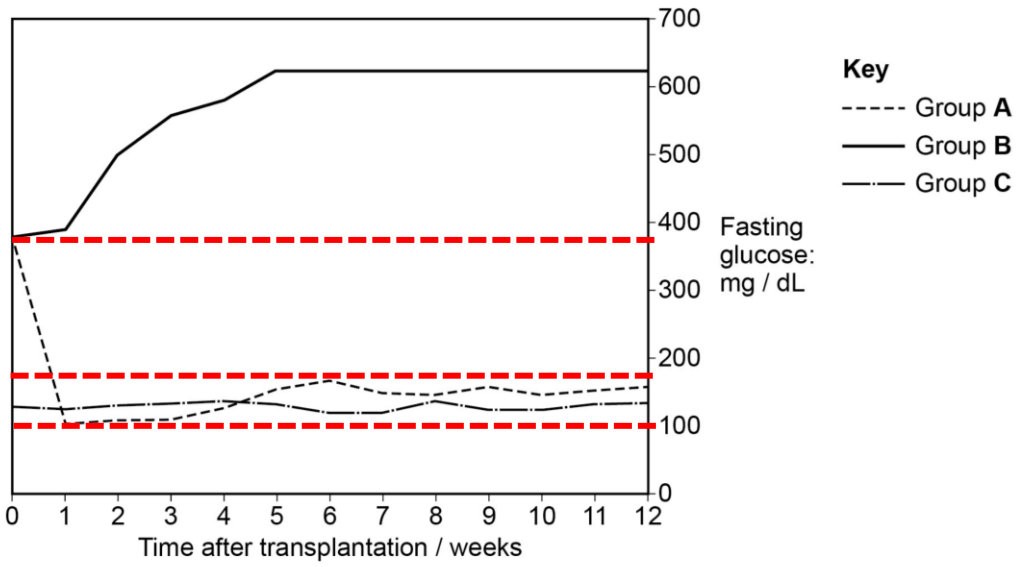

Fig 3.2

(d) Using all the information provided, discuss the effectiveness of iPSCs to treat type I diabetes in humans.

……[4]

(At least 2 points from each side for a balanced answer)

1 (Effective as) group A (treated with iPS cells) had **lower levels** in fasting blood glucose level **between 100 to 180 mg/dL** vs group B that was not treated had **higher level** of fasting blood glucose between **400 to 680 mg/dL 1 week after transplantation.**
OR (Effective as) group A (treated with iPS cells) had **sharp decrease** in fasting blood glucose from **380 mg/dL to 100 mg/dL in 1 week** after transplantation vs group B that had a **sharp increase** in fasting blood glucose **from 380 mg/dL to 630 mg/dL in 5 weeks** after transplantation.

2 (Effective as) group A (treated with iPS cells) had **similar levels** of fasting glucose as group C (without diabetes) between **100 – 180 mg/dL**.

3 (May not be effective as) study done on mice not humans, may not have the same effect

4 (May not be effective as) Only shows results for 12 weeks/short-time period / long-term effects not known;

(e) Suggest **one** advantage of using stem cell therapy in treating type I diabetes.

……[2]

1 Long term solution – self-renew/ less harm inflicted because less pain because no need for daily intravenous injection of insulin/ save cost (daily injections can be costly)

2 Cells can regulate insulin released based on negative feedback in the body vs injection is fixed dosage or there is possibility of overdose/ underdose of insulin

QUESTION 4

A cybrid (cytoplasmic hybrid cell) is produced as shown in Fig. 4.1.

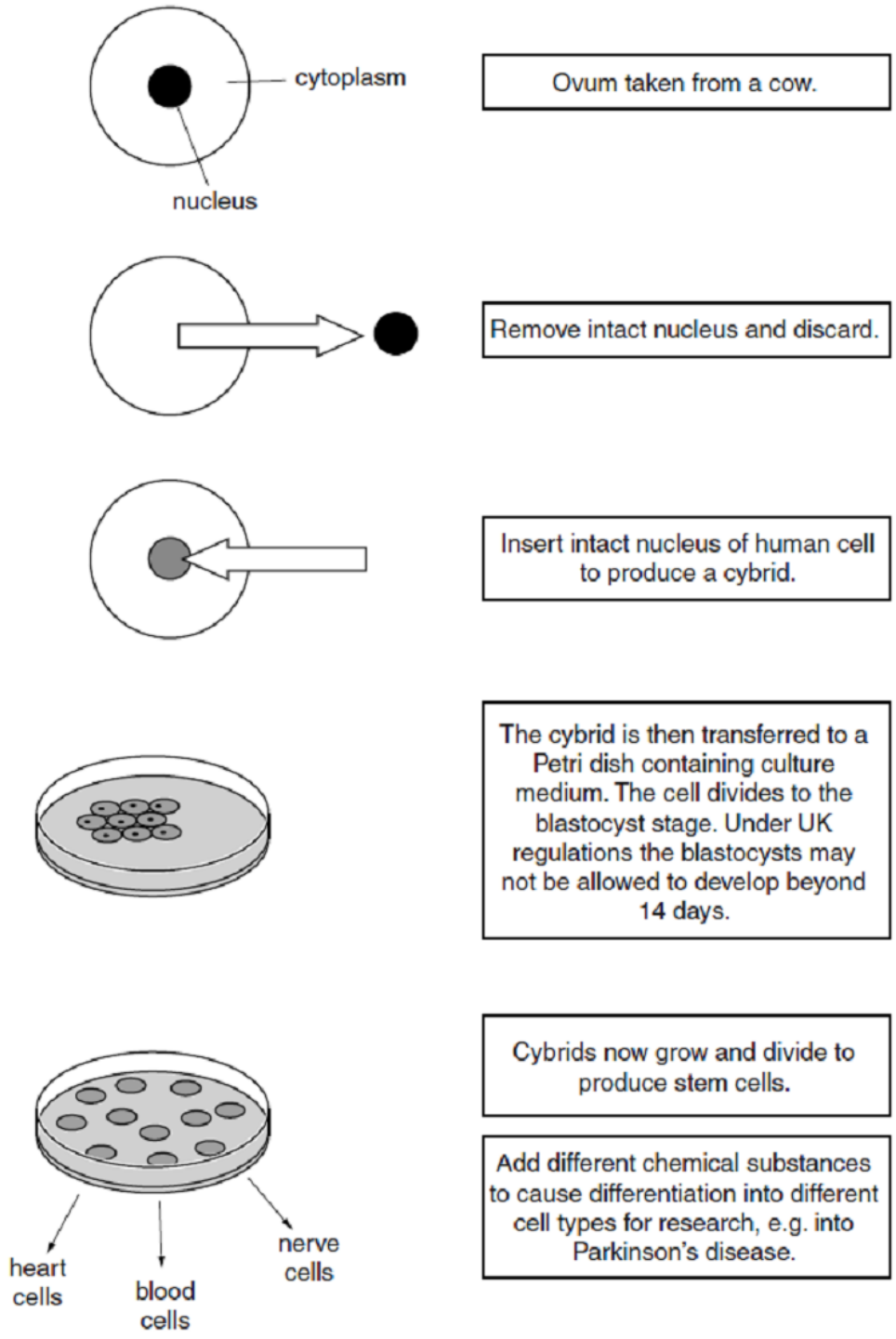

Fig 3.1

(a) The DNA of such a cybrid is 99.6% human. The remaining 0.4% of the DNA is in the cytoplasm. Explain the presence of the 0.4% DNA in the cytoplasm.

……[1]

1 Mitochondrial DNA ; from the cow ;

(b) Suggest an explanation to why the UK regulations do not allow blastocysts used in research to be developed beyond 14 days.

……[1]

1 Blastocysts that develop beyond 14 days have the **potential to form a human being** hence there will be **more ethical concerns** over using them in research.

(c) Some people argued that it is unethical to allow the production of cybrids and its use in treatment.

State whether you agree **or** disagree that this is unethical **and** explain why you reached this decision.

Choose a stand first.

……[2]

Unethical: **[Any 2]**

1 presence of human and animal DNA means it is partly human and partly cow / a human animal hybrid which would not happen in nature; unnecessary because, there already are alternative techniques (to the use of embryonic stem cells) e.g. use of adult stem cells/umbilical cord cells ;

2 claims of the benefits of cybrid stem cell research are over-rated / few (if any) examples of success in medical applications ;

3 possibility of unforeseen (irreversible) long-term consequences ;

4 idea that transplanted cells bovine proteins which would be rejected at transplantation ;

NOTE: Ignore references to 'playing God' and 'against religion'.

Ethical: **[Any 2]**

1 the amount of non-human DNA is very small/negligible ;

2 protocol limits keeping 'embryo' to 14 days (to guard against abuse) so cannot develop into a whole organism ;

3 provides a more ethical alternative to the use of embryonic stem cells from human stem cells

4 Ability to harvest more bovine ova therefore can provide many more stem cells than is possible from embryonic stem cells from human;

5 it would be unethical not to use cybrids to relieve, human suffering / e.g. diseases such as Parkinson's disease ;

If a candidate does not express an opinion, limit score to one mark unless an attempt has been made to argue that it is a finely balanced matter.

[Total: 3]

ACTIVITY – CORD BLOOD DONATION

Cord blood banks are facilities that store cord blood derived from the umbilical cord during delivery. These are either run by the government (e.g. Singapore Cord Blood Bank) or by private companies (e.g. Cordlife).

Pregnant women are approached by cord-blood banks to decide whether they want to store the cord blood of their baby for the immediate family's use for a fee or donate it to the public cord-blood bank or for research free of charge.

Task 1 (to be done before tutorial)

Imagine you are pregnant/your wife is pregnant with your first child. You are approached by the Singapore Cord Blood Bank. The agent provides you 2 resources: **#1 Brochure** explaining benefits of cord blood in therapy, Public Donation and Family Banking of cord blood and **#2 Fee schedule** for Family banking. You may also choose to not donate/store the cord blood in which case it is discarded after the baby's delivery.

Using the information provided in the brochure and fee schedule and, **your own research** about cord blood banking, take a stance on whether you want to donate/store and if you do then would you opt for Public Donation or Family Banking. Describe at least 3 reasons to support your stance. Complete the box below:

Stance (Tick 1):

- ☐ I do not want to donate/store cord blood
- ☐ Public Donation - I want to donate cord blood to the public cord blood bank
- ☐ Family Banking - I want to store cord blood for my family's use only

Reasons to support your stance:

1. ……
   ……
   ……
2. ……
   ……
   ……
3. ……
   ……
   ……

Task 2 (In class activity) – Divide the class into smaller groups based on their stance and discuss the reasons behind their stance in class.

Resource #1 page 1 – Use of cord blood in therapy

Thank you for your interest in cord blood banking

SCBB will not be able to accept cord blood from expectant mothers below 18 years of age and/or if there is more than one baby for the particular pregnancy.

To be suitable for Public Cord Blood Donation, donor parents must NOT have the following conditions:

- **Blood & Metabolic Diseases and Transfusion** e.g. red blood cell disease, white blood cell disease, immune deficiencies, multiple sclerosis, Crohn's disease, rheumatoid arthritis and lupus.
- **Infectious / Communicable Diseases** e.g. Hepatitis B or C, HIV or the AIDs Virus, West Nile virus, Tuberculosis or Malaria.
- **Sexually Transmitted Disease** e.g. Syphilis
- **Cancer – any type of cancer**
- **Organ or tissue transplant** e.g. heart, lung, kidney, bone marrow or other organ or tissue transplant.

SCBB family cord blood banking is a new service for parents who wish to store for their family.

Blood Cancers

are amongst the

TOP 10 CANCERS[1]

in Singapore

Life-saving Transplants

Stem-cell (from bone marrow, peripheral or cord blood) are commonly used for such stem cell transplants.

Cord Blood is Precious

If parents have not made a decision to bank or donate the cord blood, it is normally discarded.

Ethnicity Matters!

Stem-cell matches are most likely to be found in donors of the same ethnicity.

[1] Singapore Cancer Registry, National Registry of Diseases Office. Annual Registry Report - Trends in Cancer Incidence in Singapore 2010 - 2014

Resource #1 page 2 – Public donation vs Family banking

SCBB Community Cord Blood Banking

Public Donation

Donate. Save Lives.
- Help 60% of patients to find a match

Increase Public Inventory
- Many patients with blood cancers and disorders rely on donated cord blood for an allogeneic (unrelated) cord blood transplant.

Donor Diversity Critical
- Match only found among same race

More information on Public Donation

Family Banking

Cord Blood is Precious
- Potential use in regenerative medicine, research and clinical trials

Store for Family
- Fee for storage
- Flexible storage plan

Donate Later
- Potential donation after family storage
- If unit meets donation criteria

More information on SCBB Family Banking

"Parents who save their children's cord blood in private cord blood banks, need to be aware that should their child develop leukaemia, the child's stored cord blood already contains premalignant cells and cannot, therefore be used to treat the child (autologous transplant).

New developments in early clinical trial research for regenerative purposes may affect cord blood banking in the future. Some examples of these trials of cord blood transplants are those for Alzheimer disease, autism spectrum disorder, diabetes, cerebral palsy, hypoxic ischemic encephalopathy, systemic lupus erythematosus, and systemic sclerosis. However, no breakthrough in therapy has yet been realized."

American Academy of Pediatrics
Policy Statement, October 2017

Resource #1 page 3 – FAQs about cord blood storage

Frequently Asked Questions

1. What is cord blood?

Cord blood is rich in blood stem cells, and is usually disposed after a baby's birth. If successfully stored, it can be used to treat blood cancers and disorders.

2. What is Community Cord Blood Banking?

SCBB Community Cord Blood Banking is an ethical approach to cord blood banking which provides parents with clear and balanced information to educate and enable parents to make an informed decision, with full autonomy of choice. It includes both public donation as well as family banking services. Public banking (also known as Cord Blood Donation) remains SCBB's core mission and focus.

3. What is the difference between family banking offered by SCBB and other private banks?

The key difference is that parents can choose to donate their cord blood in future, subject to the donation criteria, if they decide not to continue with family storage. This will potentially increase the public inventory, to save the lives of more patients with blood cancer or disorder.

4. What is the storage duration for SCBB family banking?

SCBB offers an initial storage period of five years. Depending on the growth and well-being of the child in the first five years, parents can then decide if they would like to continue storage.

"The birth of a child is such a wonderful moment. Make it even more special by giving the gift of life to another person in need! Donate your baby's cord blood!"

Mandy Loh
(2-time Cord Blood Donor)

"It is wasteful to discard cord blood when we know that it could help save someone's life."

Jannathnisha Binte Mohideen Pitchay
(4-time Cord Blood Donor)

SINGAPORE CORD BLOOD BANK

Laboratory
c/o KK Women's & Children's Hospital
100 Bukit Timah Road, Women's Tower Basement 1,
Unit 0B60A, Singapore 229899

Management Office
37 Jalan Pemimpin
#04-14 Mapex
Singapore 577177

63945011
donate@scbb.com.sg
www.scbb.com.sg

Resource #2 - Fee Schedule from Singapore Cord Blood Bank for Family Banking

Fee Schedule

SINGAPORE CORD BLOOD BANK

A. Cord Blood Banking Service

Cord Blood Banking Service : ☐ Direct Family

Babies in this pregnancy : ☐ One ☐ Twins

Storage Period : ☐ Annual ☐ 5 Years ☐ 21 years

Service	Direct Family		
	Annual	5 Years	21 Years
Cord Blood Banking Fee	$1,100		
Storage Fee	$250	$1,250	$5,250
*Storage Fee Discount**	*NA*	*10%*	*26%*
Total Fee	$1,350	$2,225	$4,985

*Additional discount of 10% applies if either one or both parents are working in healthcare

B. Additional Tests ☐ **Yes** *(Select below)* ☐ **No**

☐ **Newborn Screening – Hemoglobinopathy** **$75.00**

Evaluation of inherited blood disorders like sickle cell disease and thalassemia.

☐ **Human Leucocyte Antigen (HLA) Typing**..... **$175.00**

HLA typing is a genetic test performed to determine tissue type of a person. This data will be used to perform matching of donor and recipient during transplantation.

- The Service Fee stated are in Singapore Dollars (S$) and are exclusive of and shall be subjected to payment of goods and services tax ("GST") imposed under the prevailing legislation which shall be payable by Client. The applicable GST shall be incorporated in the total amount in SCBB's invoice.
- The Client shall pay the Service Fee and any applicable fee for additional tests to SCBB within thirty (30) days[1] from the date of invoice
- If the banking services is extended for **twin pregnancy**, the Total Fee shall be multiplied by two.

Client's Name _____ Client's Signature _____ Date _____

[1] Credit terms may not be applicable if the payment is by Child Development Account.