Logbook

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7b

2023-12-21

Chosen Topic:

Study of Coagulation and Hemophilia (a rare blood disorder)

Reason of selection:

I chose Hemophilia to creat awareness and understanding of this genetic blood disorder. Research showe 1 in every 5000 men are hemophilic and 75% of them are not even diagnosed. Coagulation is a very important function of the human body and is a intresting topic to study.

Areas of science:

Human biology and health

Introduction:

Have you ever gotten a cut or scrape and wondered how it magicly stops bleeding? It's like a superpower your body has - coagulation We're going to explore this superpower and how it works.

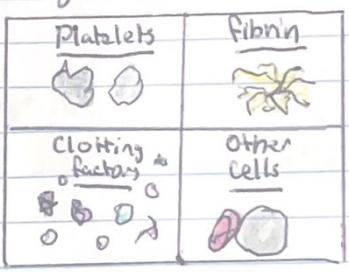
A powerful team made of tiny platlets and special proteins called clotting factors, work togather as a bandage to, stop the blood from flowing, and healing the wound.

But what if one of these factors is missing from this powerful team. There is this genetic disorder/condition named hemophilia where a person is missing a factor of this team called factor 8 / factor VIII; that is what we are going study

2023-12-22

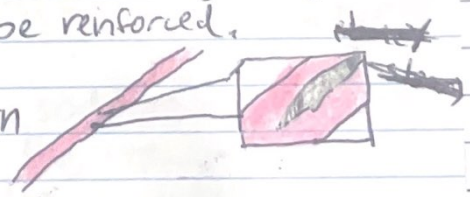
Coagulation:

Usualy everytime you have a cut or bruise your blood clots to stop the bleeding. Clotting is a complex process and there are 4 ~~more~~ main things that make it possible; platelets or cell fragments, clotting factors, or special proteins, fibrin (protein mesh), and finnaly other cells (ex: Red and white blood cells). Because cloth formation is so important, platelets and clotting factors are alway available; floating around in your blood.

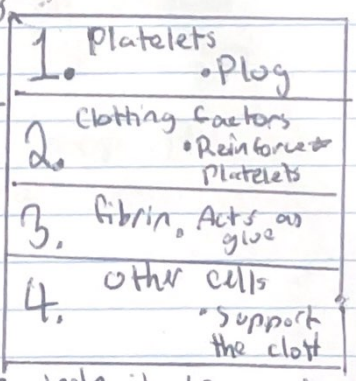


4 Steps for blood clotting:

When there is a tear in a blood vessel, the first thing that happens is that the nearby platelets are activated, and becom sticky. they start sticking to each other and to the sides of the hole, usualy the platelets can form a temporary plug but this plug isnt strong enough to hold for long, so it must be reinforced.



Passing by clotting factors turn themselves on or activate and add themselves to the platelets plug. A special kind of clotting factor can weave itself together with others of the same kind and form a web of fibrous tissue called fibrin this web act as a glue. Other cells like red and white cells can also help reinforce the clotte that help it become stronger.



23-12-25

Understanding coagulation through a experiment

Meterials

- Red sodium Alginate (10 ml)
- White sodium Alginate (1.2 ml) - optional
- Calcium chloride (1/8 tsp / 600 mg)
- Pipette
- Cup
- Water (50 ml)
- Stir stick
- Vial - optional

Procedure

Fill your cup with 50 ml of water and add 600 mg of calcium chloride and stir until the powder is dissolved.

In a sepperate bowl squeeze 10 ml of sodium alginate. Grab a pipette and and gentely drop blobs of sodium alginate into the calcium chloride bowl; Red blood cells are formed!!! Repeat until empty.

Optional: Drop 6 drops of white sodium alginate into a spoon and hold the spoon in the calcium chloride mixture for ten seconds; a white blood cell is formed!!!. Repeat thrice.

Optional: Drain the water and scoop the red and white blood cells and place them into a empty vial to keep.

	In the Human body	What I used in the experiment
Substance that requires calcium to coagulate	Blood	Sodium aliginate solution
Source of calcium for coagulation	Platelets that increase the amount of calcium around the wound	Calcium chloride solution
end product of coagulation process	Blood clot	Semisolid balls of calcium aliginate

26-12-23

Hypothesis 1:

If the strategy of gene therapy i.e ✗ engineering special stem cells having the ability to produce high levels of factor VIII and transplanted into the patient, succeds, it could potentialy revolutionize hemophilia treatment by significantly improving blood clotting and creat a more effective treatment method

Hypothesis 2:

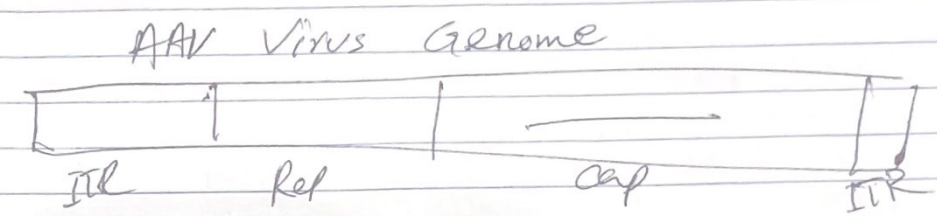
If a educational program was made to creat awarness about hemophilia, ~~and~~ how geneticaly passes from 1 person to another and promote well informed family planning, I hypothesize that there will be more genetic counseling and testing services. This increased awerness will increas smart decisions and decrease the chances of hemophilia passing to the next generation

not used

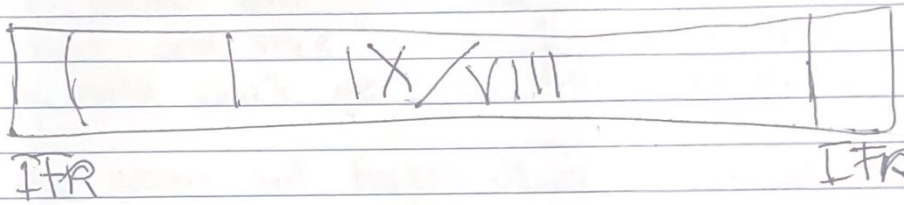
06-01-24

Gene therapy

Adeno Associated Virus (AAV) has a genom which is encapsulated in just 1 chromosome.



Recobinant AAV vector genome



So we use a AAV to inject into the blood that contains either factor VIII or IX and a promoter which makes sure it regenerates. Originaly it contains 1 chromosomes and 2 genes and the lining on the sides, to protect it

01-13-24

Hemophilia gene therapy dream or reality? NIC

Dr. David Lillicrap - episode 1 - Reality

- Children are not able to get therapy done because the vector mostly can't get into the chromosomes and stays floating in the nucleus in structures called episomes. When the cell devides the episomes are left behind. Because of this when the childs liver grows and the episomes are left behind, and since it's a 1 time treatment the child can't get gene therapy again.

- The reason that factor IX therapy is more effective then factor VIII is the fact that we are making the hepatocytes cells make factor VIII when normally its another type of cell and so though it can make it it won't be as good as the normal factor VIII, factor IX though is produced in the hepatocytes cells soo it works pretty good.

- Hepatotoxicity - happens 2-4 months after infusion - liver cells are leaking or dieing - treatment: supression of immune system (steroids) for 1-10 months - big issue

Dr. Brian Ommani - episode 2 - mid

- 60% hemophilia A defficient people are NOT eligible
- 40% hemophilia B deficient people are NOT eligible

- children <18 are not eligible (liver is still developing)
- gene therapy is only for severe hemophiliacs
- those with inhibitor or past inhibitors are not eligible
- those with past or present liver issues are not eligible
- those who have pre-existing antibodies against AAV vector (have had that specific virus before) might not be eligible (depending on where you live)
- irreversable treatment (no-matter outcome)
- No-alchohol 1st and/or 2nd year
- Once infussion you must go to clinic quite often to get blood tests to check your liver enzymes and blood factor levels among other things.
- Occasioaal proflaxys and clinic cheack ups and blood tests

Dr-David Lillicrap-episode 3

- Starts working after 2-4 weeks ~ month
- ~~Start~~ continues increasing ~ 6 months
- factor IV after 3-6 months stays steady- a number of years

- factor XIII after 3-6 months start to fall - fall about 50% over the course of about 2 years

- 5% have no responce to therapy

Dr. Brian Ommani - episode 4 *has gotten gene therapy for factor ~~XIII~~ IX 5

- outcomes may vary on person to person (some may get 40% some may get 100%)
- If planing to get therapy be ready for diffrent outcomes
- easy infussion
- Twice a week visits (for him) and 30 visits cos for

Dr. Glenn Pierce - episode 5

Uknowns:

- Imune responce
  - strong = bad result weak = good result
- Long term risks
- Why some have no responce while others have
- Why the levals of factor ~~VIII~~ IX may decline over time
- Rare toxicitys
- If you can get CANCER because of it

Dr. Jerry Tidle - episode 6

- Shared decidion making – Very important
  - information - treatment steps
  - Councilling - Diffrent ideas / prospects
  - Risks - qualifacations
  - Research - After procedure care
  - potetial problems eg:, cant do this or that, avoid this, ect
- Uknown responce (new technology)
  - migh even have to go back to proflaxis (not able to do again)

Dr. Duran Wang - episode 7 - about financing

Dr. Jerry Tidle - episode 8 - delivering gene therapy in canada – (already done - 3 weeks ago)

Dr. Glenn Pierce - episode 9

- New technology – start of process
- Timeline:
  - identifaction of agro participated by Judith in 1964 helped plasma fraction industry for factor IX & VIII

- mid 80s most products were completly safe for HIV ushered recombonant for factor IX & XIII
- cloned / identified at their gene structures in 1984 for factor XIII - 1982 for factor IV
- 1992 first factor XIII recombonant aproved
- 1997 first factor IV recombonant aproved
- long period of no activity
- 2014 half life products aproved
- 2017 bispecific antibod - a facto XIII mimetic aproved
- 2018 for non-inhibitor patients

- Normal people have anti-clotting factors and clotting factors - if you have less clotting you can decrease anti clotting factors so it might clott normally (only for hemophilia B) (very less chances) - ant-tfpi

- 2023 gene therapy starts getting approved

(information collected from online logs)
Work on slideshow:

- 27-12-23 Start
- 28-12-23 logbook - research
- 29-12-23 continue logbook & problem & hypothesis
- 30-12-23 abstract & Genetic transfer & hypothesis redo
- 3-01-24 start case study & transfer from logbook
- 4-01-24 history of hemophilia
- 5-01-24 Transfer from logbook
- 6-01-24 small experiment
- 7-01-24 hemophilia gene therapy start
- 10-01-24 more research & continuing gene therapy
- 11-01-24 more research
- 12-01-24 observation
- 13-01-24 analysis and conclusion
- 14-01-24 more research finish case study & finishing touches

(information collected from Online)

Jan 24 - Informed that I got selected

Jan 30 - school round

Feb 5 - selected for city round

Feb 6 - started online - Basic project info

Feb 12 - ethnic due care down & approved

Feb 13 - Problem, Method, Conclusion done

Feb 15 - citation, declarations done

Feb 16 - AKnowlagements done

Feb 17 - Research done

Feb 20 - Data done

March 7 - Presentation done

March 8 - atachments & final touches