ADHESION OF SICKLE CELLS TO BLOOD VESSELS

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Introduction

Sickle cell disease is a hereditary blood disorder that occurs because of a mutation on the Hemoglobin gene.

Quick facts about sickle cell
- Mutation causes sickle shape and increases stickiness
- 85% of people affected are in African countries
- 3.3 million cases of sickle cell worldwide
- Stickiness leads to blood vessel being blocked
- Blockage in blood vessel = Sickle cell crisis
- Has no cure

Symptoms affected by stickiness
- Anemia
- Stroke
- Jaundice
- Acute Chest Syndrome
- Spleen dysfunction:
- ❖ **What is a crisis?**

A crisis event occurs when sickle cells are blocking the movement of oxygenated blood throughout the body.
- ❖ **What influences a crisis?**

P-Selectin is a molecule responsible for adhesive properties in cells. For sickle cells, P-selectin is higher, leading cells to stick to blood vessels at higher rates. A study published recently looked at the effects of reducing P-selectin on vaso-occlusion.

Methods

What is being tested?
I want to see how different P-selectin levels affect crisis time.
When does a crisis occur?
Crisis occurs when too many cells are blocking the blood vessel.
Question: Do sickle cell crises occur faster if they collide with other cells that are already stuck, or if their P-selectin levels are high?

Hypothesis: Sickle cells crises occur faster when sickle cells have higher collisions compared to when they have high P-selectin values.

- ❖ **Classes**
  - ❖ Cell Class
    - ❖ Contains info similar for sickle and regular red blood cell
    - ❖ Regular shape
    - ❖ Location, velocity
    - ❖ Movement, acceleration
    - ❖ Collision detection
  - ❖ Sickle Class, has information for sickle cell only
    - ❖ Shape
    - ❖ Stickiness P-selectin value/ stickA value
    - ❖ Collisions, when cell has stickiness
    - ❖ Is cell blocking blood vessel?
    - ❖ Lifetime decrease
    - ❖ Checks whether cell is alive
  - ❖ Main Tab
    - ❖ Creates 20 sickle cells
    - ❖ Tracks stickA value for cells alive
    - ❖ Tracks number of cells collided
    - ❖ Tracks time taken for crisis
    - ❖ Tracks total number of cells stuck
    - ❖ Calls methods from other classes
    - ❖ Prints out sketch of cells

Results

Sketches

I ran 20 trials with stickA range 0-0.001 and stickA range 0-0.01. For each trial I tracked the value of P-selectin/stickA for the cells that were alive during a crisis, the number of cells that are stuck but not collided, the number of cells that had collided, and the time it took for a crisis to occur.

- ❖ Cells that are in the same position have stopped
- ❖ Cells are closer together in 0.001 because they can move and collide more

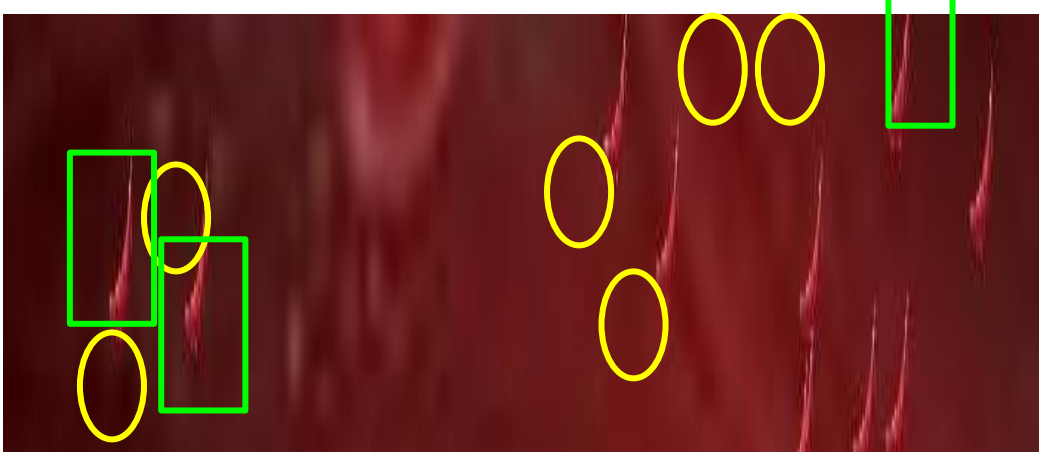Figure 5. Sickle Cell StickA random (0-0.001) vs Frame Count 200 Frame Count vs 300

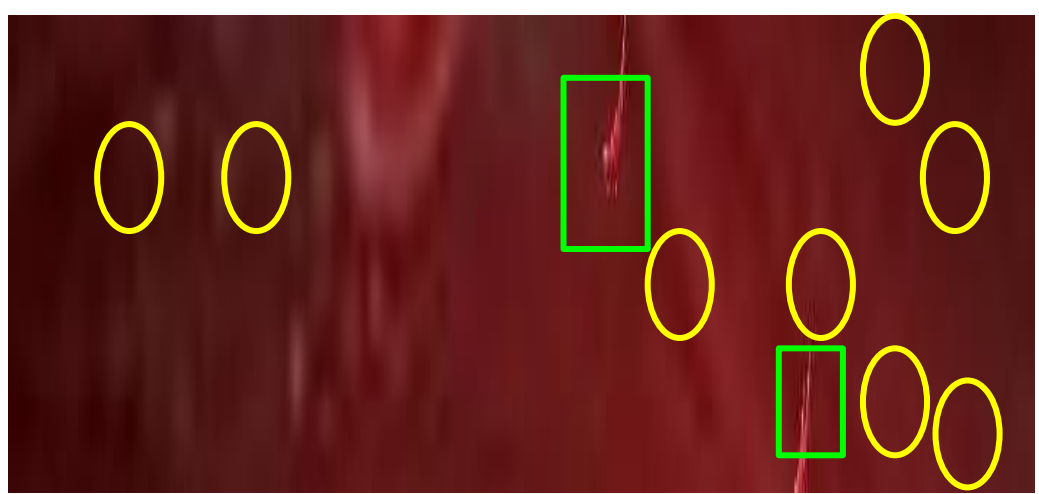Figure 5a. Sickle Cell StickA random (0-0.001) Frame Count 200

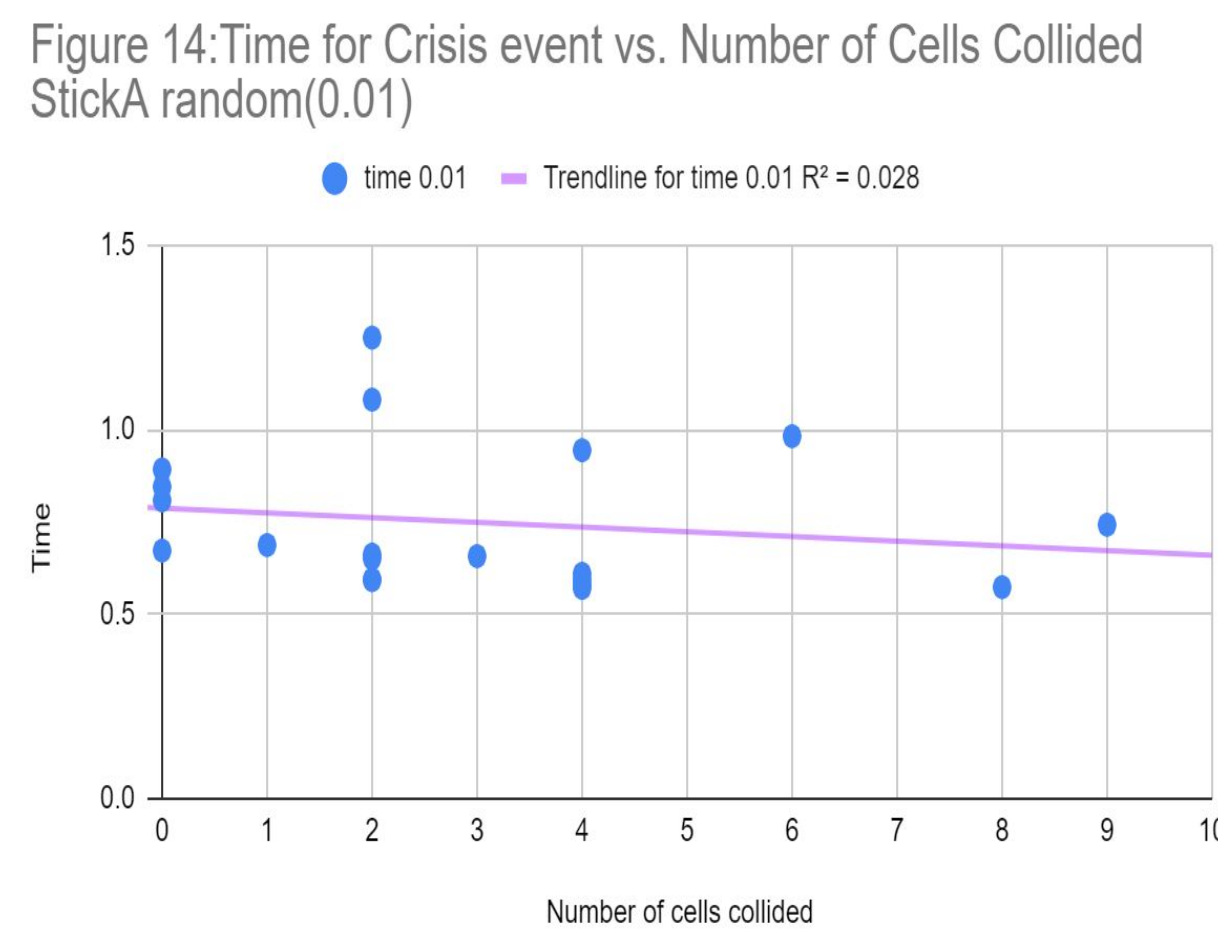Figure 5b. Sickle Cell StickA 0.001 Range Frame Count 300.

Key
Dead Cells
Collisions Stuck

When StickA is 0.01, there are more cells stuck by themselves.

Figure 9. Sickle Cell StickA random (0-0.01) vs Frame Count 100 Frame Count vs 200

Figure 9a. Sickle Cell StickA random (0-0.01) Frame Count 200

Figure 9b. Sickle Cell StickA 0.001 Range Frame Count 300.

Key
Dead Cells
Collisions/ Stuck

Time Taken for Crises Comparison Collision

Figure 5 shows the effects of collisions on the time taken for a crisis to occur. The chart shows the general effect of collisions on time.

Figure 13:Time for Crisis Event vs . Collisions for StickA random (0.001)

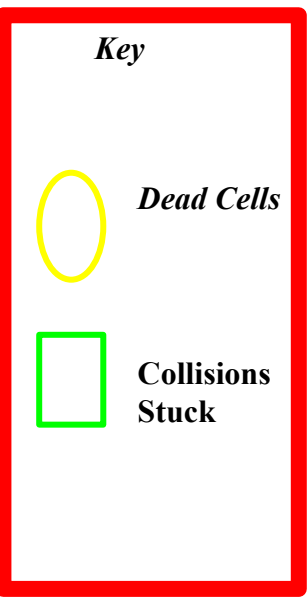Figure 14:Time for Crisis event vs. Number of Cells Collided StickA random(0.01)

Figure 5: Figure 13 +14: Collisions vs Time

- ❖ More collisions = lesser time
- ❖ The trendline has a downward slope
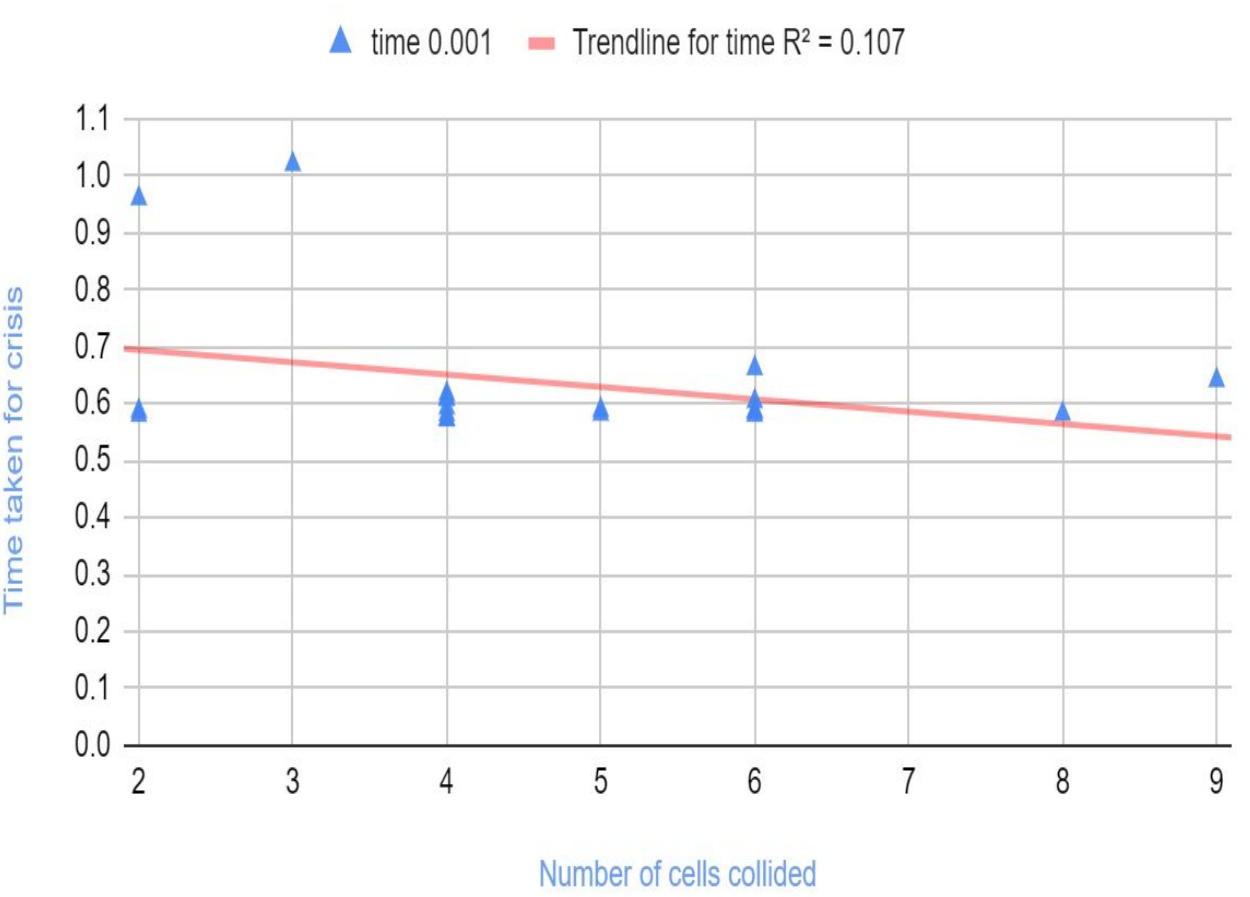
Time Taken for Crises Cells That Are Stuck but Did Not Collide

Figure 6 shows the effects of lack of collisions on crises time.
- ❖ More cells stopped without collision = higher time taken for crises
- ❖ Upward trend in crises

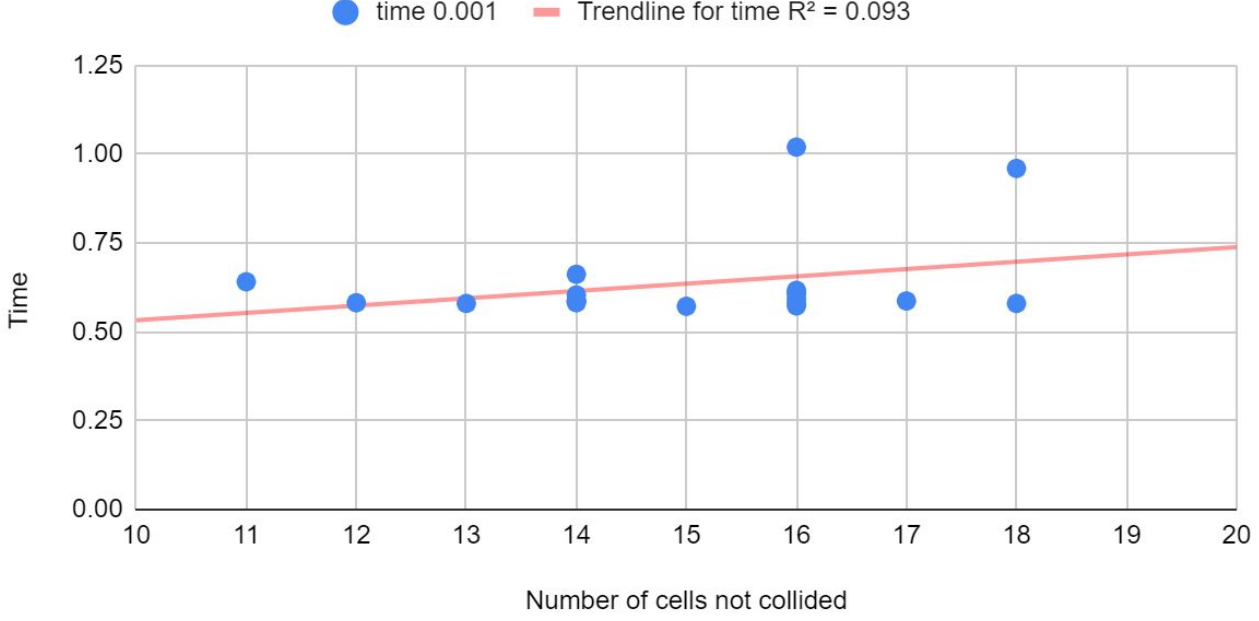Figure 11:Time for Crisis Event Vs. Number of Cells Stuck but not collided for StickA random(0.001)

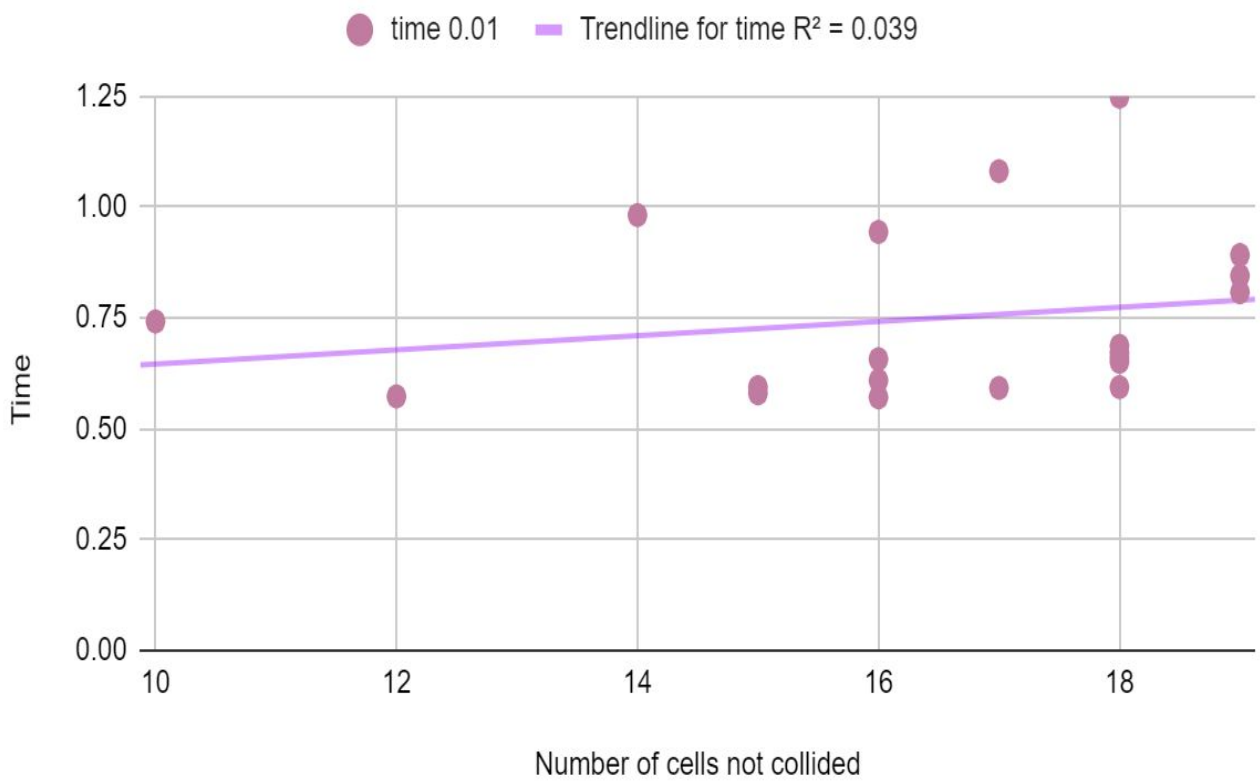Figure 12:Time for Crisis Event vs Number of cells not collided for StickA random(0.01)

Figure 6. Figure 11+ 12: Stuck but not collided vs Time

Looking at Influence of P-Selectin/StickA Concentration

The average stickA for 0.001 was 5.03E-04 while the one for 0.01 was 0.00484803995.

More cells on average collided when the stickA value was 0.001 than when the range was 0.01.

More cells on average get stuck but do not collide when the stickA ranges 0.01.

T-Test

I conducted a two-sample T-test to check if there was any difference in the means of time between stickA value of 0.001 and 0.01. The t-test showed that there was a difference in means between the two ranges.

```
Welch Two Sample t-test for Time
Taken for Collision

data: datatime0.001 and
datatime0.01
t = 2.2185, df = 32.392, p-value
= 0.03365
alternative hypothesis: true
difference in means is not equal
to 0
95 percent confidence interval:
 0.009344032 0.217755968
sample estimates:
mean of x mean of y
 0.74920   0.63565
```

Figure 9. Two Sample T-test on Crises Time

I also conducted a two-sample t-test to check the difference in collisions. The t-test showed there is a difference in means between the 0.001 sample and the 0.01 sample.

```
Welch Two Sample t-test for
Number of Collisions

data: collided0.001 and
collided0.01
t = 2.4936, df = 35.004,
p-value
= 0.01752
alternative hypothesis: true
difference in means is not
equal to 0
95 percent confidence
interval:
 0.32531 3.17469
sample estimates:
mean of x mean of y
 4.70       2.95
```

Figure 10. Two-Sample T-tests collisions

Discussion

The results show that trials with higher levels of collisions took less time to reach crises. Alternatively, those with lower levels of collisions resulted in longer crisis times. There were more collisions when the value of stickA/P-electin were lower. This makes sense because when the stickA is 0—0.01, more individual cells will get stuck in place. Less collisions occur because the cells are less free to move. When stickA is at the lower range 0—0.001, the cells are able to move freely and more collective collisions occur between cells.

The data is not consistent with the trial I was referencing because when P-selectin was reduced, sickle cells still got stuck in blood cells faster. The research showed that there were less cells getting stuck. This aligns with my findings as in the 0.001 cell trial, cells were less likely to get stuck unless they stuck to each other.
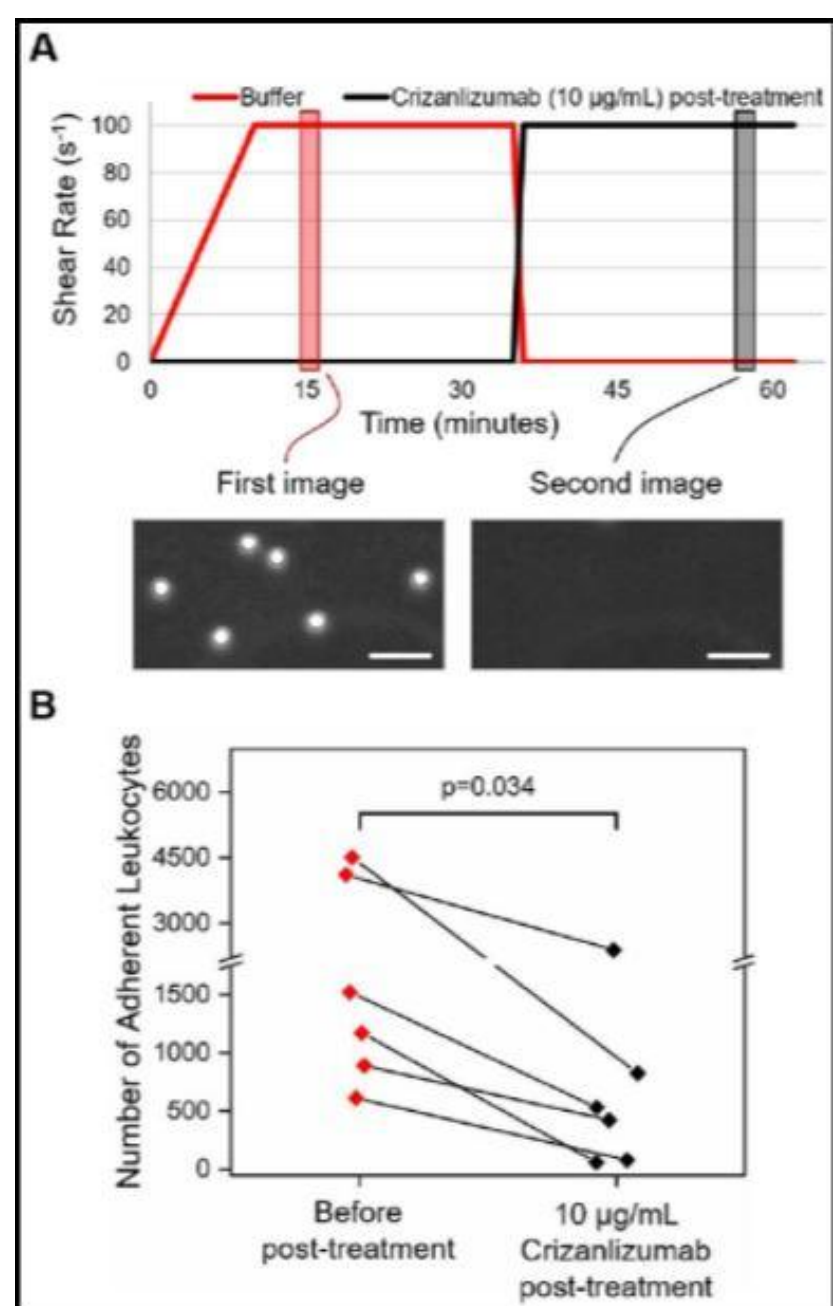

Figure 11. Adhesion to blood vessel P-selectin. (Manwani, D., 2021)

References & Acknowledgments

1. Sickle Cell Disease | Cedars-Sinai. (2021). Retrieved 23 November 2021, from https://www.cedars-sinai.org/health-library/diseases-and-conditions/s/sickle-cell-disease.html

1. Manwani, D. (2021). P-selectin and sickle cell disease: a balancing act. Blood, The Journal of the American Society of Hematology, 137(19), 2573-2574.