

# Multiscale Model of Keloid Scar Expansion

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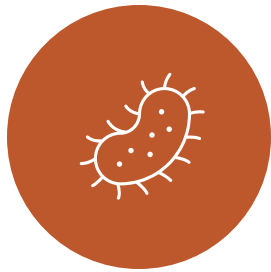
ANGELIZ VARGAS CASILLAS

PHD CANDIDATE

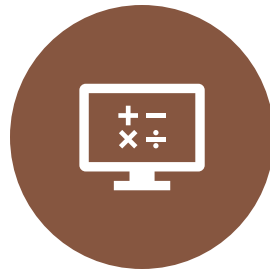
DEPARTMENT OF MATHEMATICS

# Overview

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BIOLOGY  
BACKGROUND



AGENT-BASED  
MODEL



RESULTS



CODE

# Keloid Scars

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- Tumor-like growth in genetically predisposed individuals that continues to grow past the initial wound region
- Itchy, painful, burning sensation during growth
- Overproduction of collagen
- Regression is rare
- Surgery is not a good treatment option
- Current treatments:
  - Steroid injections, cryotherapy, laser therapy, radiation therapy, or steroid creams



U.S. Dermatology Partners

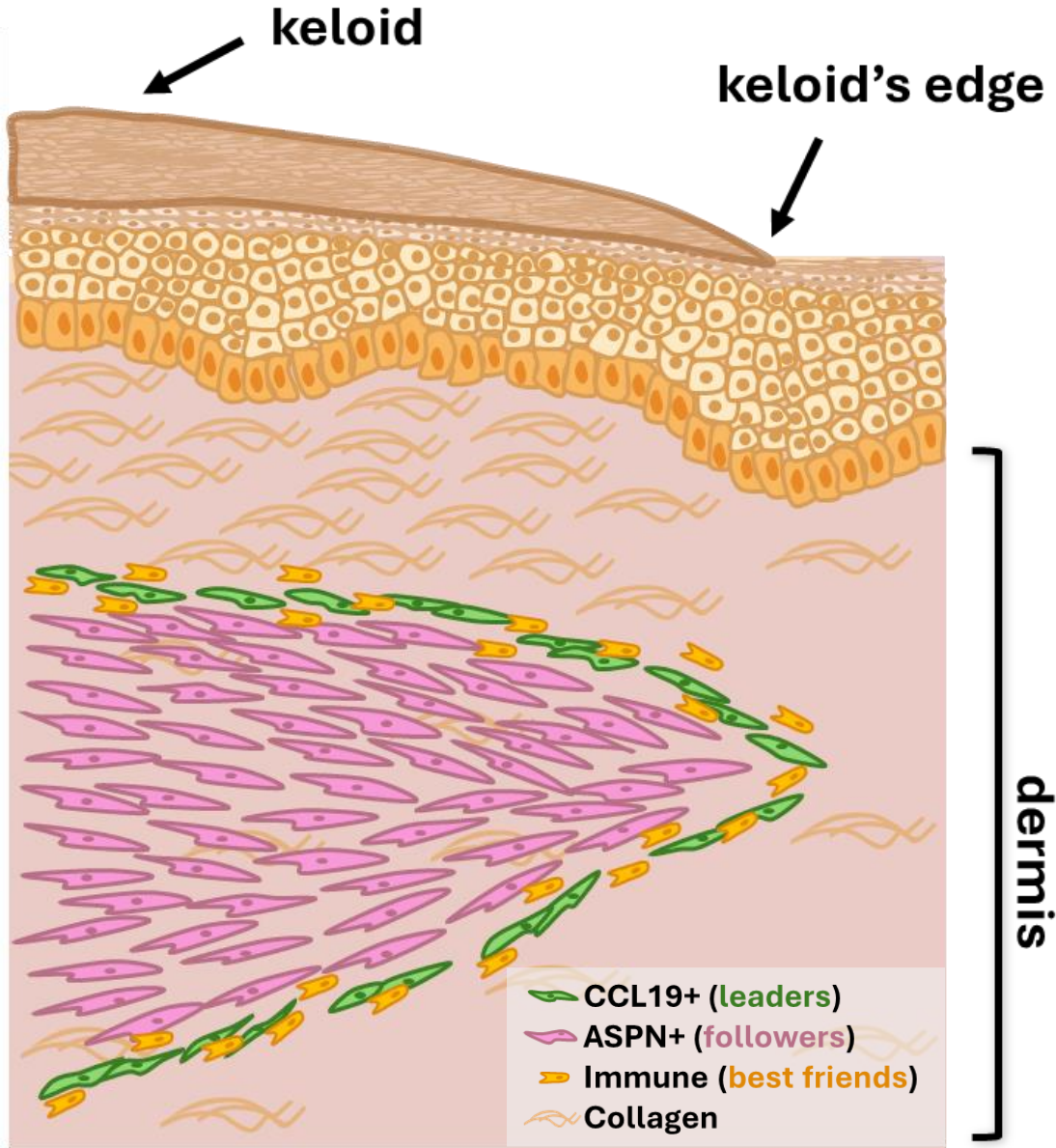
# Why a Mathematical Model?

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Exclusive to human skin

No valid animal models

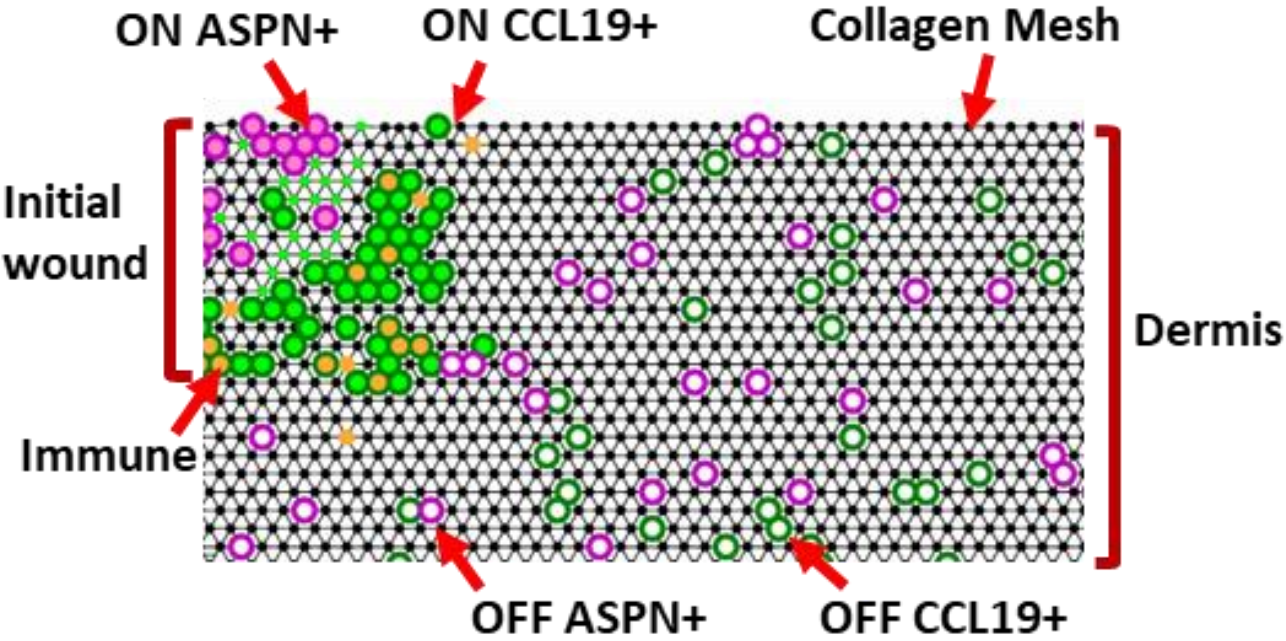
Allows for virtual experiments without injuring or further scarring patients



# Spatial Pattern

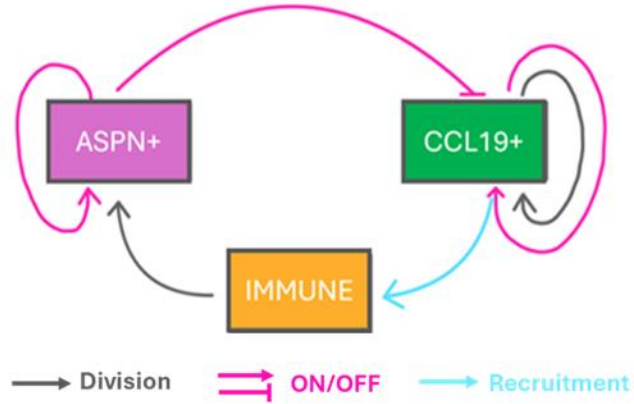


# An Agent-Based Keloid Model

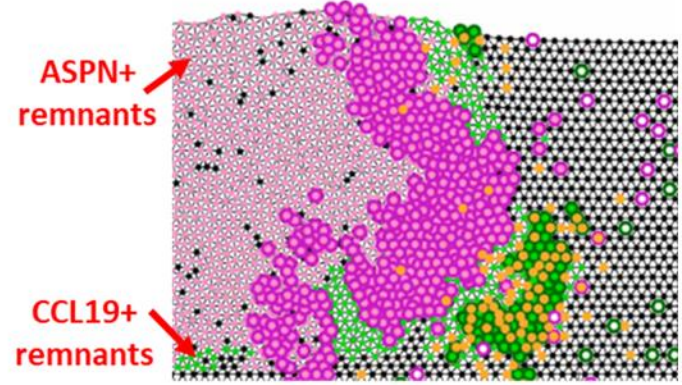


- **Dermis layer cells and fibers in the model:**
  - Collagen fibers
  - CCL19+ and ASPN+ fibroblasts
  - Immune cells
  
- **Fibroblasts have 2 states:**
  - ON – may produce collagen fibers, may divide, and may interact with immune cells or other fibroblasts
  - OFF – quiescent cell

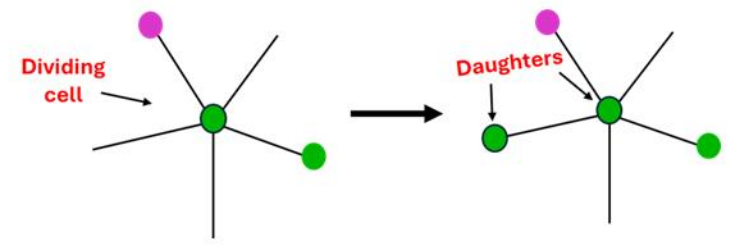
### Cell Interactions



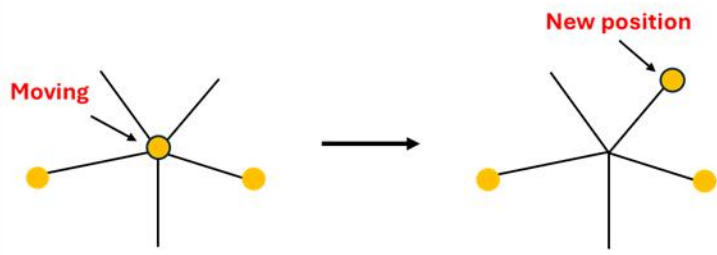
### Fibroblast Death



### Fibroblast Division



### Immune Cell Movement

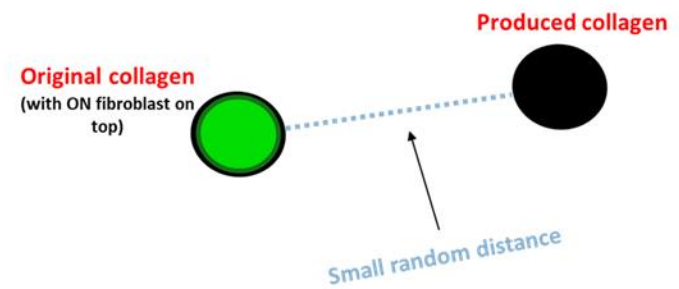


### Collagen Movement

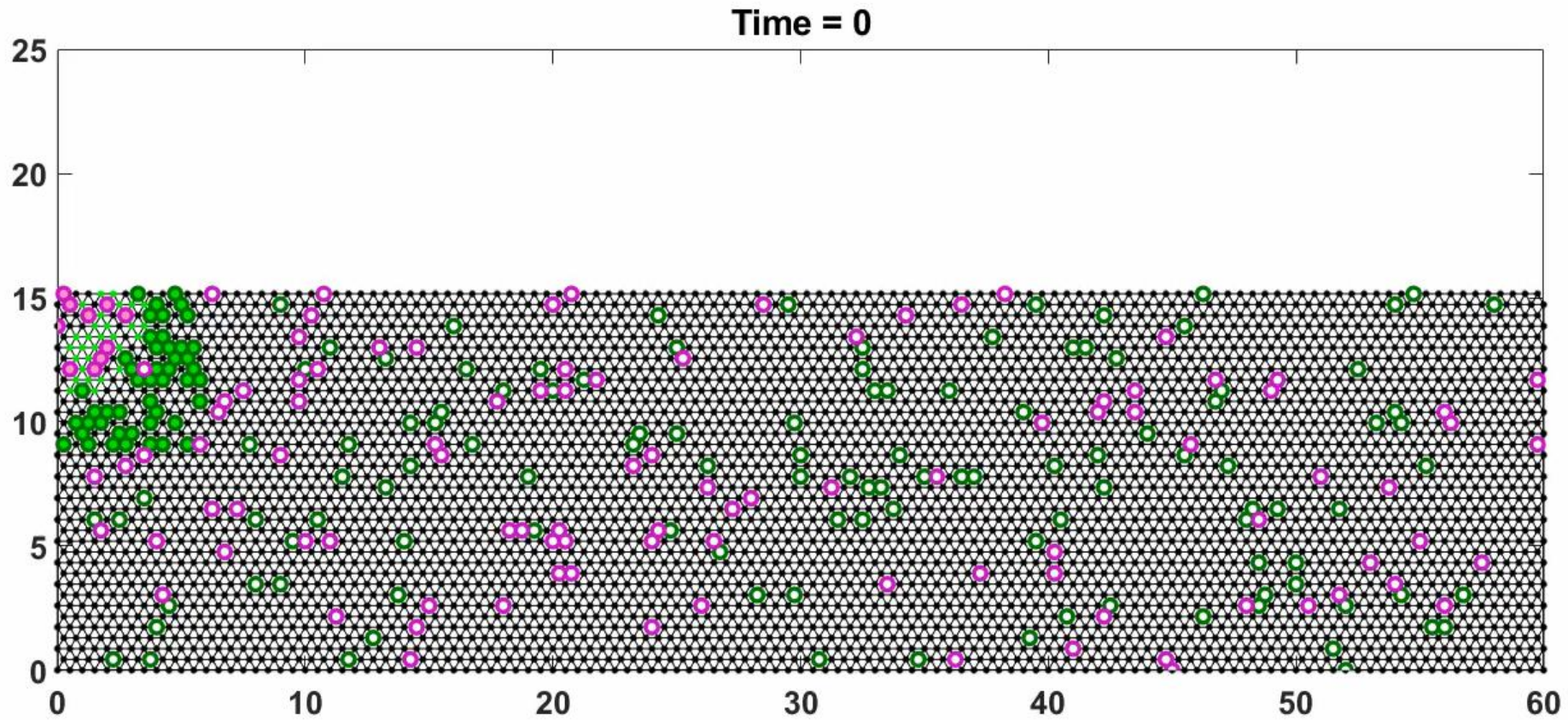
$$\frac{dx_i}{dt} = - \sum_{j=1}^K \mu (\|x_i - y_{p_{i,j}}\| - l) \frac{x_i - y_{p_{i,j}}}{\|x_i - y_{p_{i,j}}\|}$$

- **Determining  $\mu$  for collagen fibers:**
  - Strong attachment (against stretching)
  - Weak repulsion (weak compression)

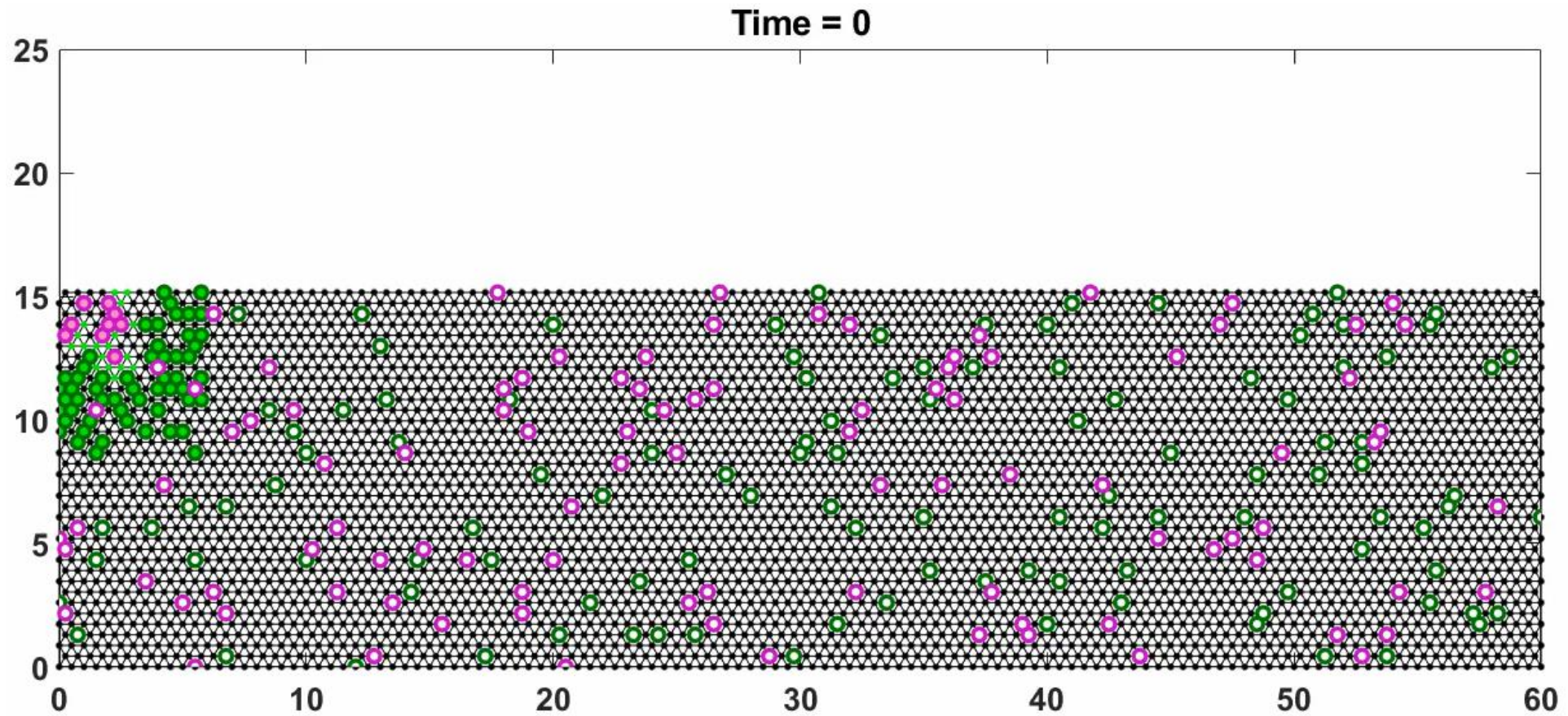
### Collagen Production



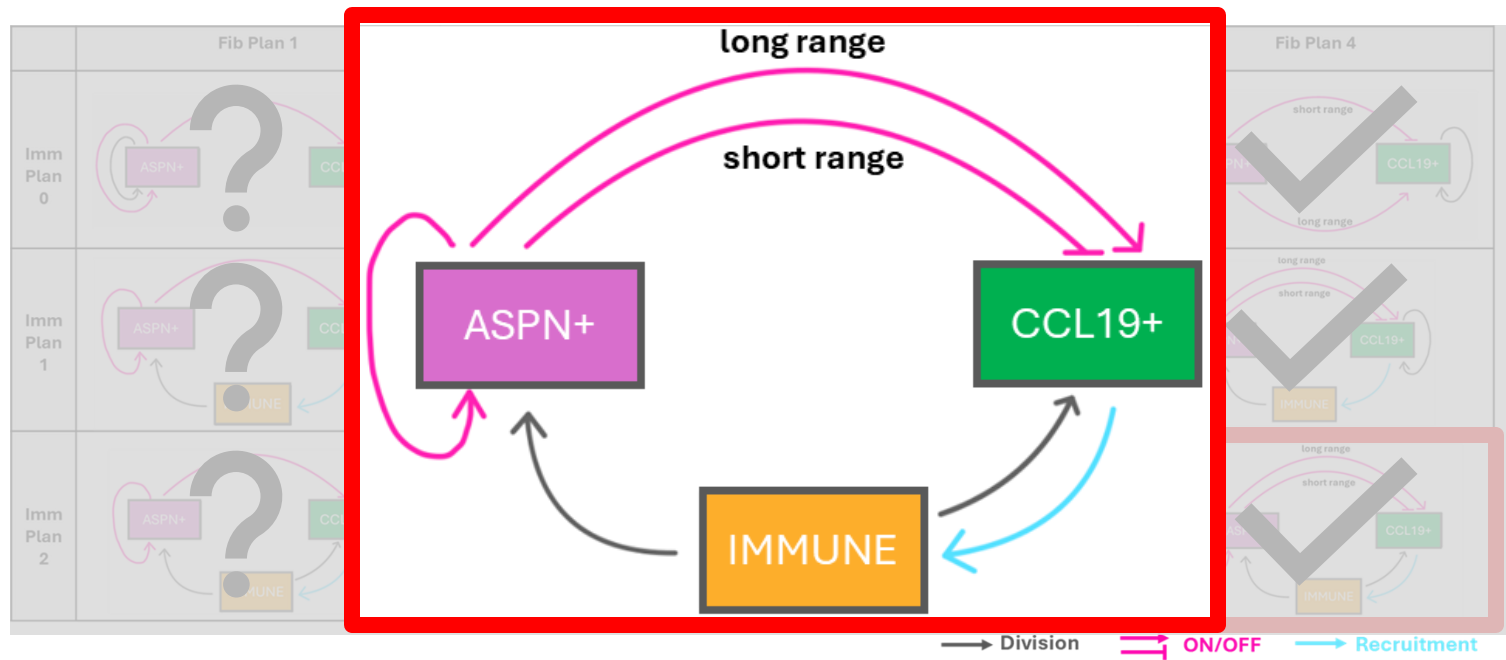
# An ABM Simulation – Successful Expansion



# An ABM Simulation – Failed Expansion



# Preliminary Results



- Collaborators can test these predictions
- If the model and biological experiments agree, then we can suggest potential keloid treatments

# Code Snippet

```

MainPlan4_KL.m x DeMesh_KL.m x HPCC_Run_KL.m x KL_Imm.sh x +
1 function MainPlan4_KL(nsim)
2
3 %Keloid
4 %Plan 4
5 %Version2
6 %Two types of cells, purple (FB2) and green(FB1)
7 %Each type of cells has ON and OFF states
8 %A purple ON cell can turn on a purple OFF cell within a distance
9 %A purple ON cell can turn on a green OFF cell within a long distance
10 %Purple ON cells can remove nearby green cells
11 %ON cells automatically divide
12
13 %green FB1 recrute immune cells
14 %immune cells perform random walk, and quit the system after a while
15 %immune cells activate purple FB2
16 %For an ON purple cell, if there's an immune cell nearby, then it may
17 %divide
18 %For an ON green cell, if there's an immune cell nearby, then it may
19 %divide
20 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
21 % clc;clf;clear all; close all
22
23 global Id_Fib Id_Fib_Col Id_Fib_Fix
24 global Id_FibB1 Id_FibB2
25 global Id_Imm
26 global Intl_Wound_Width Intl_Wound_Depth
27 global St_ON St_OFF d0 d_CutOff FB1_DivT_Avg FB1_DivT_Std FB2_DivT_Avg
28 global d_Kill_2to1 d_Act_2to2 d_Act_2to1
29 global dt Max_FB1_Gen Max_FB2_Gen Min_CellTime
30 global Imm_DivT_Avg Imm_DivT_Std d_Imm_FB2

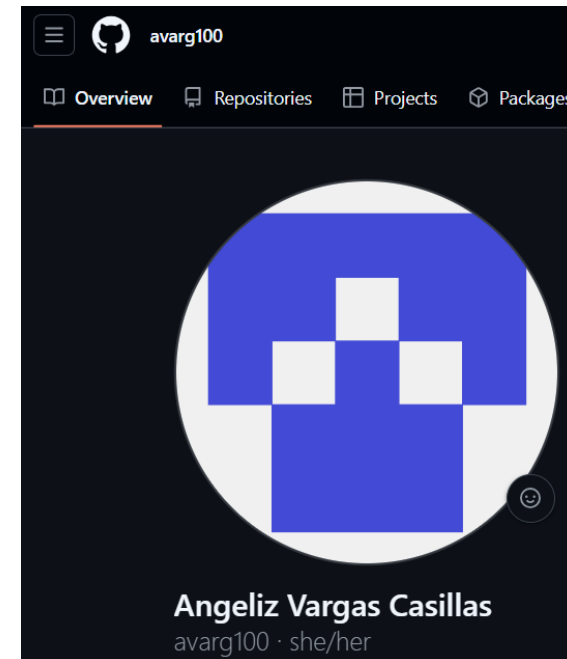
```

Some variables

# Launch Plan

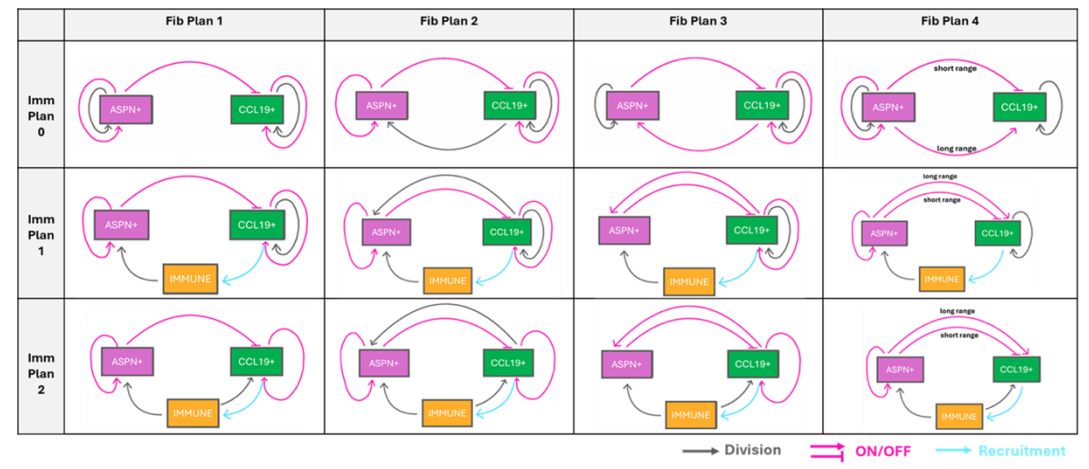
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- Repository for **code** and **data**: GitHub
  - Will be included as supplementary material on published paper (Nature Communications)
- Multiple versions of code so I will include the cell interaction diagram
- README file indicating the adjustable parameters, their meaning, and acceptable range of values as well as instructions for how to run the code
- MATLAB code for visualizing data (movies or snapshots)



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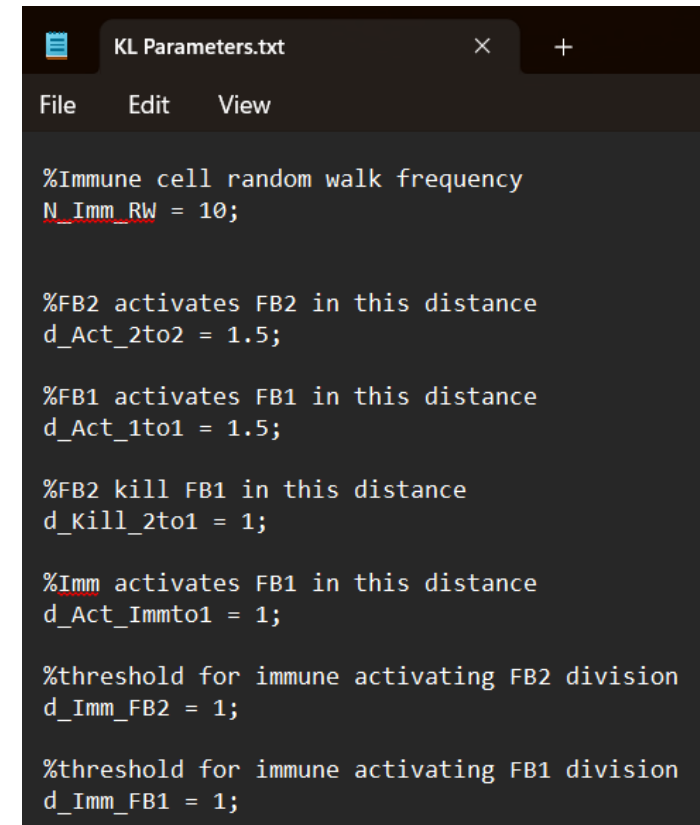
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```
KL Parameters.txt
File Edit View
%Immune cell random walk frequency
N_Imm_RW = 10;

%FB2 activates FB2 in this distance
d_Act_2to2 = 1.5;

%FB1 activates FB1 in this distance
d_Act_1to1 = 1.5;

%FB2 kill FB1 in this distance
d_Kill_2to1 = 1;

%Imm activates FB1 in this distance
d_Act_Immto1 = 1;

%threshold for immune activating FB2 division
d_Imm_FB2 = 1;

%threshold for immune activating FB1 division
d_Imm_FB1 = 1;
```

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```

SimSnapshot_KLm x +
1 %Keloid
2 % function SimSnapshot_KL(nsim)
3
4 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
5 clc;clf;clear all; close all
6
7 global Id_Fib Id_Fib_Col Id_Fib_Fix
8 global Id_FibB1 Id_FibB2
9 global Intl_Wound_Width Intl_Wound_Depth
10 global St_ON St_OFF d0 d_CutOff FB1_DivT_Avg FB1_DivT_Std FB2_DivT_Avg FB2_DivT_Std
11 global d_Act_2to2 d_Act_1to1 d_Kill_2to1 Max_FB1_Gen Max_FB2_Gen Min_CellTime
12 global dt
13
14 %Close existing workers
15 %delete(gcf('nocreate'));
16
17 plan = "Plan4";
18 nsim=1;
19 version = "_Version0";
20
21 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
22
23 %Bottom & sides boundary fixed.
24
25 %Computation domain: [XL, XR] x [YB, YT]
26 XL = 0;
27 XR = 60;
28 YB = 0;
29 YT = 15;
30
31 d0 = 0.5;
32 h0 = d0*sqrt(3)/2;
33
34 d_CutOff = 2*d0;
35

```

# Acknowledgements

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- Advisor:

- Dr. Qixuan Wang



- Biology collaborators from UC Irvine:

- Dr. Maksim Plikus
- Dr. Yingzi Liu



Thank you!

Questions?