# BME: 200/300 Adhesion Dissolution

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# Overview

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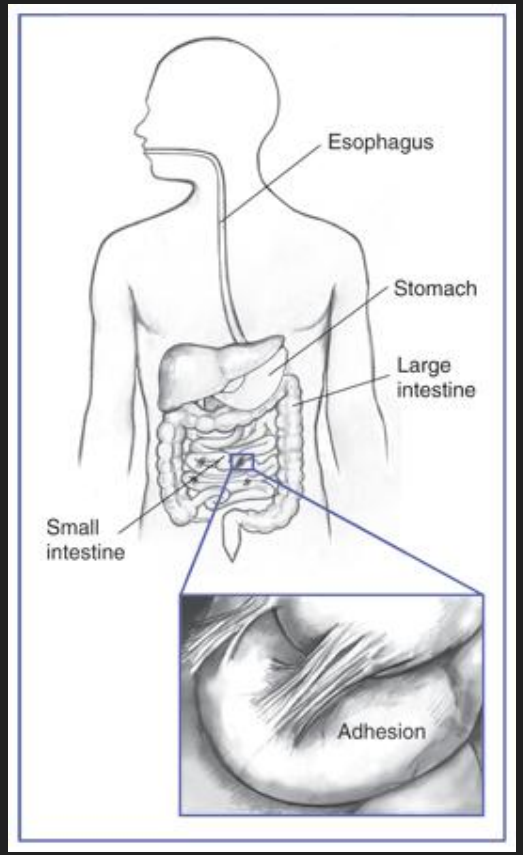
# Background on Adhesions

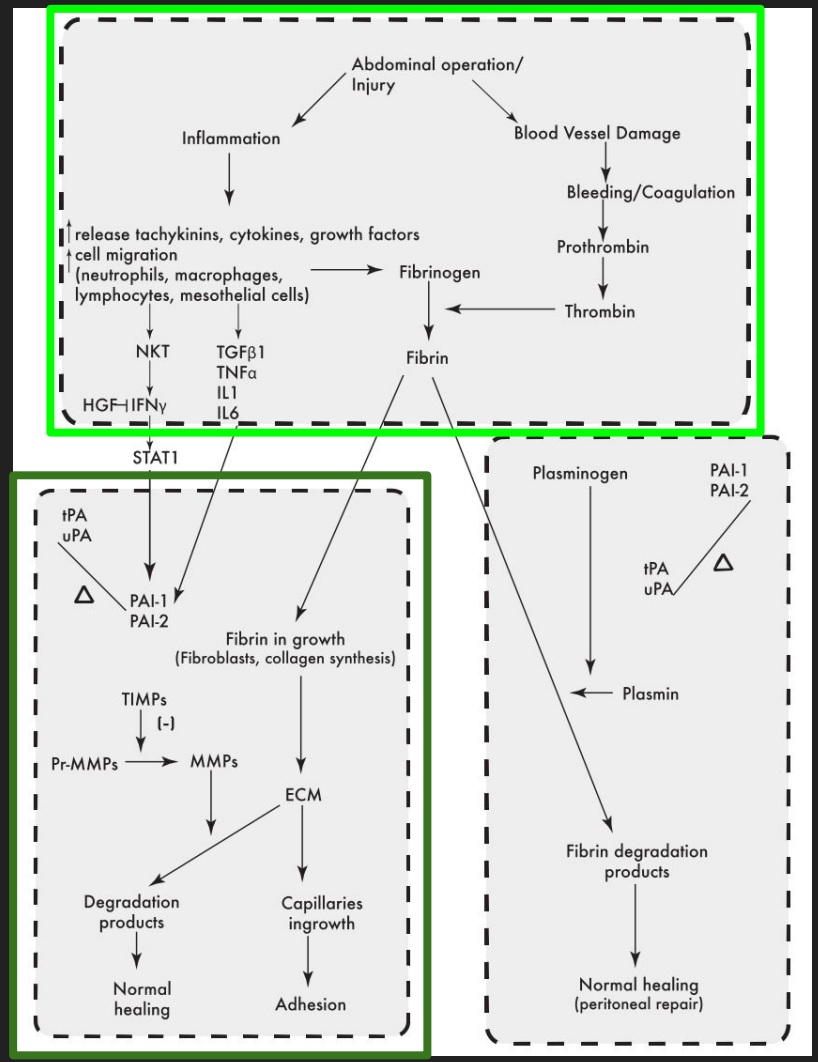
- What are adhesions?
  - bands of scar-like, connective tissue that connect organs that are usually unattached
- What causes adhesions?
  - Adhesions can be caused by upper and lower abdominal surgeries
  - They form in anywhere from 67-100% of patients who undergo abdominal laparotomies
- Why do we care?
  - 15-18% of those with adhesions face complications (i.e. small bowel obstructions) that require surgical removal




Buåureanu et al 2014
https://www.niddk.nih.gov/health-information/health-topics/digestive-diseases/abdominal-adhesions/Pages/facts.aspx

# Adhesion Formation & Maturation

- New adhesions are made of fibrin
- As they mature, they become a collagenous extracellular matrix

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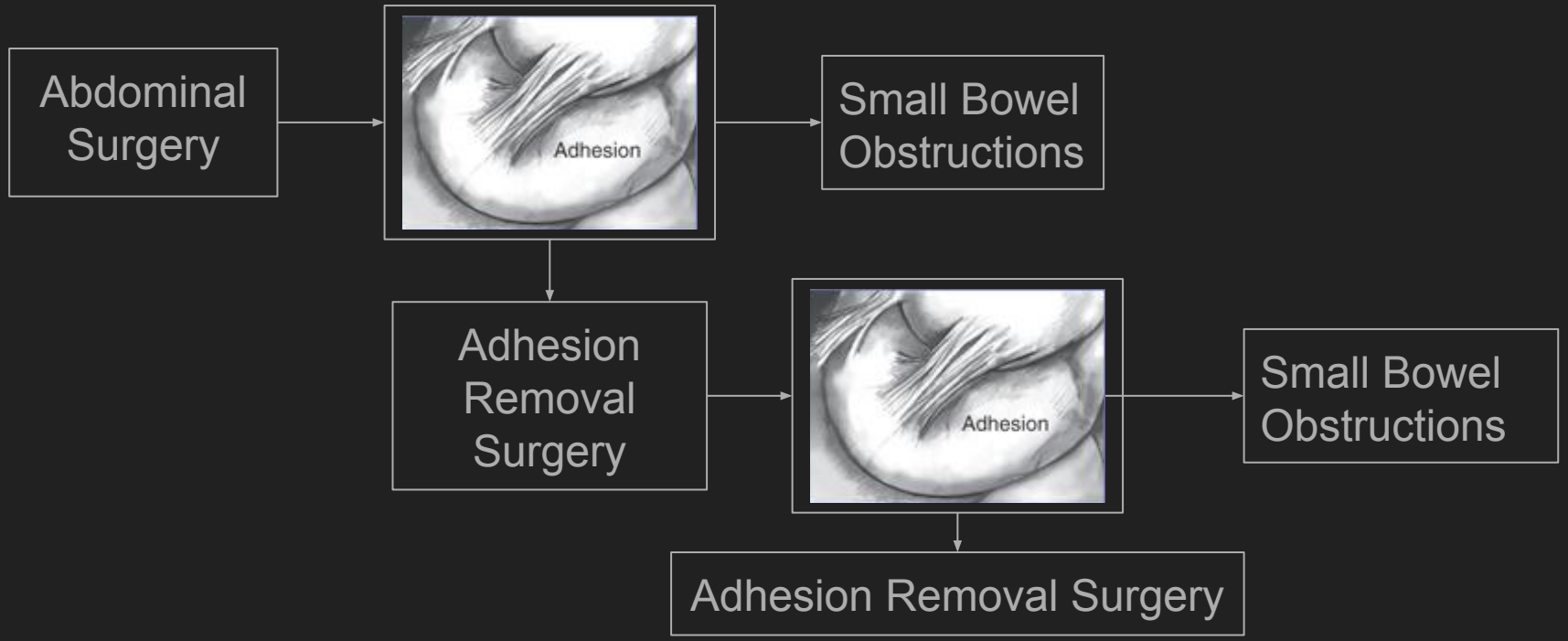
# Project Problem Statement



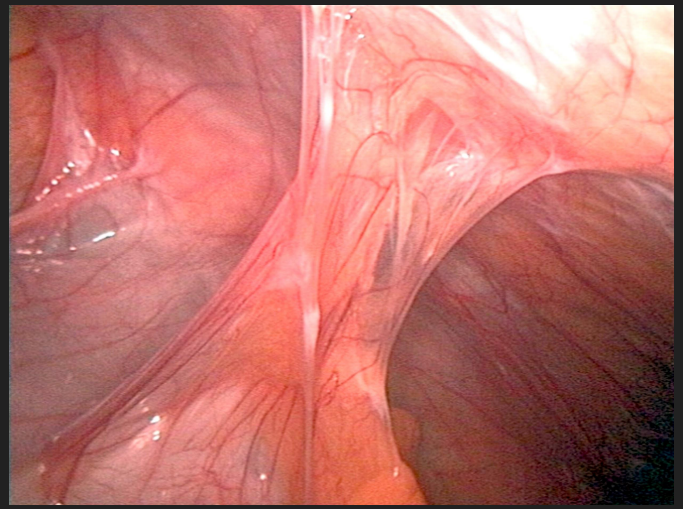

- Our task: less invasive, more natural solution

# Design Specifications

- Must sever and reduce adhesion volume by >50%
- Must degrade mature adhesion (not preventative)
- Contain 98% of administered enzyme to adhesion
- Device and enzyme must be viable for FDA approval

# Possible Targets for Adhesion Dissolution

1. Vasculature
2. Cells
3. Extracellular Matrix (collagen)



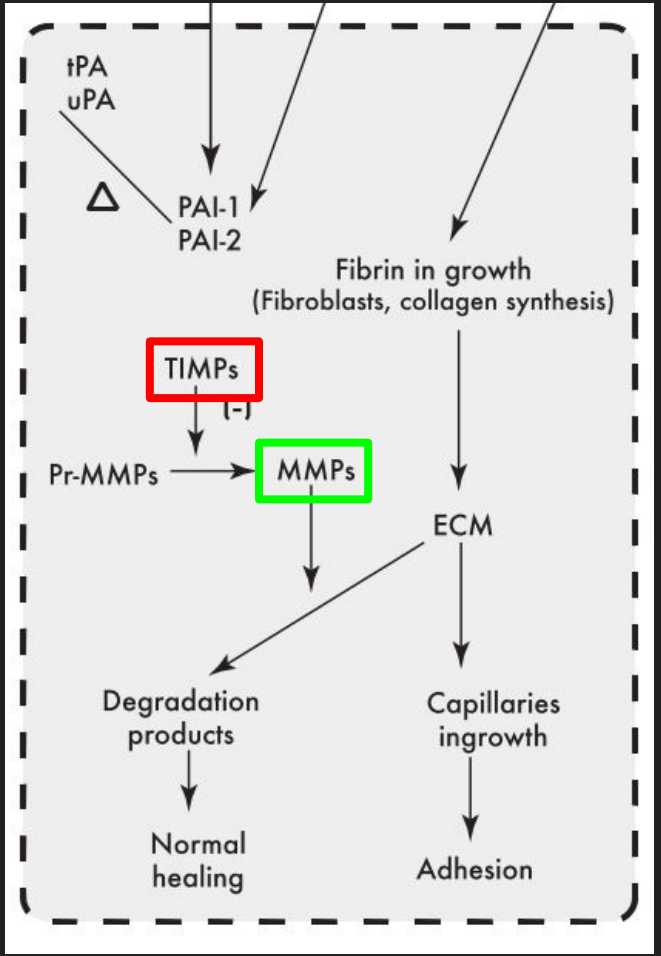
- Vascular/cell removal - prevent growth
- ECM removal - degrade structure

https://www.niddk.nih.gov/health-information/health-topics/digestive-diseases/abdominal-adhesions/Pages/facts.aspx, https://en.wikipedia.org/wiki/Adhesion_(medicine)

# Solution: ECM degradation

- ECM regulation:
  - Matrix Metalloproteinases (MMPs)
    - degrade ECM
  - Tissue Inhibitor of Matrix Metalloproteinases (TIMPs)
    - inhibit MMPs

- Target ECM with MMP delivery

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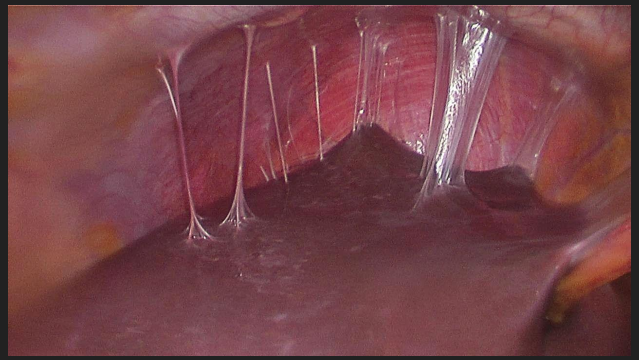
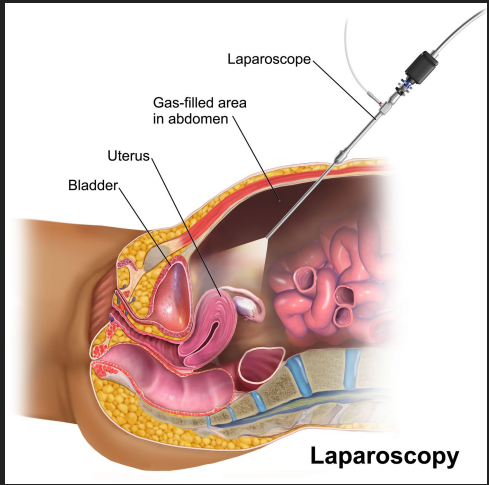
# Design 1: Hydrogel

- Hydrogel
  - Diffuse MMPs selectively to the adhesion ECM
  - Controls the MMP
  - Laparoscopic Techniques



http://www.healthbenison.com/abdominal-adhesions-treatment/

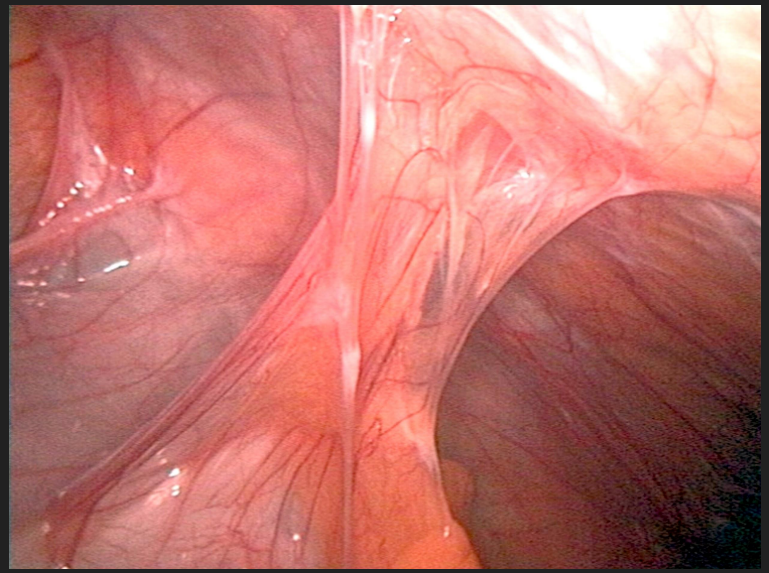



https://en.wikipedia.org/wiki/Laparoscopy

http://newatlas.com/temperature-controlled-hydrogel-movement/38865/

# Design 2: Chemical Scalpel

- Chemical Scalpel
  - Laparoscopic Method
  - Localized MMP release
  - Probe like design
  - User takes the probe and ‘spots’ the adhesion with MMPs
  - Need to use an MMP with short half life

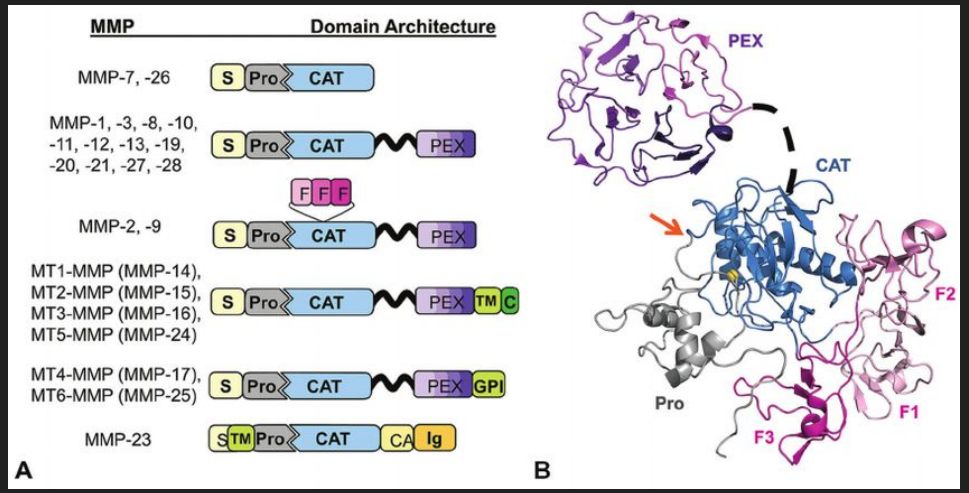


https://en.wikipedia.org/wiki/Adhesion_(medicine)

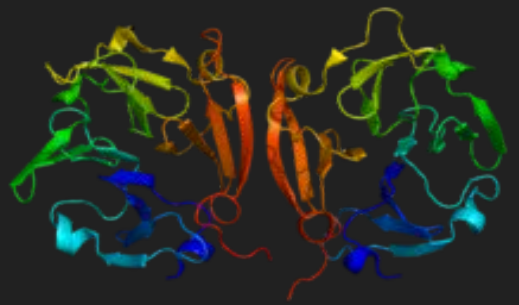
http://www.directindustry.com/prod/solartron-metrology/product-4818-57437.html

# Design 3: Gene Therapy-Endogenous MMP

- Gene Therapy
  - Endogenous MMP attack
  - Internally produce excess MMPs in the cells in adhesions
  - Uses the body's natural processes




https://www.researchgate.net/figure/273955929_fig1_Figure-1-MMP-domain-structure-and-protein-fold-A-The-various-domain-organizations-of



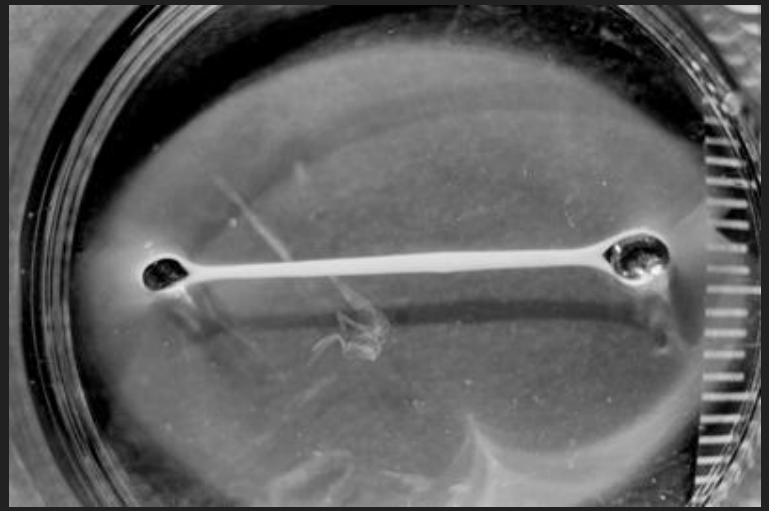
https://en.wikipedia.org/wiki/Matrix_metalloproteinase

# Design Matrix

| Criteria | Weight | Design 1: Hydrogel | | Design 2: Chemical Scalpel | | Design 3: Gene Therapy | |
|---|---|---|---|---|---|---|---|
| Safety | (30) | 4/5 | 24 | 3/5 | 18 | 4/5 | 24 |
| Performance | (25) | 4/5 | 20 | 3/5 | 15 | 5/5 | 25 |
| Simplicity (Ease of Use, Risk of Failure) | (20) | 3/5 | 12 | 4/5 | 16 | 1/5 | 4 |
| Cost | (15) | 4/5 | 12 | 3/5 | 9 | 1/5 | 3 |
| Fabrication | (10) | 4/5 | 8 | 3/5 | 6 | 1/5 | 2 |
| Total | (100) | | 76 | | 64 | | 58 |

# Future Work

- Choose appropriate MMP
  - Criteria: collagen-specific, appropriate half-life, effective degradation performance
- Hydrogel Selection and fabrication
- Testing
  - MMP
    - Determine concentration
  - Hydrogel
    - Effectiveness
    - Surgical feasibility



http://labs.bio.unc.edu/harris/Courses/biol441/two_point_aligned_collagen.jpg

# Acknowledgements


- Prof. Kristyn Masters
- Dr. Philip Bain
- Dr. Ross Molot


# Questions?

# References

R.T. Beyene et al. (2016). Intra-abdominal adhesions : Anatomy , physiology , pathophysiology , and treatment, *52*(2015), 271–319. http://doi.org/10.1067/j.cpsurg.2015.05.001

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