

When Innate Immunity Hurts: Implications for Medical Device Failure

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Learning Targets

- Explain innate immunity/inflammatory response
- Relate phagocytosis to the inflammatory response
- Explain how the inflammatory response is regulated

Immunity

Outside

Inside



Physical &
Chemical Barriers
(skin & mucus
membranes)

<http://www.republicmortgage.com/wp-content/uploads/How-To-Keep-Your-Home-Germ-Free.jpg>

Barriers to infection

- Epithelial layers produce protective substances
 - Acidic pH
 - Enzymes
 - Antimicrobial peptides
 - Psoriasin



Figure 5-4
Kuby Immunology, Seventh Edition
© 2013 W. H. Freeman and Company

- Why does our skin secrete psoriasin?

Immunity

Outside

Inside



Physical &
Chemical Barriers
(skin & mucus
membranes)

Innate Immunity

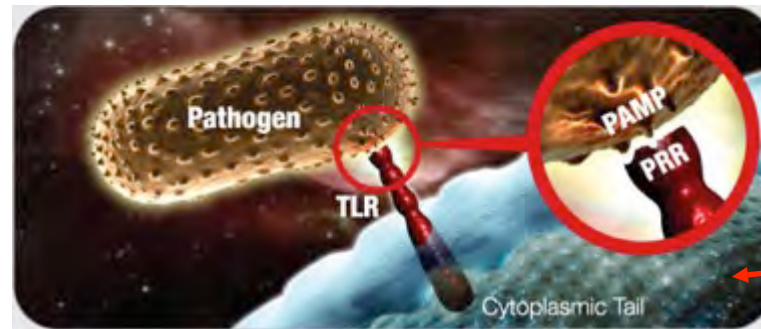
- First line of defense
- Non-specific
- No memory
- Same response to repeat infection

Adaptive Immunity

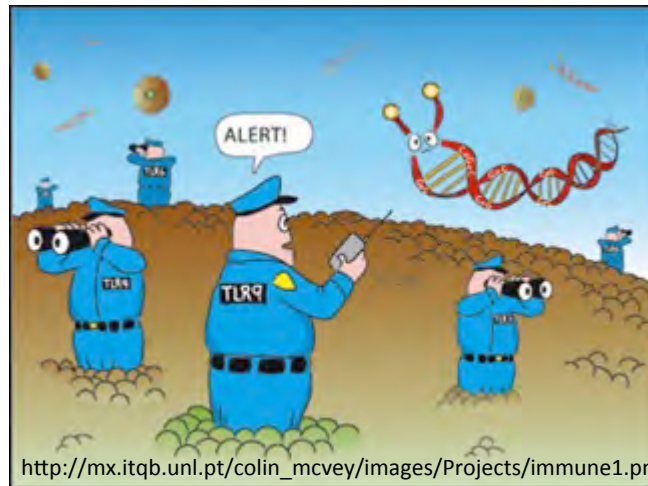
- Max response in days
- Specific
- Memory
- More rapid response to repeat infection

<http://www.republicmortgage.com/wp-content/uploads/How-To-Keep-Your-Home-Germ-Free.jpg>

Pathogen Recognition



- **PAMPs** – Pathogen-Associated Molecular Patterns
- **PRRs** – Pattern Recognition Receptors



- **Inflammation** is triggered when innate immune cells detect infection or tissue injury

Inflammatory Response

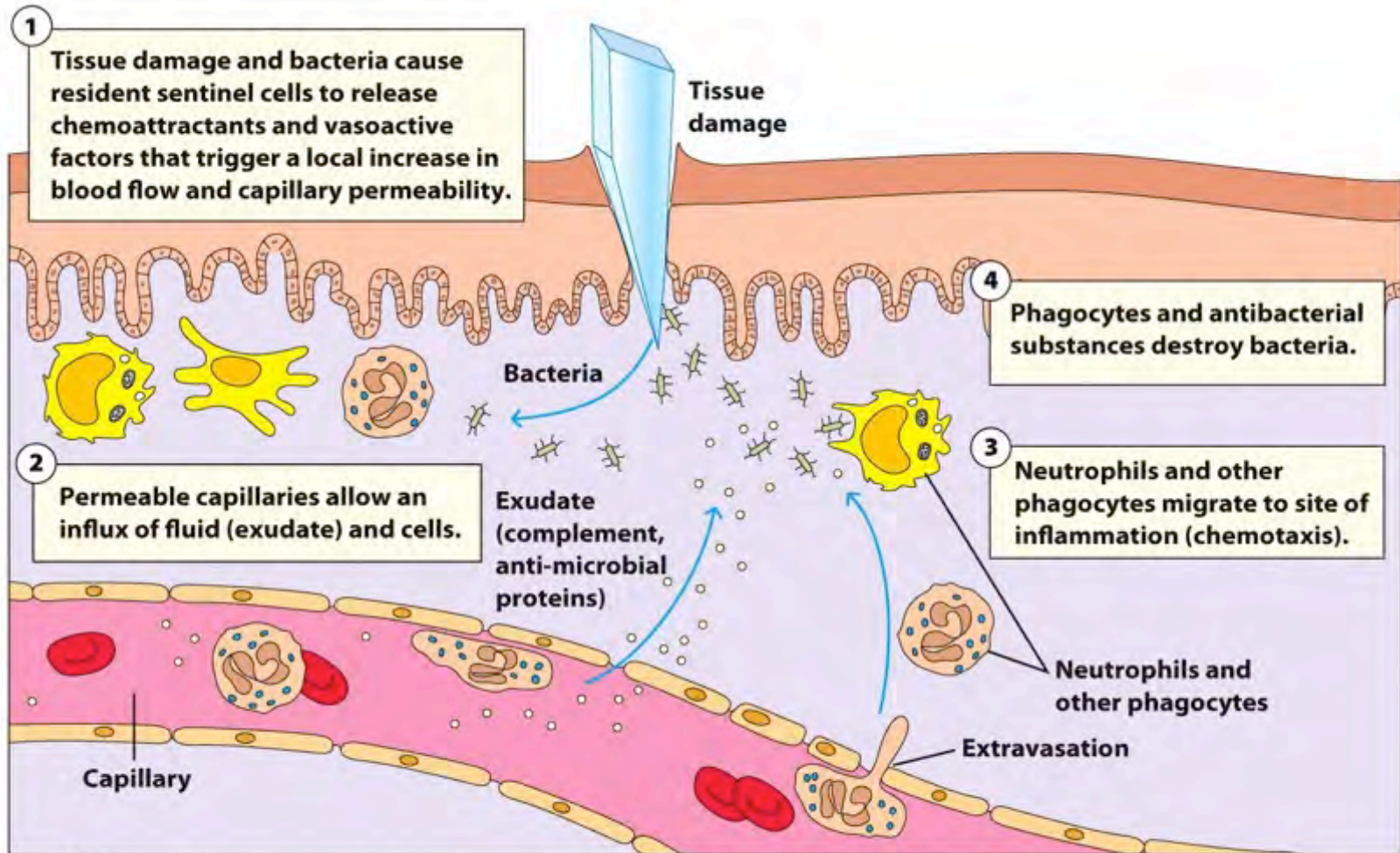
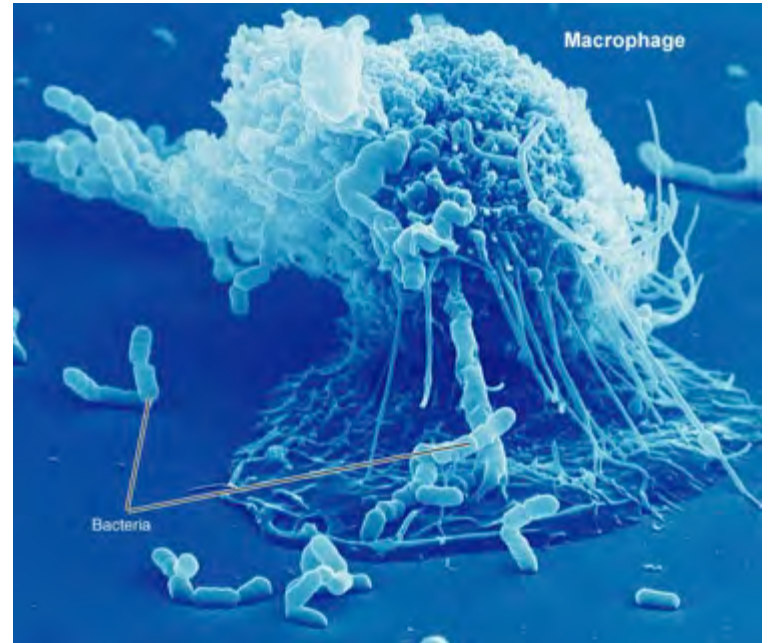
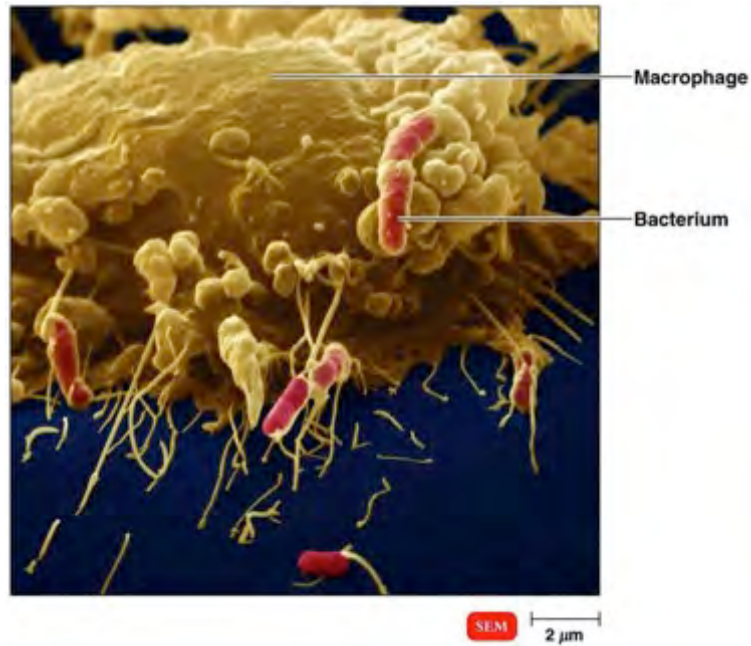
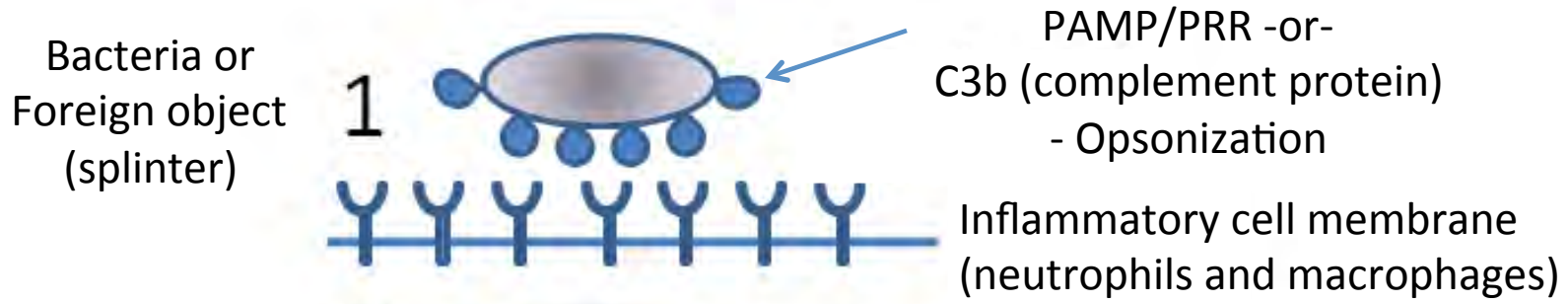


Figure 5-17

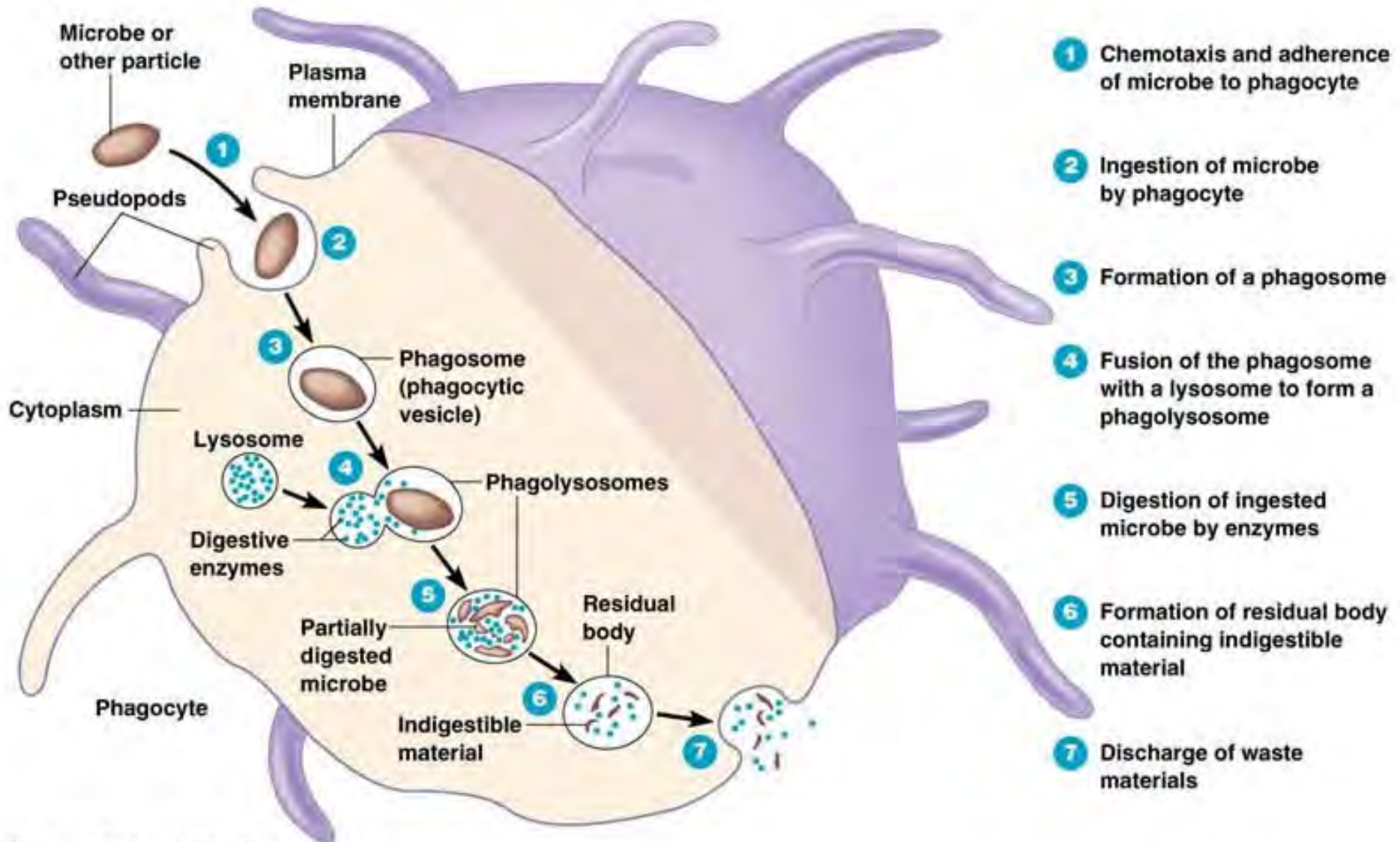
Phagocytosis



Phagocytosis

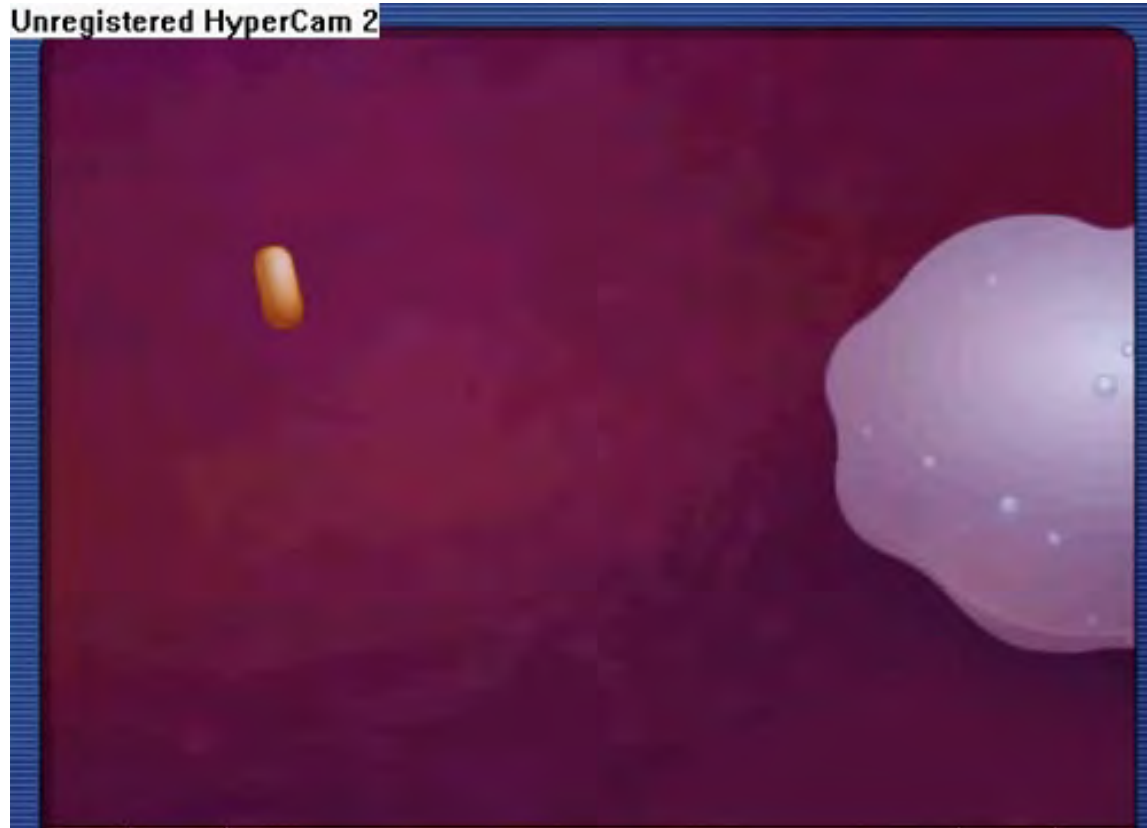


Phagocytosis



Phases of phagocytosis

Phagocytosis Video 1



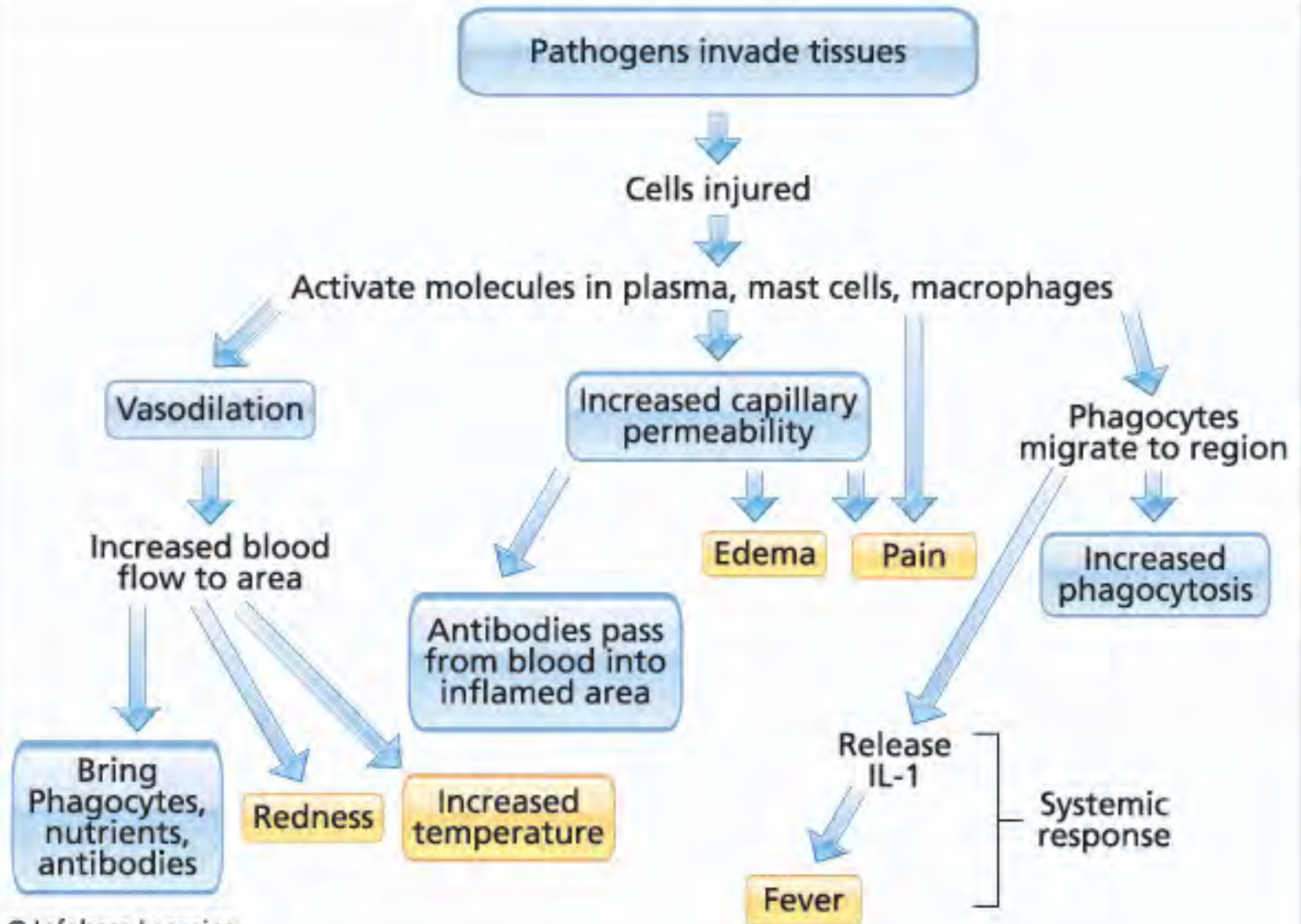
http://highered.mheducation.com/sites/0072495855/student_view0/chapter2/animation__phagocytosis.html

Phagocytosis Video 2

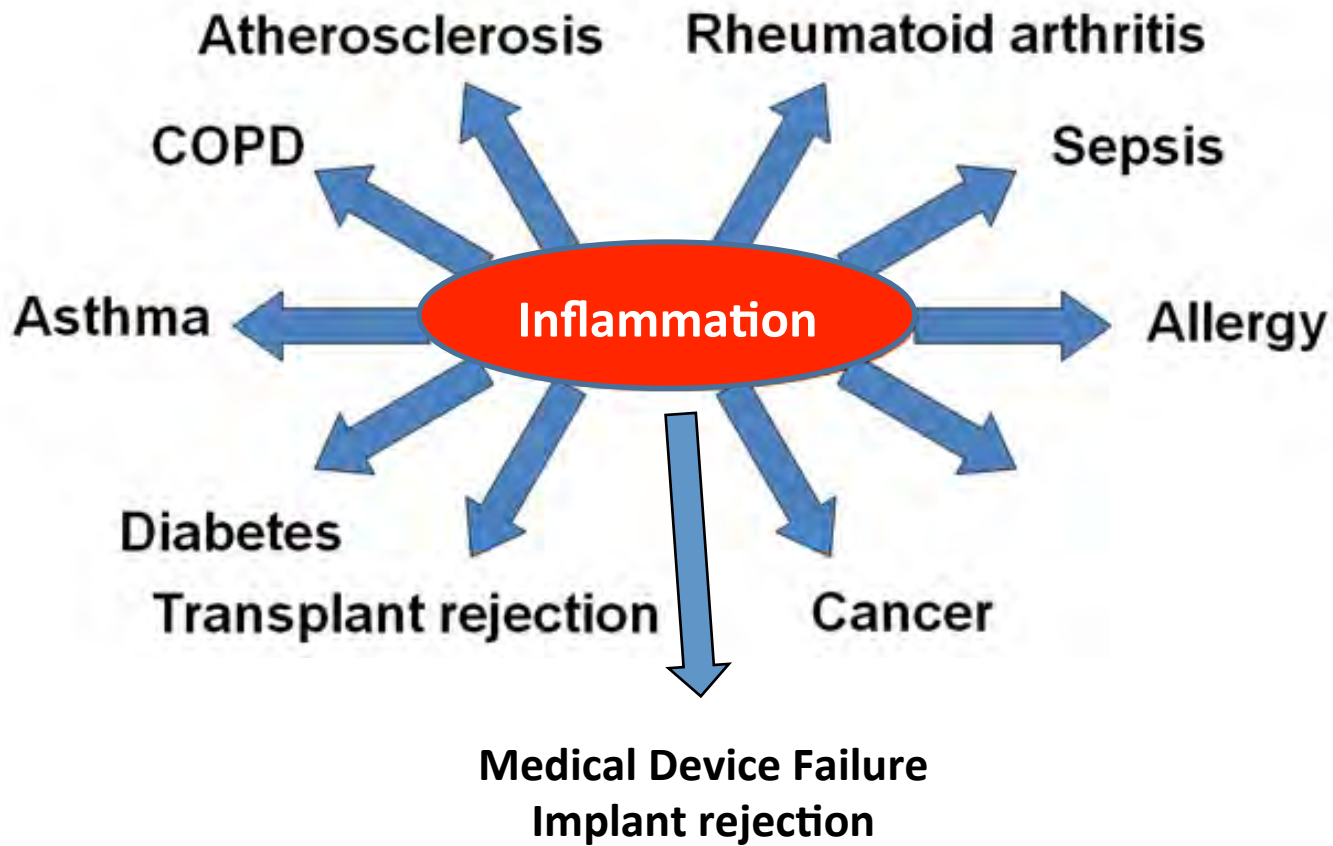
www.BetaGlucans.info

https://www.youtube.com/watch?v=Z_mXDvZQ6dU

Inflammatory Response



Inflammation-Related Diseases



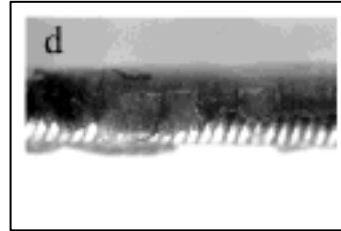
Discussion Question

- What do you think causes diseases associated with inflammation?

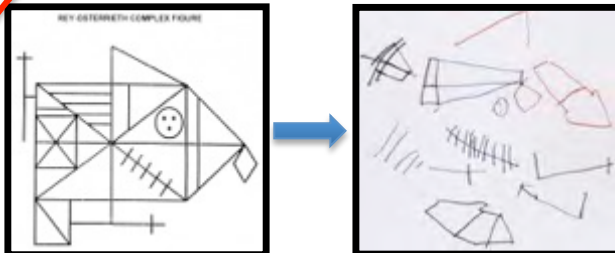
Issues with Innate Immunity



Restenosis



Cracked pacemaker lead insulation



Post-surgical complications of cardiopulmonary bypass



Wiederman et al
Ann Thorac Surg 2010

Fig 1. The degenerated St. Jude valve is shown after explantation.

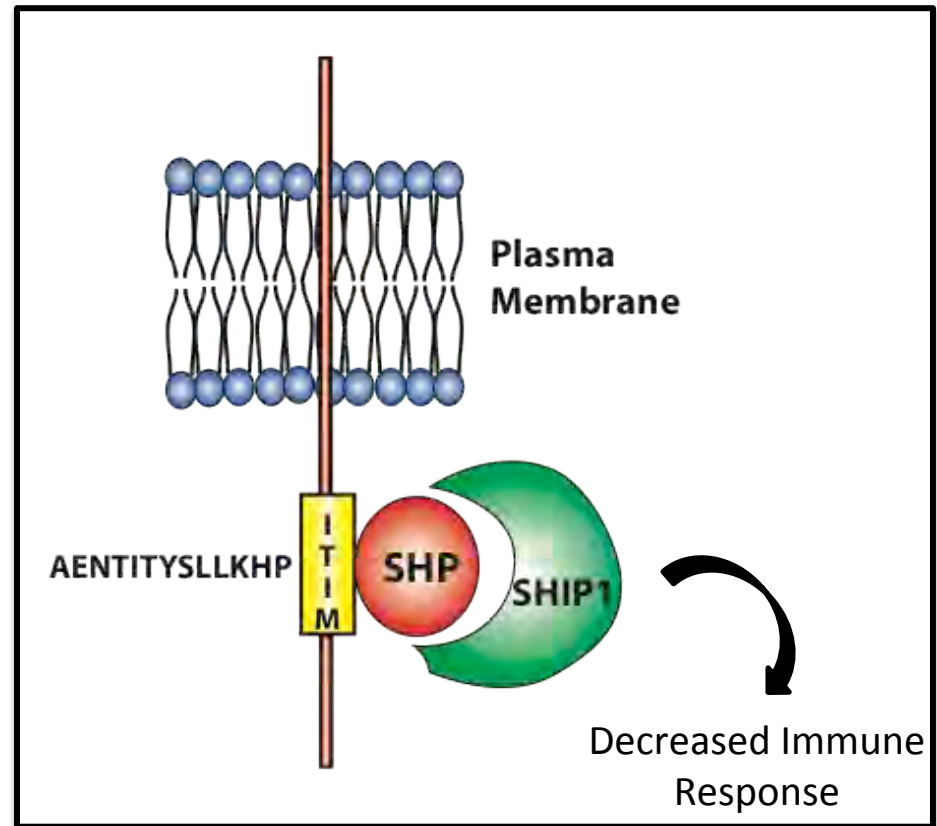
Bioprosthetic valve calcification

Biocompatibility

“The condition of being compatible with living tissue or a living system by not being toxic or injurious and not causing immunological rejection”

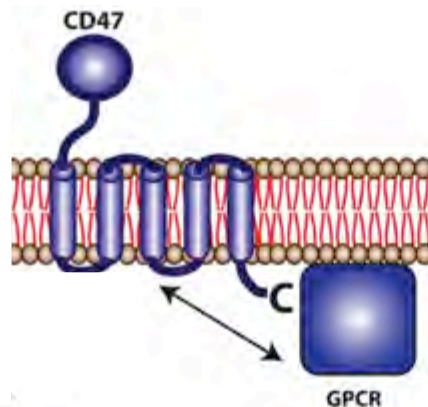
Regulation of the inflammatory response

- Under homeostatic conditions, response to foreign stimuli closely regulated
- Inhibitory immune cell surface receptors
- Immunoreceptor Tyrosine Inhibitory Motif (ITIM) protein family
 - **Signal Regulatory Protein Alpha (SIRP α)**



CD47

- Expressed in virtually all cells
- CD47-SIRP α interaction inhibits immune response
- Over-expressed in most cancer cells



Questions?

The use of CD47 as an anti-inflammatory agent on medical polymers

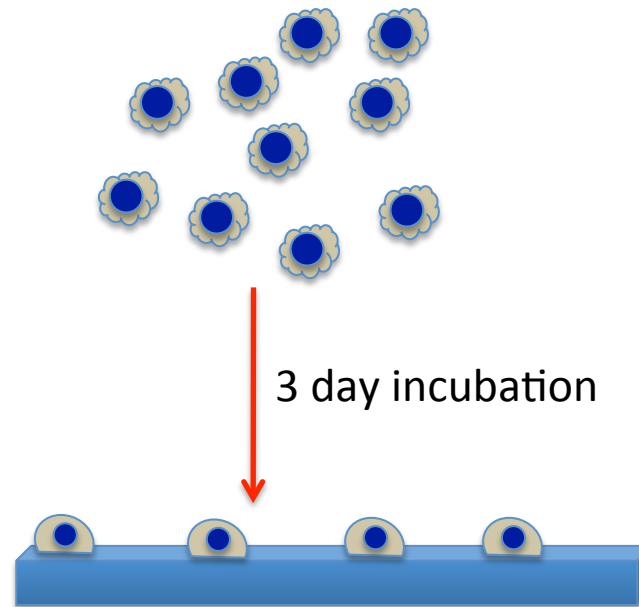
Pacemaker leads, glucose sensors, cardiopulmonary bypass tubing, hemodialysis tubing, & LVAD tubing

Does CD47 prevent *in vitro* cell attachment?

In vitro assay

Attachment Assay

THP-1 = human
monocyte-derived
macrophage cell line

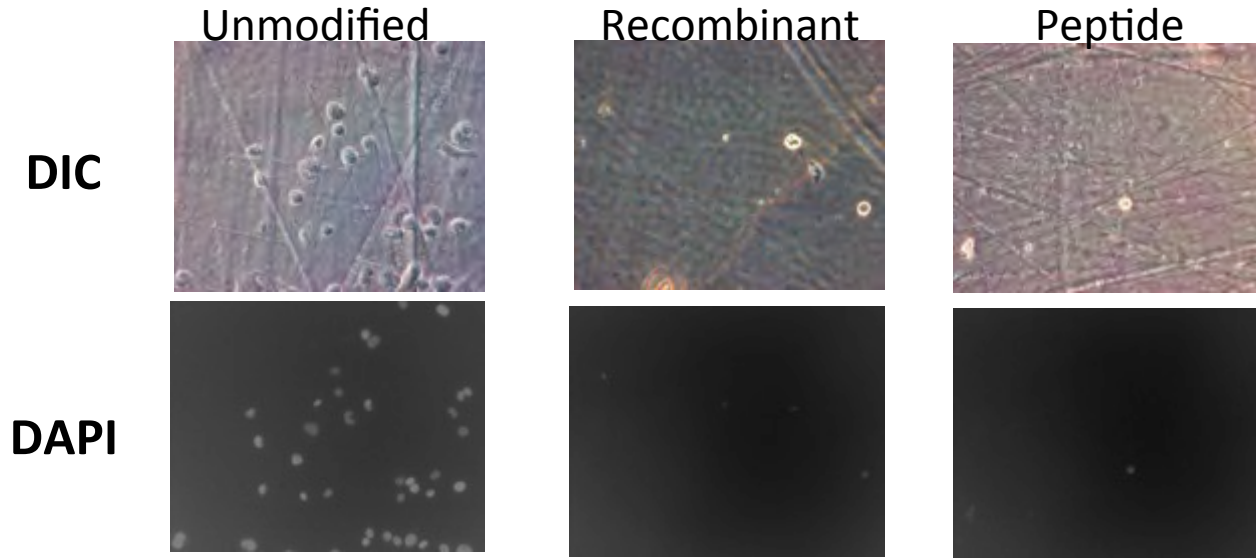


Wash with PBS
Fix cells
Stain with DAPI
Count adhered Cells

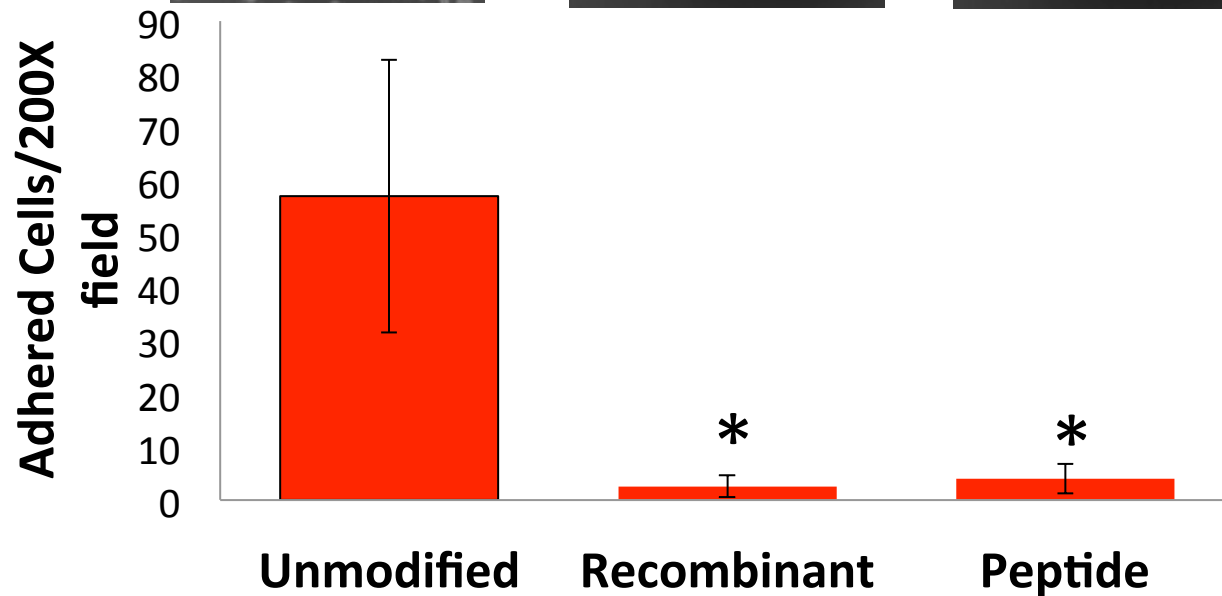
Modified vs
Control Surfaces

THP-1 Attachment Assay

A.



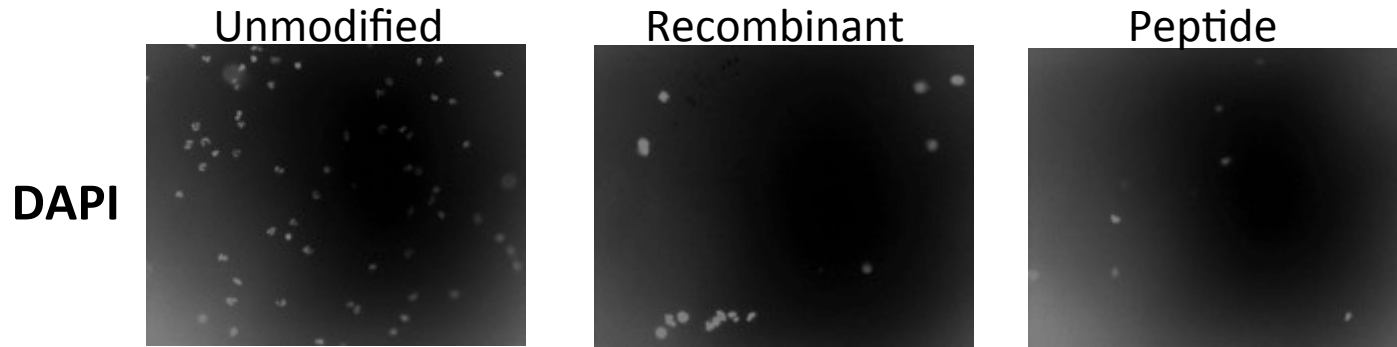
B.



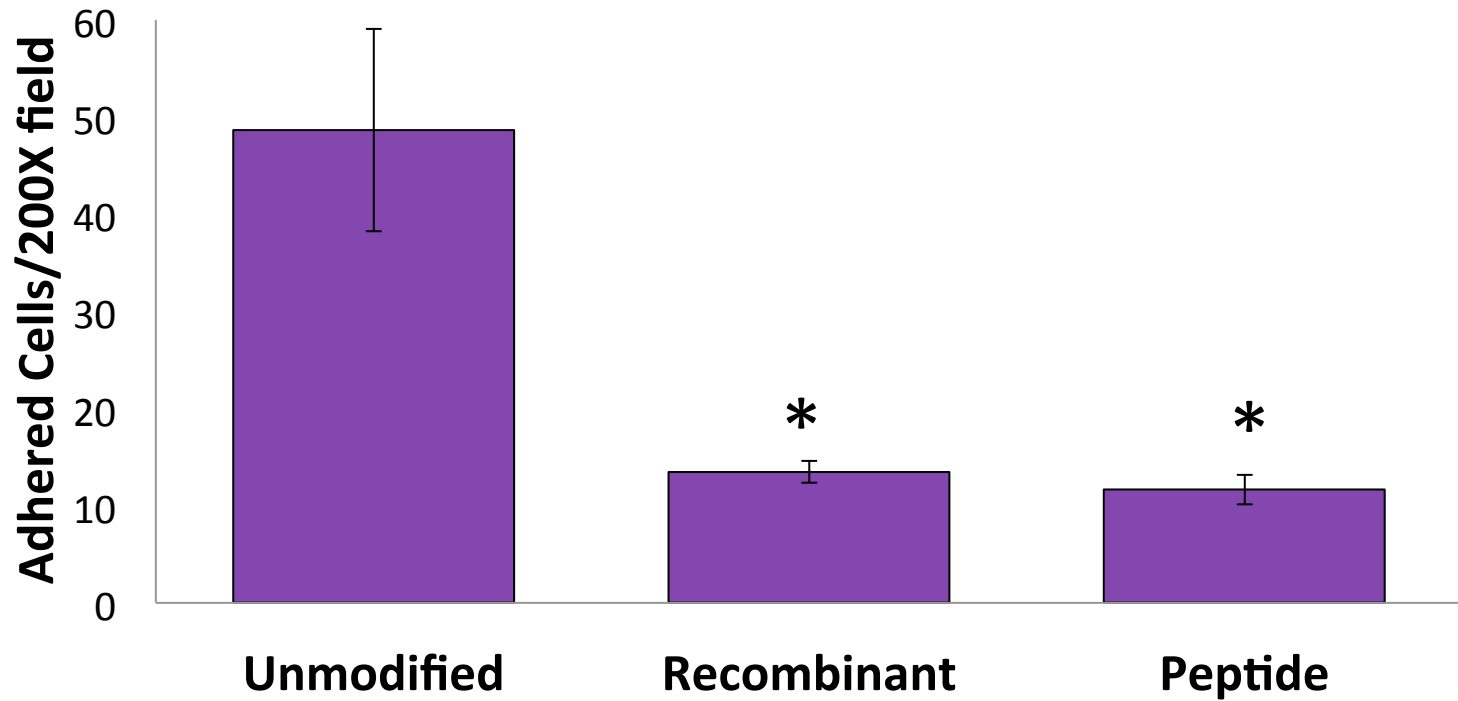
Does CD47 prevent *ex vivo* blood cell attachment?

Chandler Loop Assay

A.



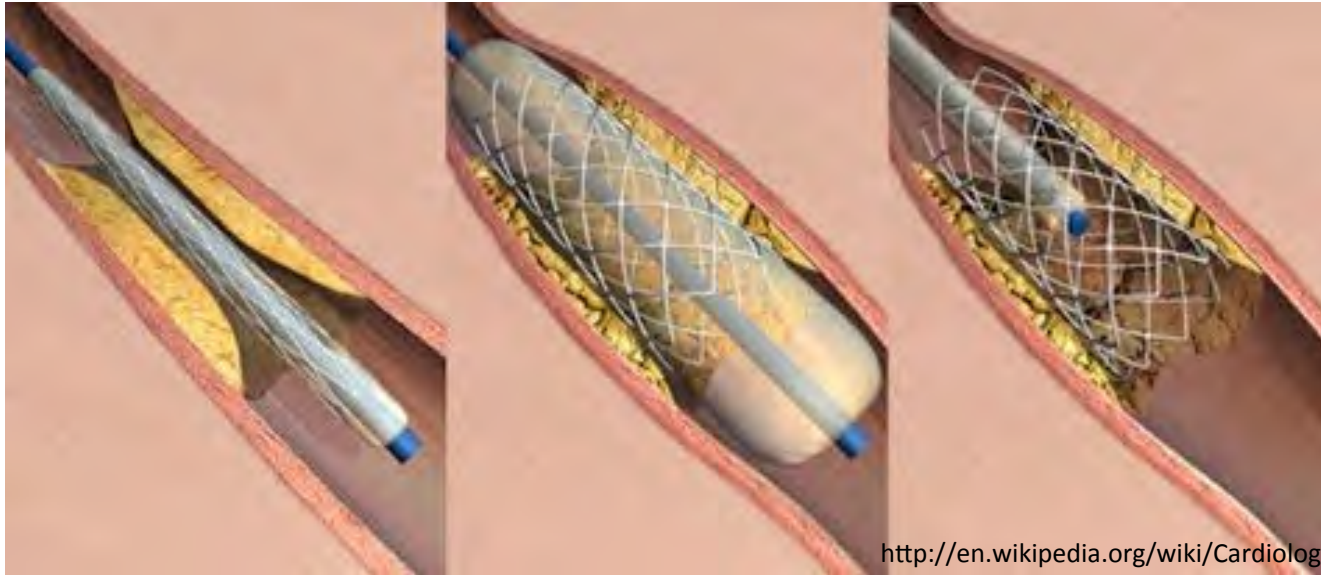
B.



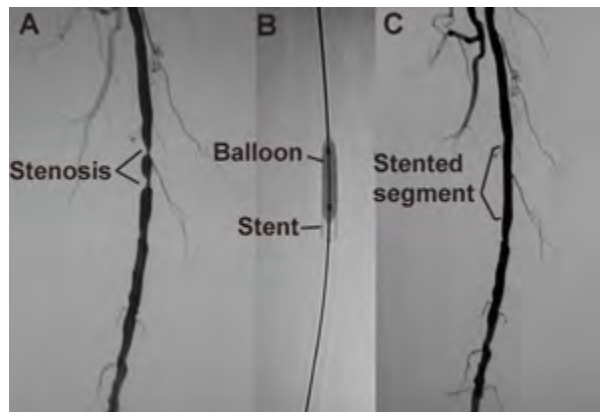
The use of CD47 as an anti-inflammatory agent on vascular stents

Steel stents, orthopedic implants,
dental implants

Vascular Stents



<http://en.wikipedia.org/wiki/Cardiology>



<http://www.yoursurgery.com/ProcedureDetails.cfm?BR=5&Proc=33>



Restenosis

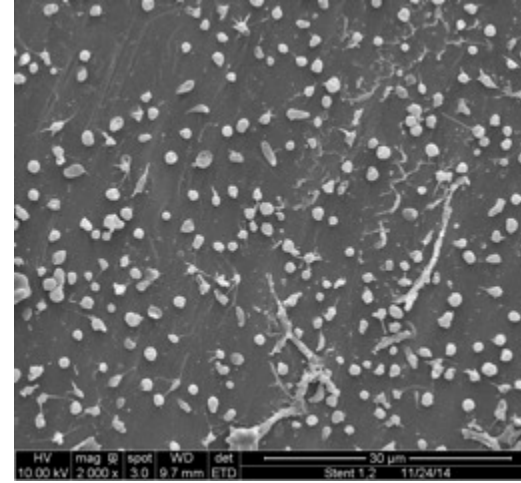
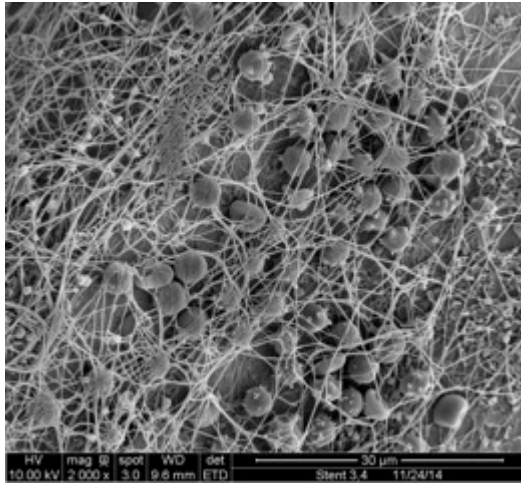
Does CD47 prevent *in vivo* cell attachment?

CD47 Prevents Cell Attachment *In Vivo*

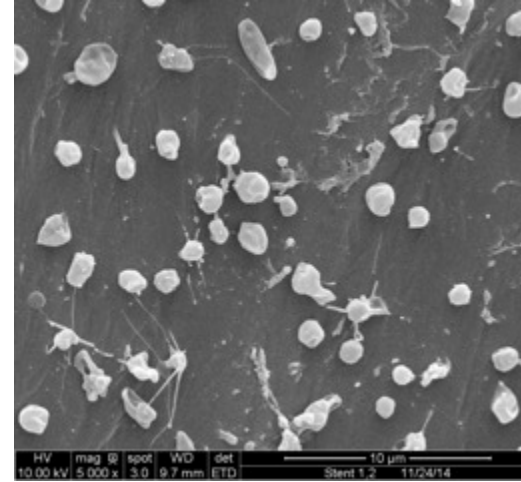
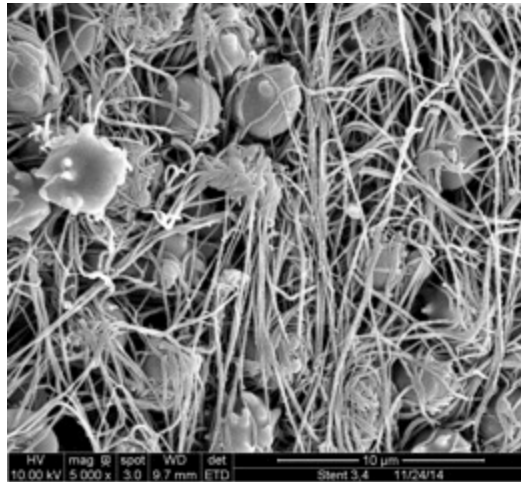
Bare Metal Stent

CD47 stent

2,000X

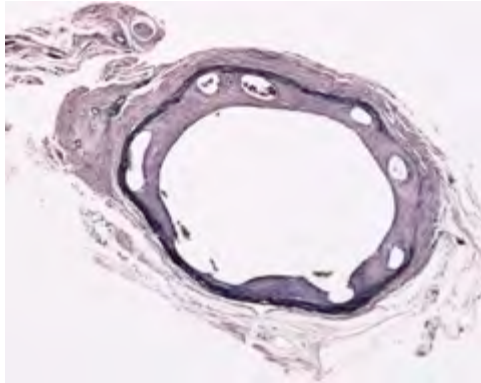


10,000X

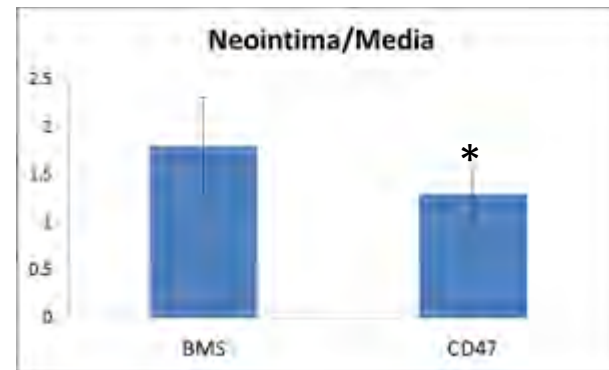
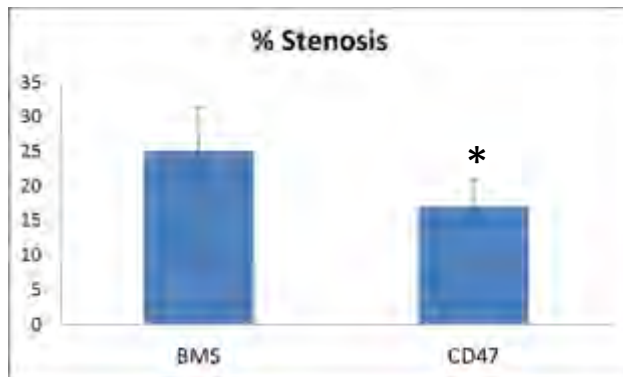


CD47 Prevents Restenosis *In Vivo*

Bare Metal Stent



CD47 stent



CD47 decreases restenosis measures by almost 30%

Summary

- Pathogens and foreign objects trigger an inflammatory response in the body.
- Innate Immunity is the first way the body deals with eliminating pathogens and foreign objects from the body.
- CD47 is a marker of “self” to immune cells.
- CD47 can be used on medical devices/ implantable materials to prevent the inflammatory response.

Thank You! Questions?

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