

# Atherosclerotic Heart Disease: Atherogenesis for USMLE Step One



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# Atherosclerotic Heart Disease:

*(a five part series)*

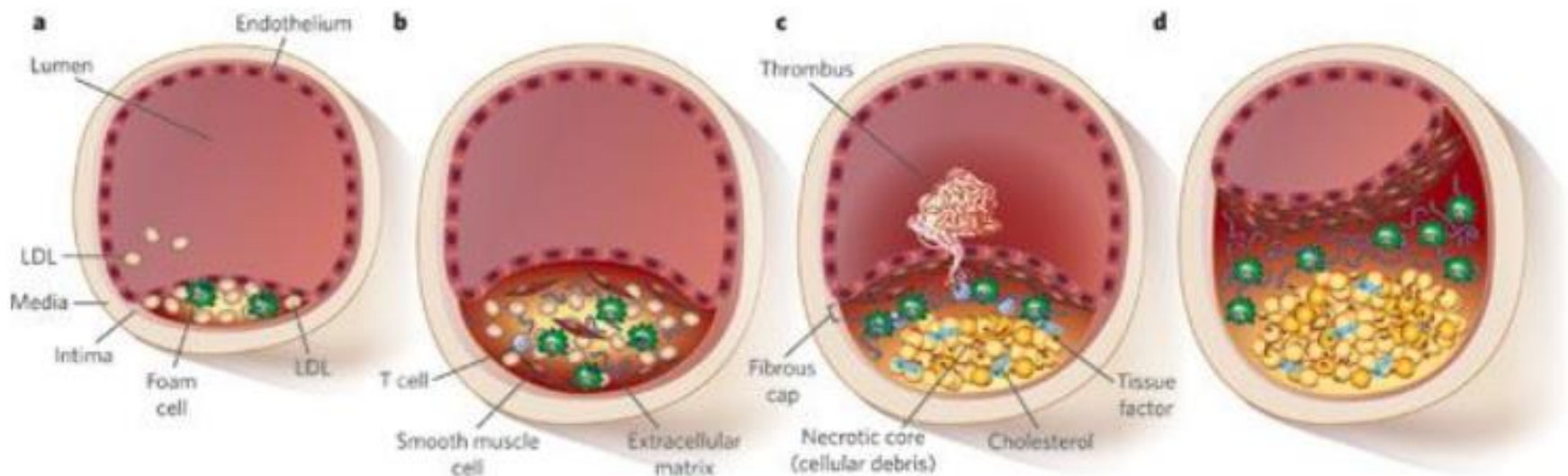
- I. Atherogenesis
- II. Chest Pain and The Anginal Syndromes (17:23):  
<https://youtu.be/UTCz2EC8bNw>
- III. EKG localization of Myocardial Infarction (13:54):  
<https://youtu.be/tY1CaJemXGA>
- IV. Cardiac Pathology and Complications of Myocardial Infarction (15:00): [https://youtu.be/JKo\\_PqlTW6k](https://youtu.be/JKo_PqlTW6k)
- V. Lipoprotein Metabolism and Lipid Lowering Drug Therapy (*Live Lecture*; 16:13): <https://youtu.be/ixuAoVqtUOY>

# Four Key Steps in Atherogenesis

1. Initiating Event (e.g. tobacco, HTN, DM) → Endothelial Damage
  - Platelet Adhesion and Aggregation
2. Endothelial Damage and Dysfunction
  - Monocyte/Lymphocyte Migration into Intima
  - LDL cholesterol Oxidation (accelerated by free radicals)
3. Smooth Muscle Cell Migration and Proliferation
  - Stimulated by Growth Factors and Cytokines
    - Platelet-derived Growth Factor, Endothelial GF, MΦ cytokines
4. Cytokines/Growth Factors (TGF- $\beta$ ) → SMC
  - Fibrogenesis → interstitial collagen and extracellular matrix production



# Four Key Steps in Atherogenesis



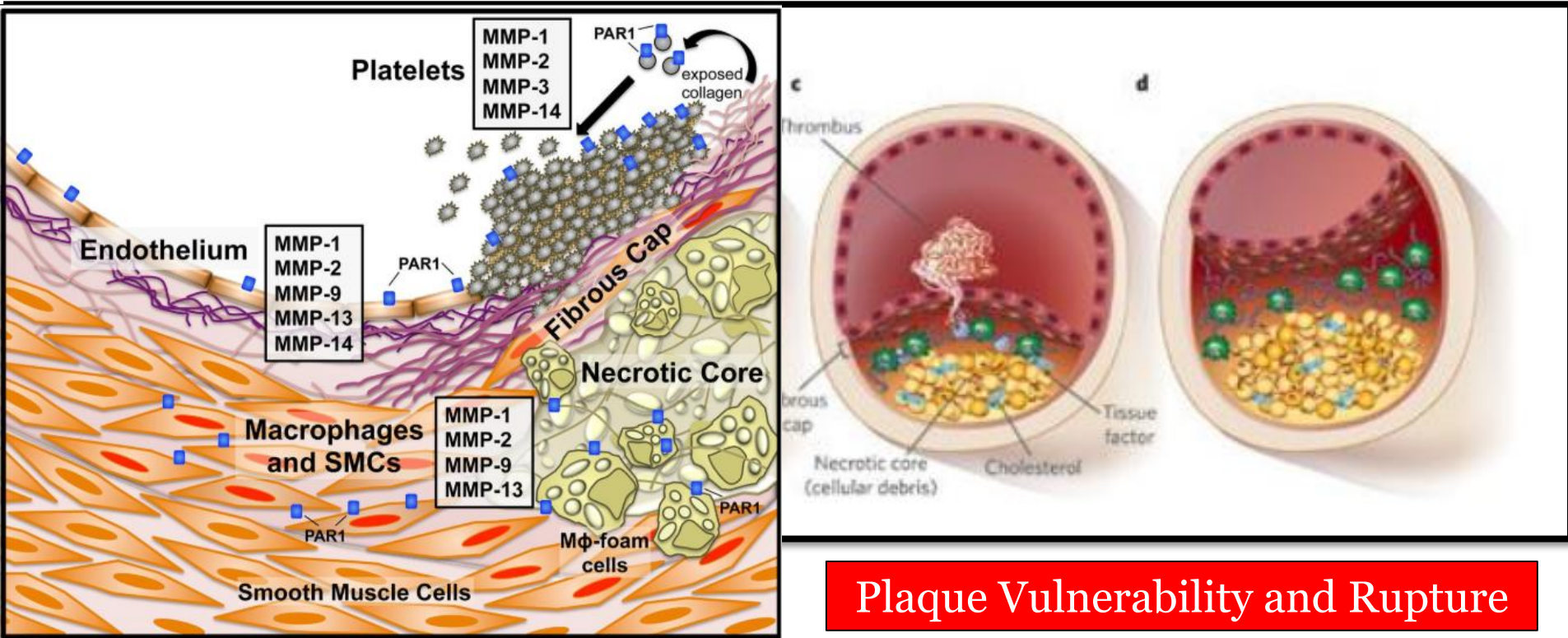
## 4. Cytokines/Growth Factors (TGF- $\beta$ ) & SMC

- Fibrogenesis, interstitial collagen and extracellular matrix production

Angina

Plaque Vulnerability and Rupture

# Four Key Steps in Atherogenesis



Plaque Vulnerability and Rupture

Matrix Metalloproteinases



# Four Key Steps in Atherogenesis

1. **Initiating Event** (e.g. tobacco, HTN, DM, HLD) → Endothelial Damage

– Platelet Adhesion and Activation

2. Endothelial Damage → ↑ Permeability

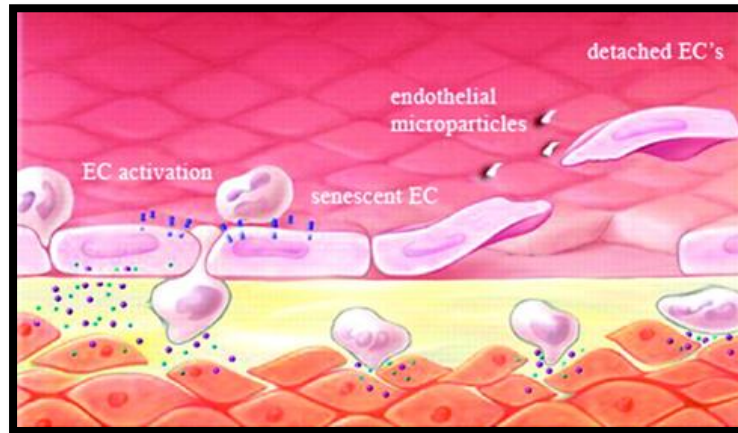
3. *A Series of Activations*

• Platelet-derived GF, Vascular Endothelial GF, MΦ cytokines

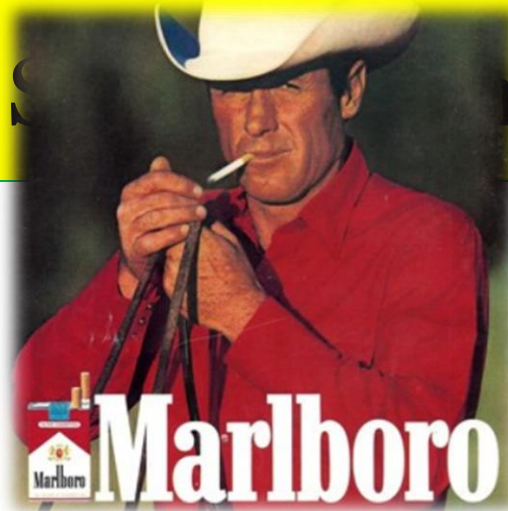
4. Cytokines/Growth Factors (TGF-β) → SMC

– Fibrogenesis → interstitial collagen and extracellular matrix production

# Four Key Steps in Atherosclerosis

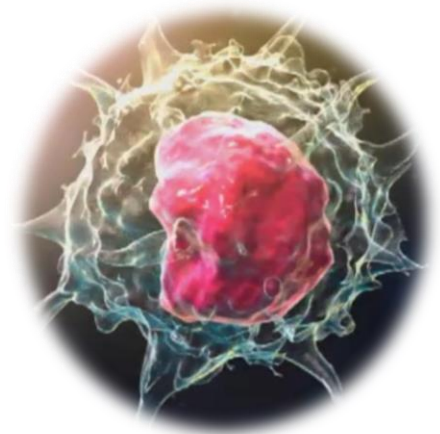
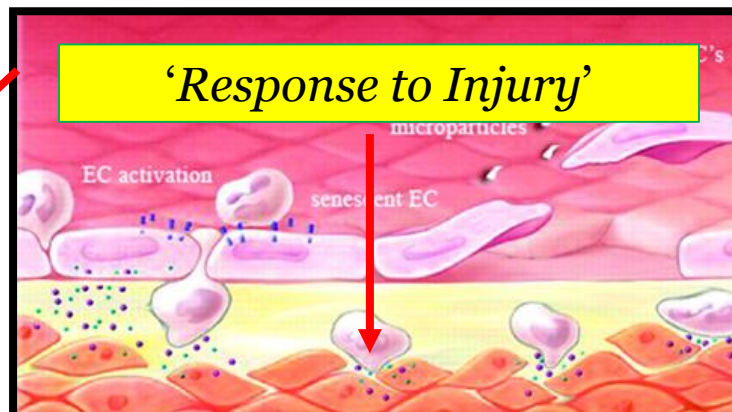
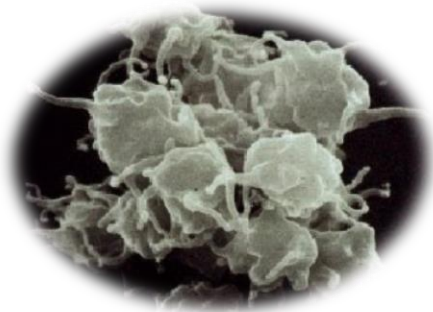


# Four Key Steps in Atherosclerosis

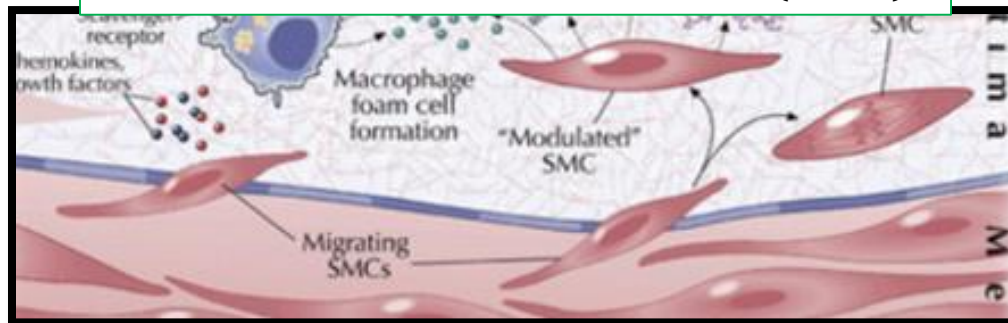


Platelets

Monocytes

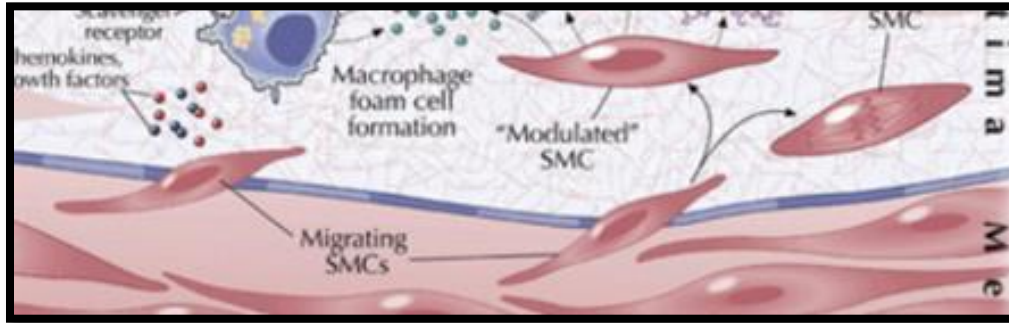
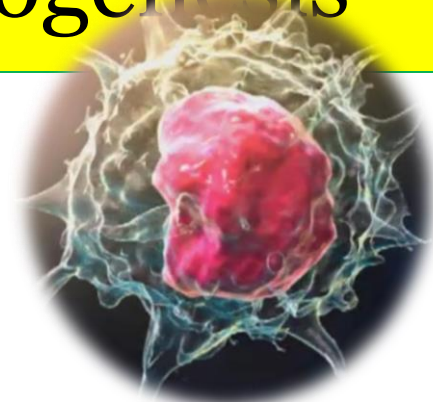
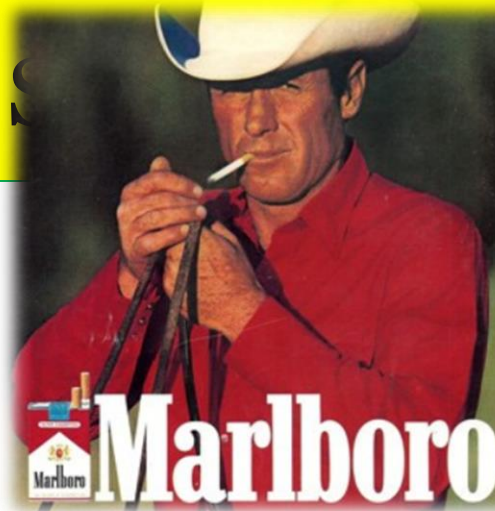
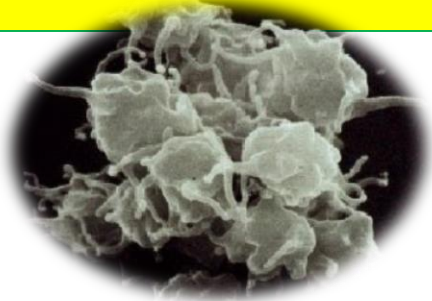


Vascular Smooth Muscle Cells (SMC)





# Four Key Steps in Atherogenesis

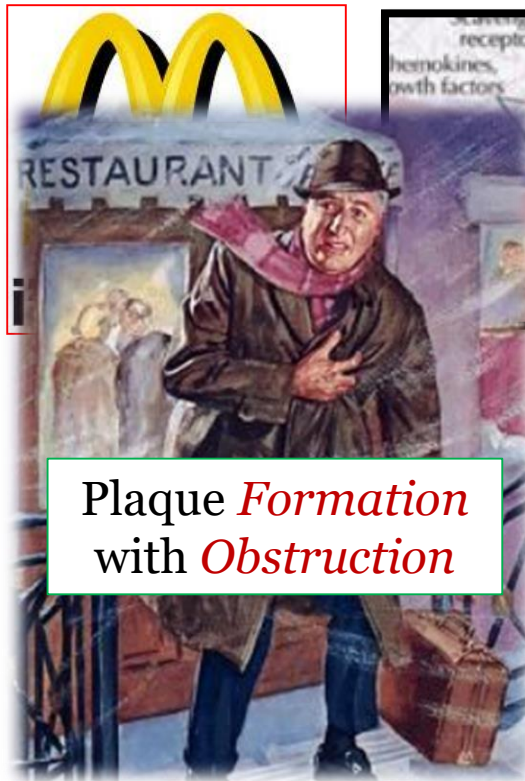
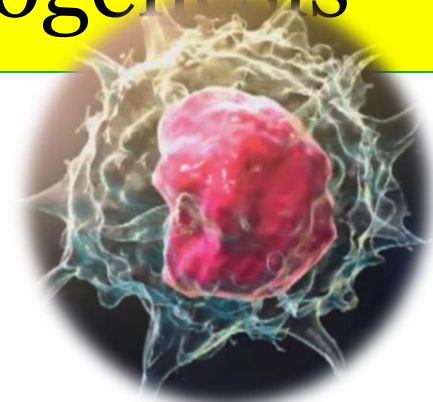
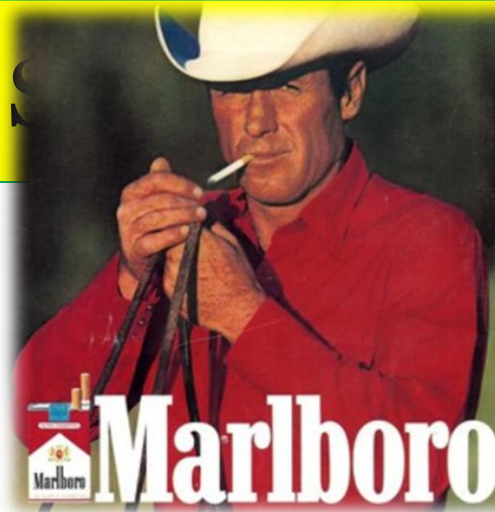
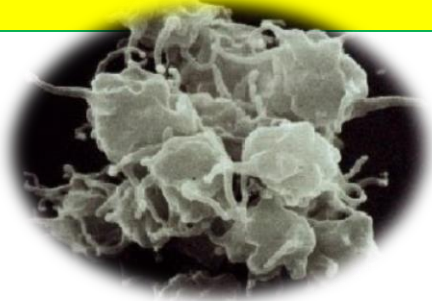


SMC → ECM  
(*Fibrous Cap*)

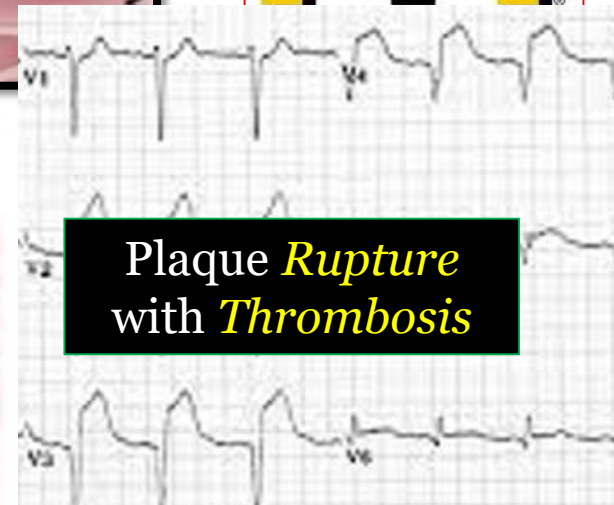
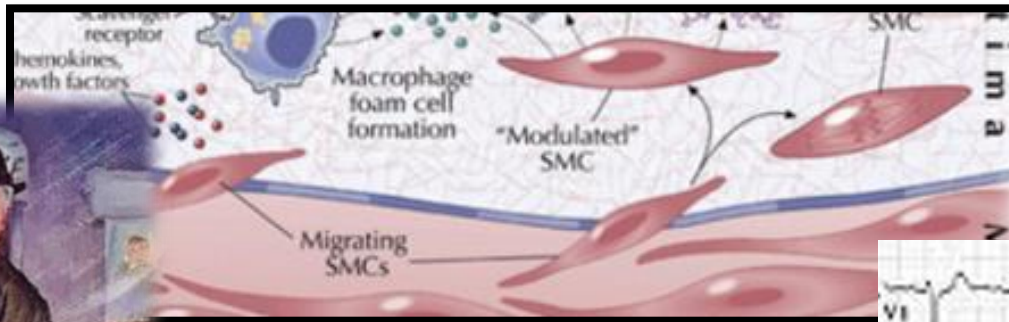


Lipid-Laden MΦ  
(*Foam Cells*)

# Four Key Stages of Atherogenesis



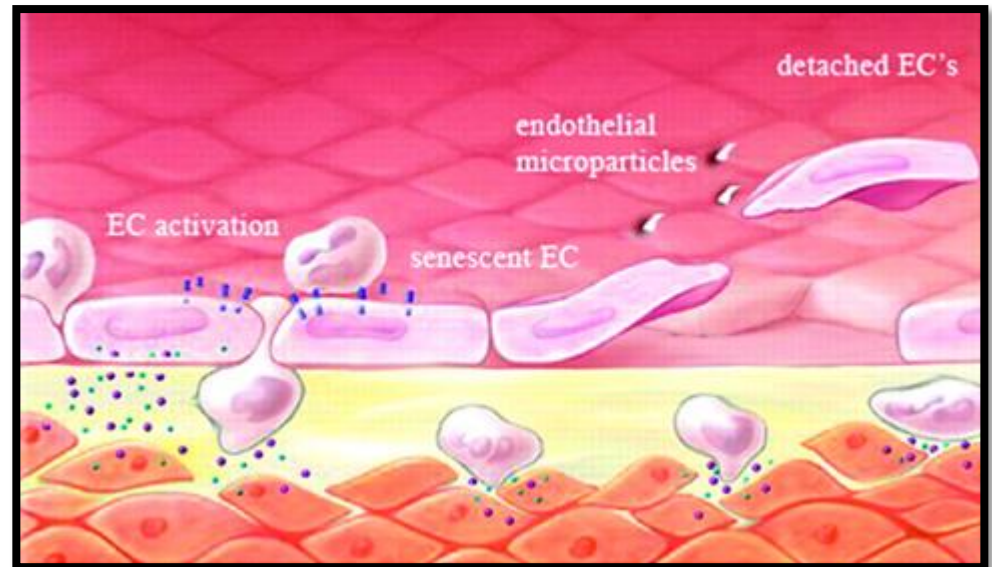
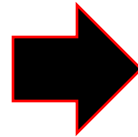
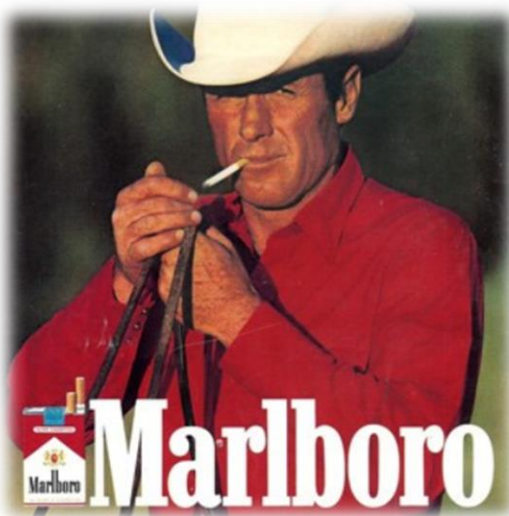
Plaque *Formation*  
with *Obstruction*



Plaque *Rupture*  
with *Thrombosis*

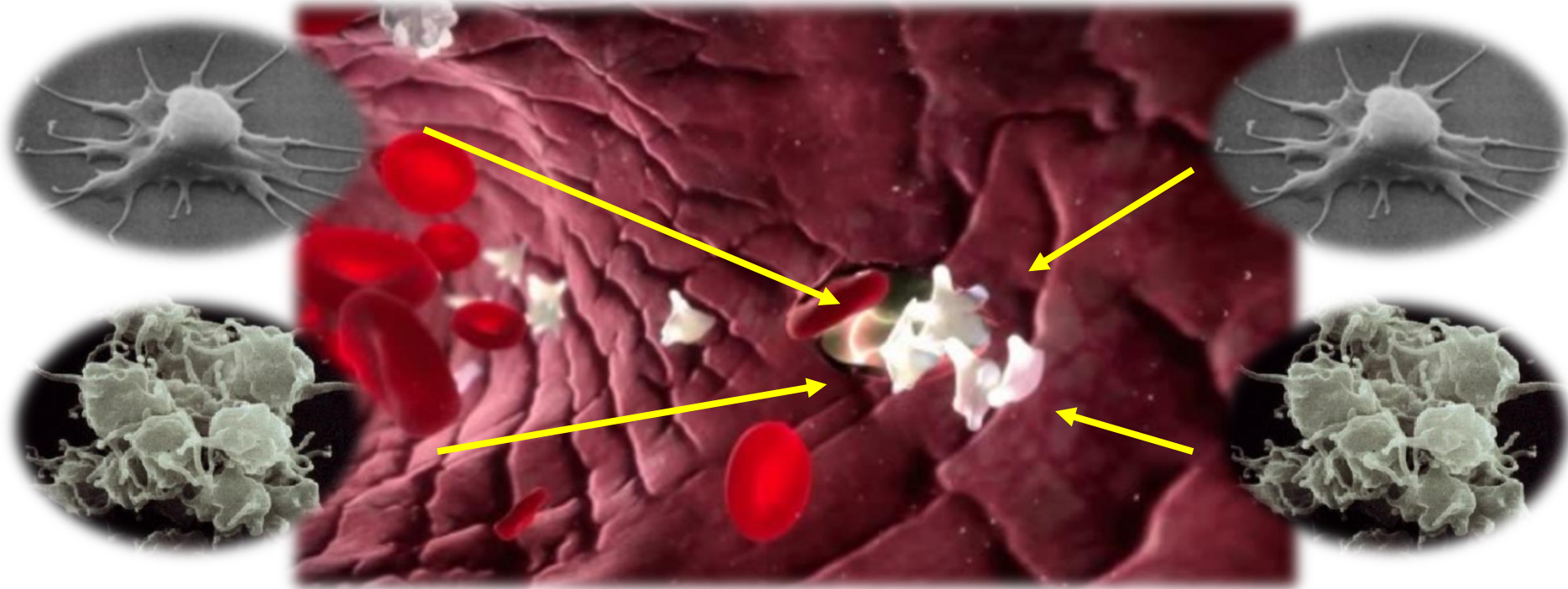
# Four Key Steps in Atherogenesis

1. Initiating Event (e.g. tobacco, HTN, DM, HLD) → Endothelial Damage



# Four Key Steps in Atherogenesis

1. Initiating Event (e.g. tobacco, HTN, DM, HLD) → Endothelial Damage
  - Platelet Adhesion and Activation



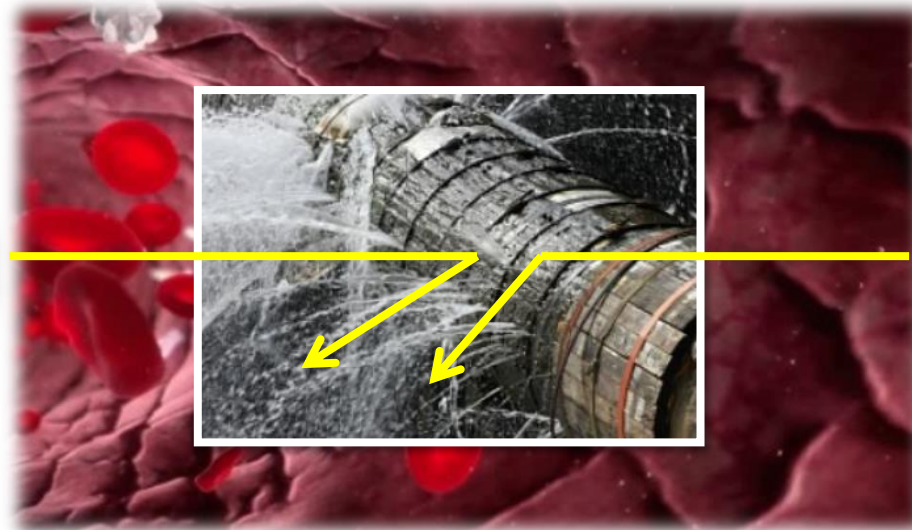
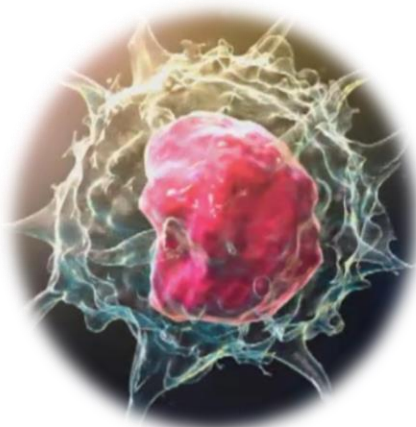
# Four Key Steps in Atherogenesis

1. Initiating Event (e.g. tobacco, HTN, DM, HLD) → Endothelial Damage
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2. Endothelial Damage → ↑ Permeability
  - Monocyte/Lymphocyte Adhesion and Migration into Intima
  - LDL cholesterol enters the Intima (oxidized by free radicals)



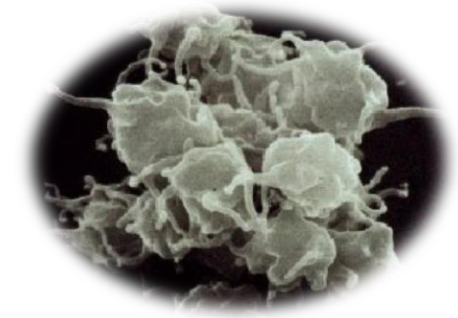
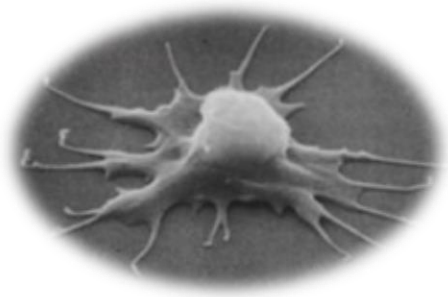
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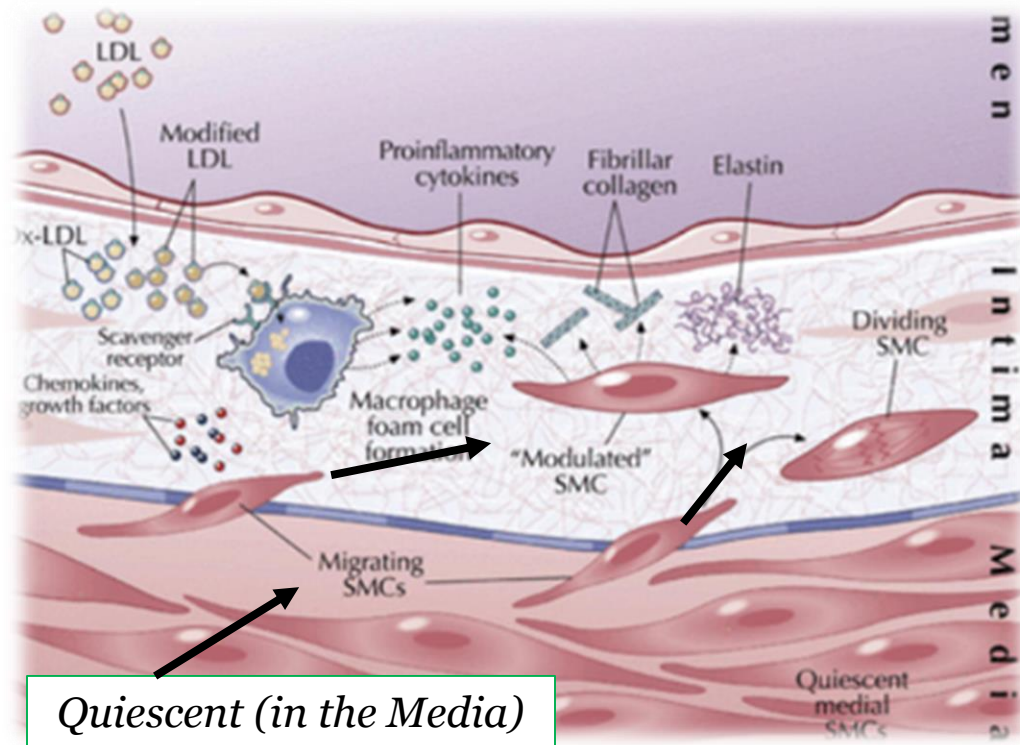


# Four Key Steps in Atherogenesis

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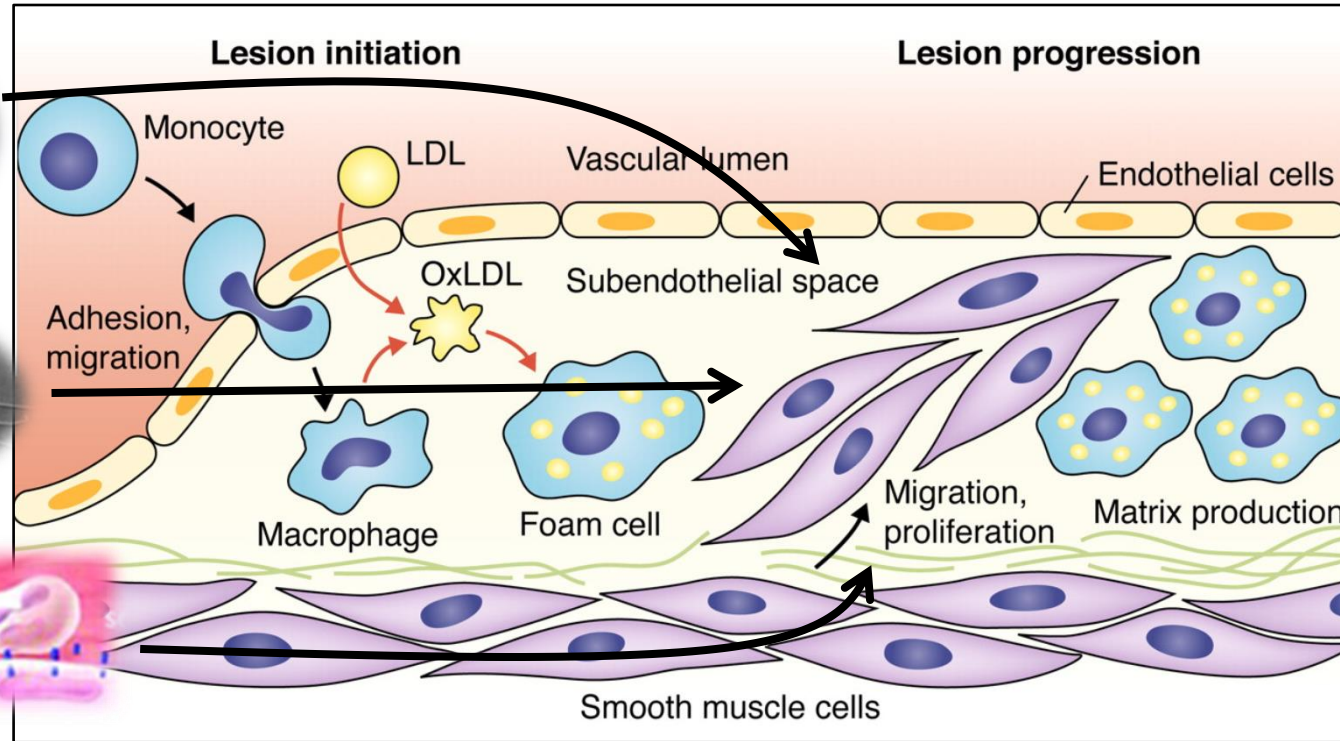
# Key Steps in Atherogenesis



## 3. Smooth Muscle Cell (SMC) Migration and Proliferation



# Key Steps in Atherogenesis



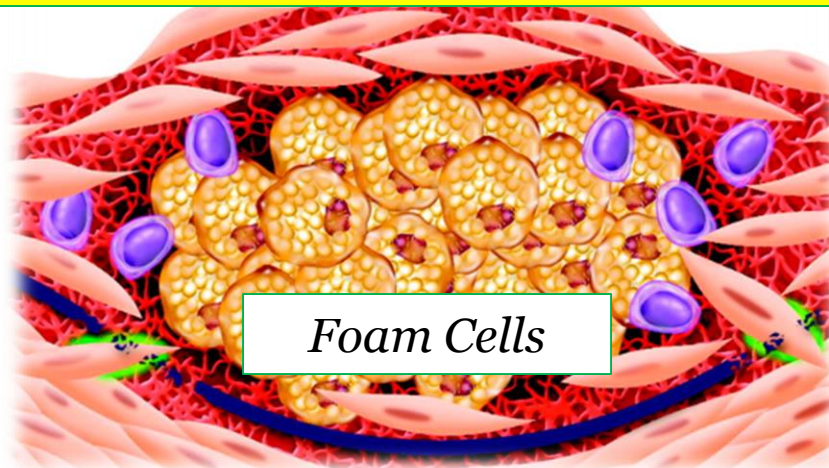
## 3. Smooth Muscle Cell (SMC) Migration and Proliferation

- Stimulated by Growth Factors and Cytokines
  - Platelet-derived GF, Vascular Endothelial GF, MΦ cytokines (e.g. TGF)

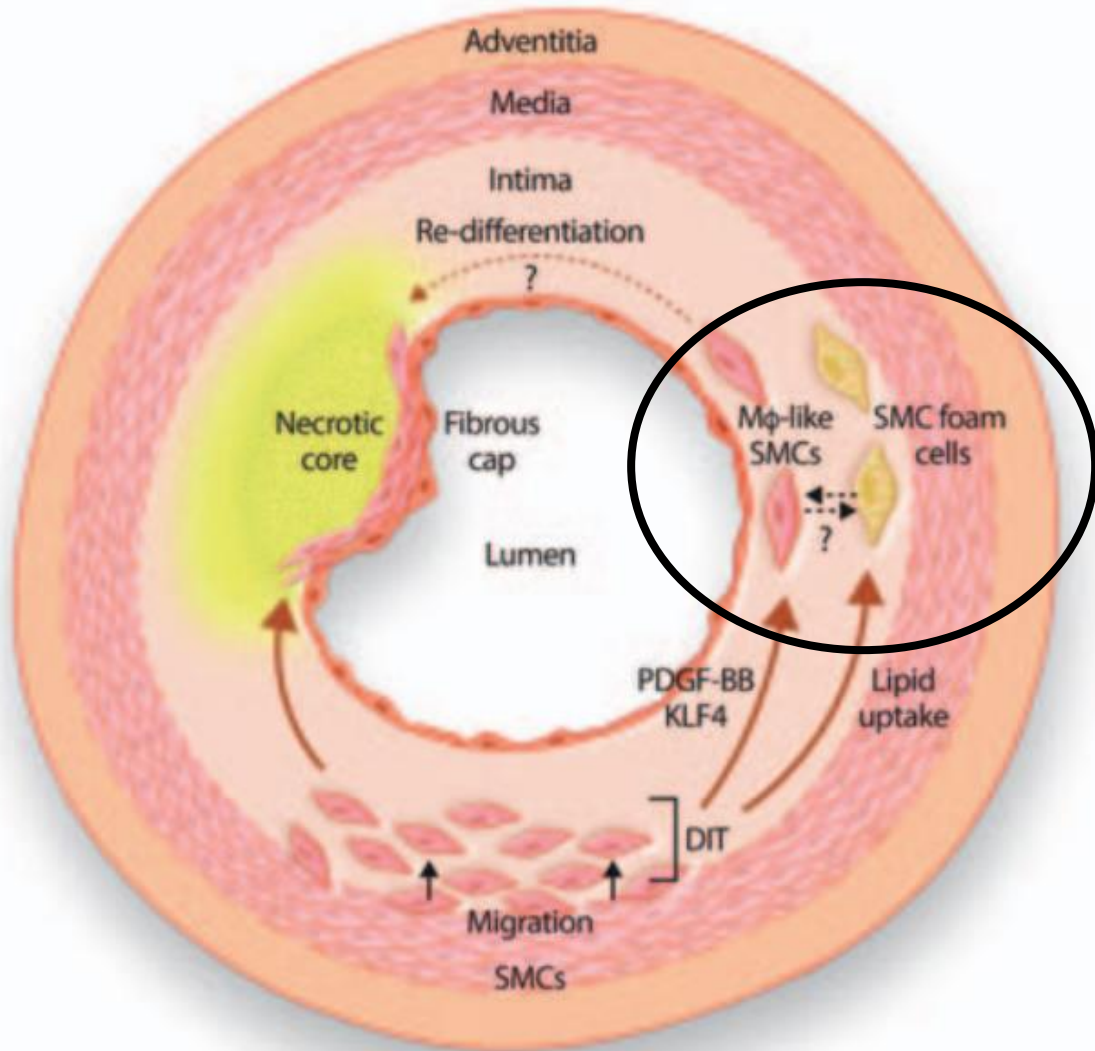
# Four Key Steps in Atherogenesis

2. Endothelial Damage → ↑ Permeability
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3. Smooth Muscle Cell (SMC) Migration and Proliferation
  - Stimulated by Growth Factors and Cytokines
    - Platelet-derived GF, Vascular Endothelial GF, MΦ cytokines

Key Step: Tissue MΦ and Activated SMC both ingest oxidized LDL cholesterol to form *Foam Cells*



# Four Key Steps in Atherogenesis



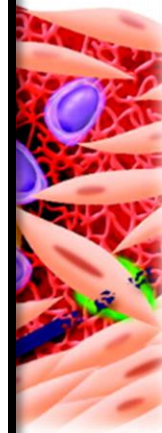
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Migration into Intima  
(induced by free radicals)  
Proliferation and Proliferation

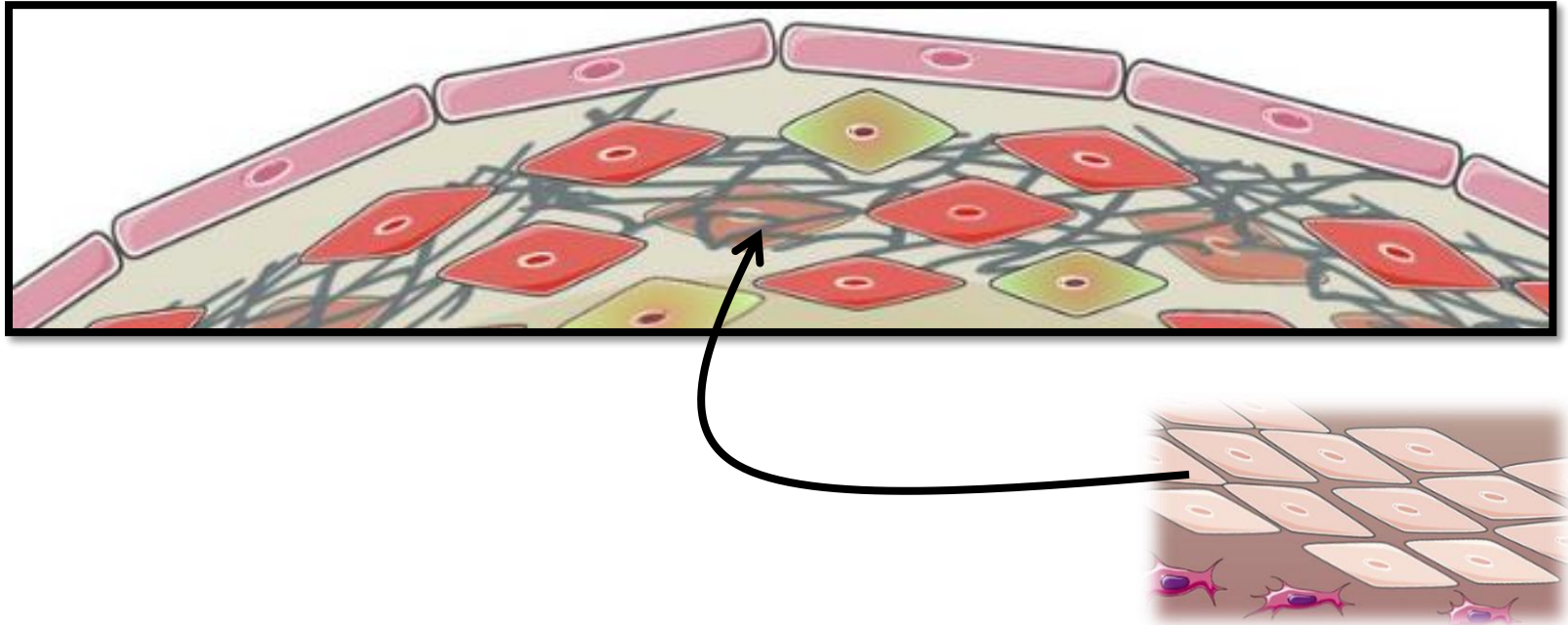
lines

PDGF, Mφ cytokines

SMC both ingest  
*Foam Cells*

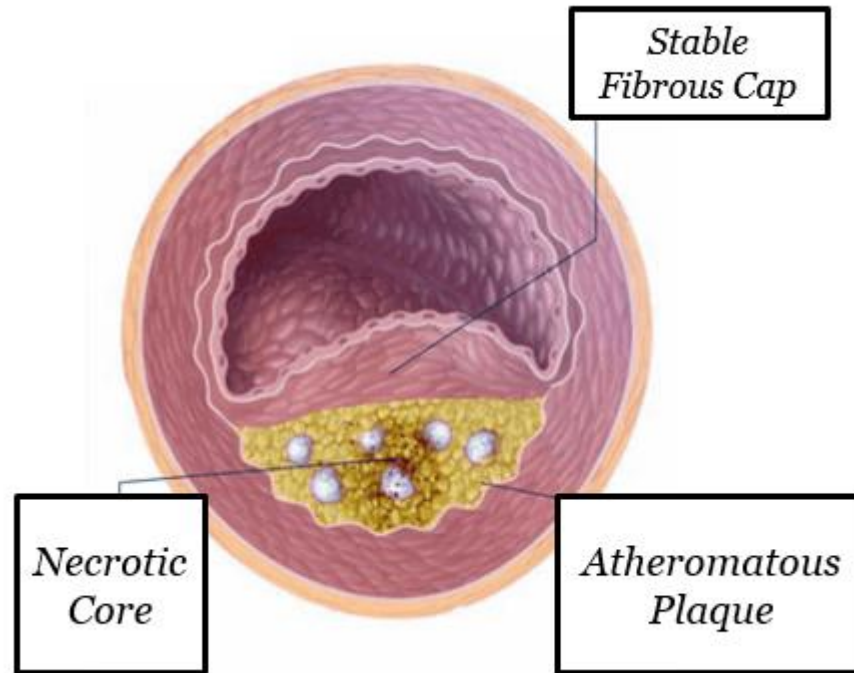


# Key Steps in Atherogenesis



4. Cytokines/Growth Factors ( $\text{TGF-}\beta$ )  $\rightarrow$  *SMC*
  - Fibrogenesis  $\rightarrow$  *interstitial collagen and extracellular matrix production*

# Key Steps in Atherogenesis



4. Cytokines/Growth Factors ( $\text{TGF-}\beta$ )  $\rightarrow$  *SMC*
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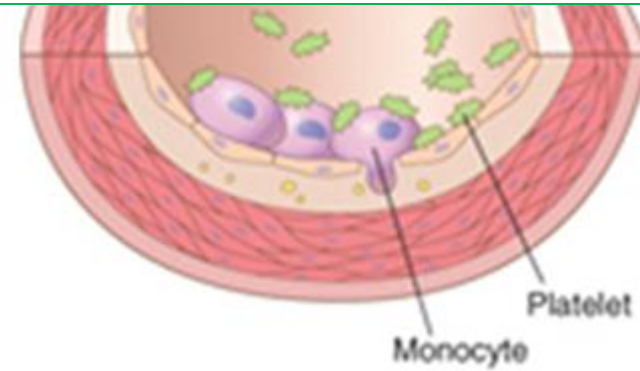
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    - Platelet-derived GF, Vascular Endothelial GF, MΦ cytokines
4. Cytokines/Growth Factors (TGF-β) → SMC
  - Fibrogenesis → interstitial collagen and extracellular matrix production

1. Endothelial Damage  
(e.g. HTN, Tob, DM, HLD)

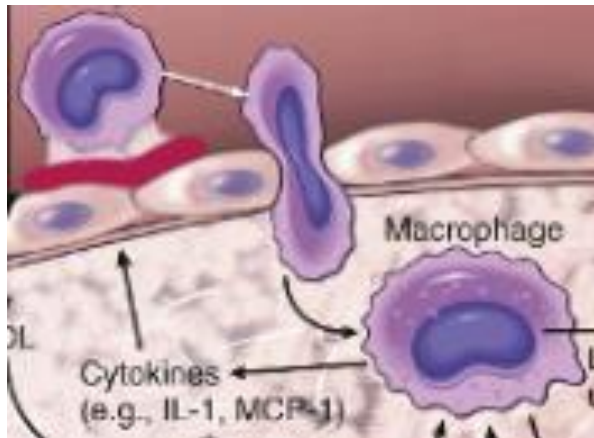
Initiating Event

Platelet adhesion and activation  
with release of PDGF

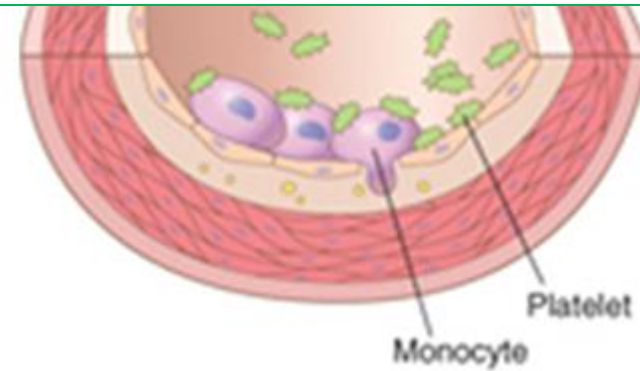


1. Endothelial Damage  
(e.g. HTN, Tob, DM, HLD)

Initiating Event



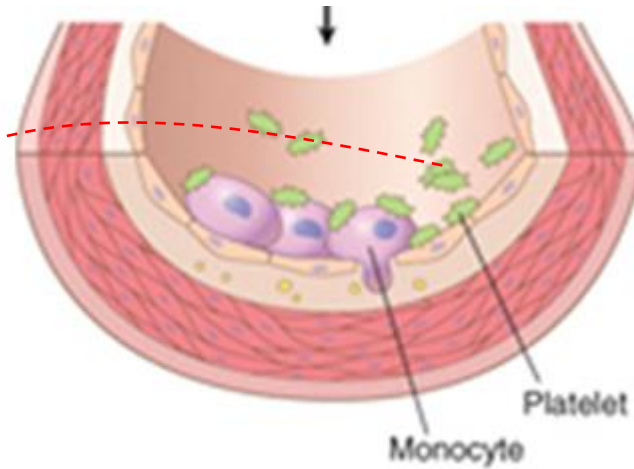
Platelet adhesion and activation  
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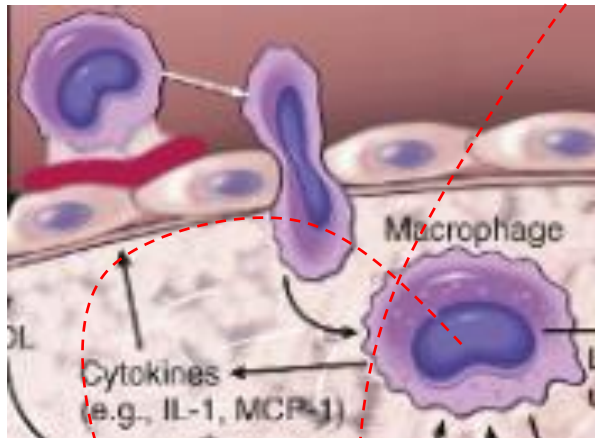
2. Tissue monocyte/MΦ Response



# 1. Endothelial Damage (e.g. HTN, Tob, DM)



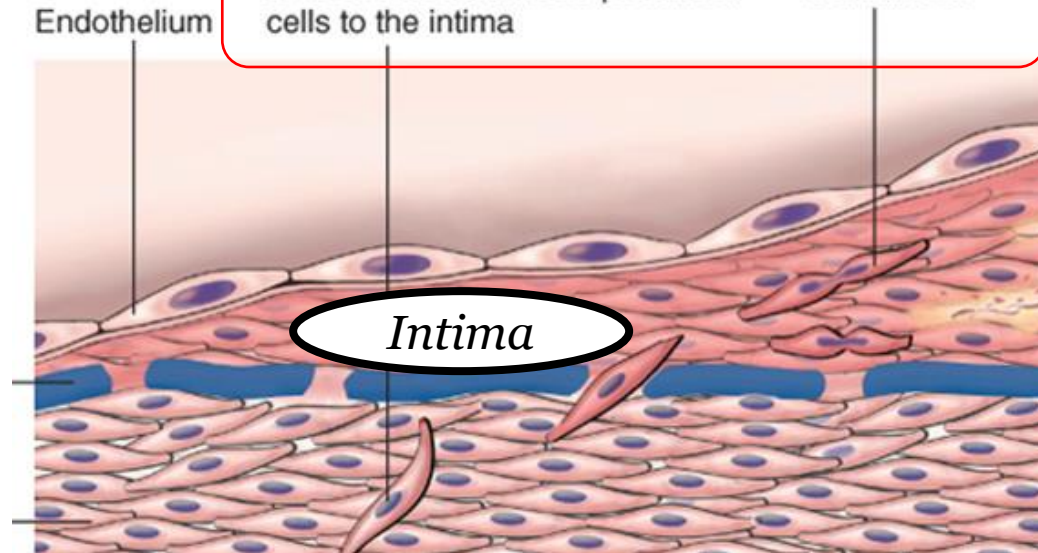
# 2. Tissue monocyte/MΦ Response



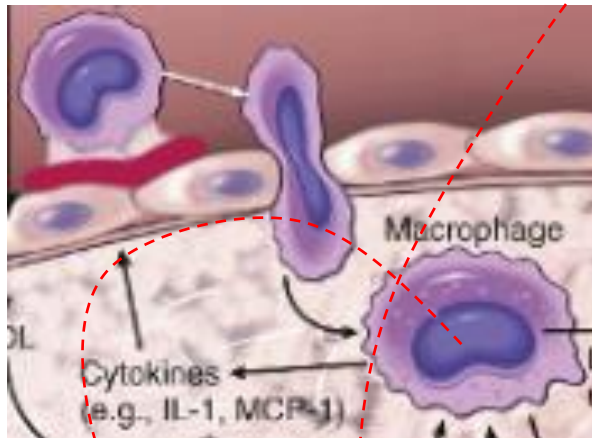
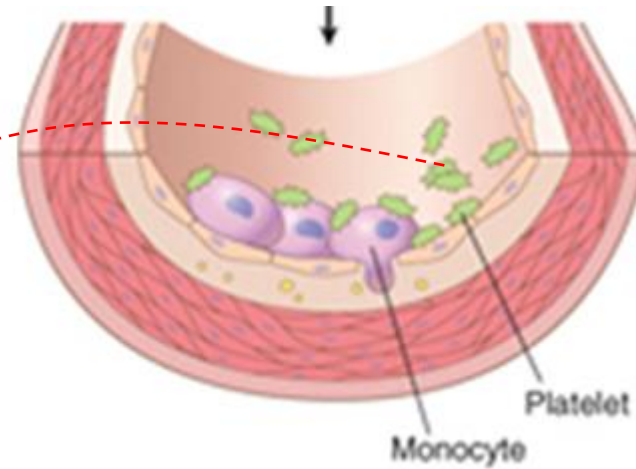
1. Recruitment of smooth muscle cells or smooth muscle precursor cells to the intima
2. Smooth muscle cell mitosis

PDGF, VEGF, cytokines

3. Smooth muscle (SMC) migration & proliferation



# 1. Endothelial Damage (e.g. HTN, Tob, DM)



# 2. Tissue monocyte/MΦ Response

- 1. Recruitment of smooth muscle cells or smooth muscle precursor cells to the intima
- 2. Smooth muscle cell mitosis

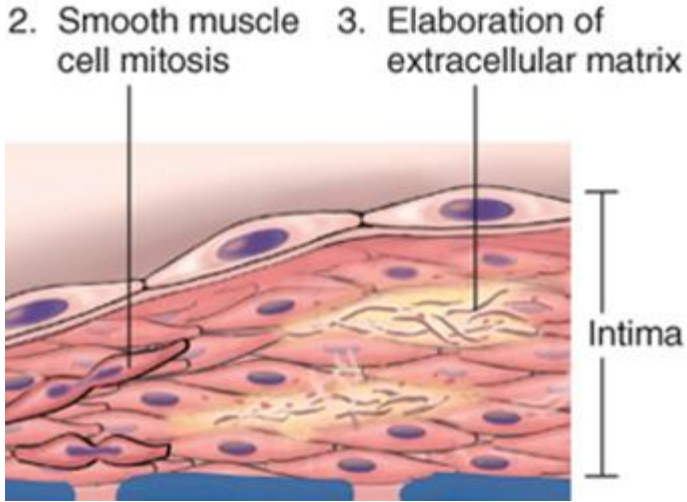
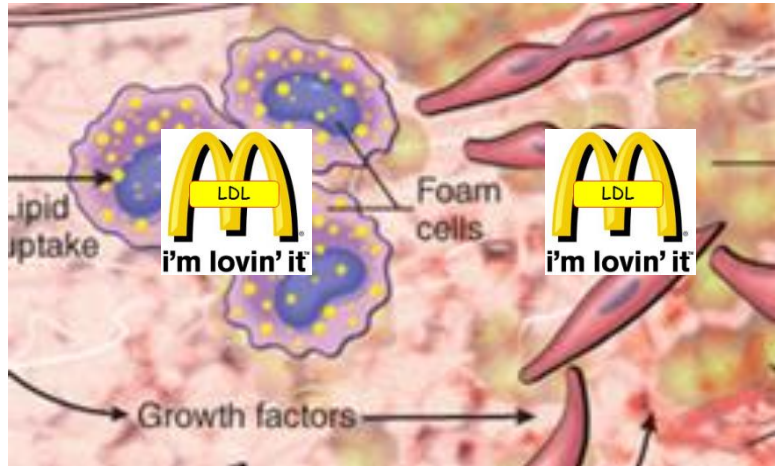
PDGF, VEGF, cytokines

# 3. Smooth muscle (SMC) migration & proliferation

Foam Cells: MΦ and SMC

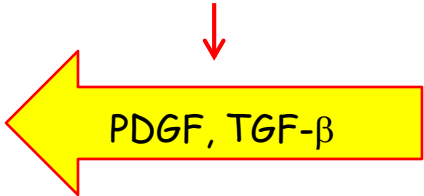


**MΦ** and **SMC** ingest oxidized LDL to form foam cells

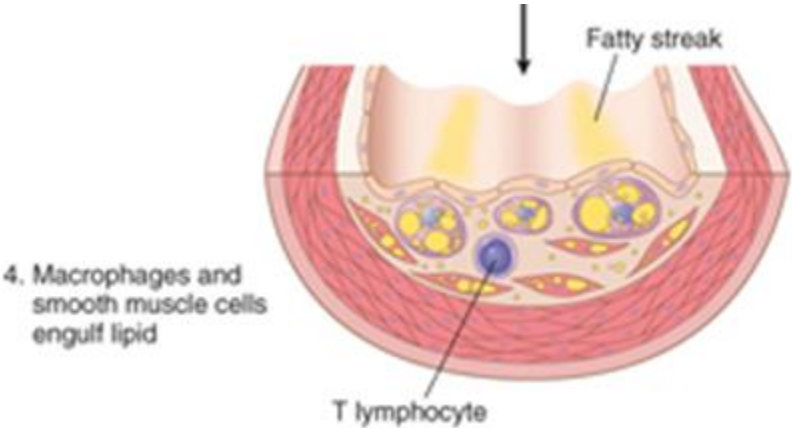


**SMC** produce collagen and extracellular matrix

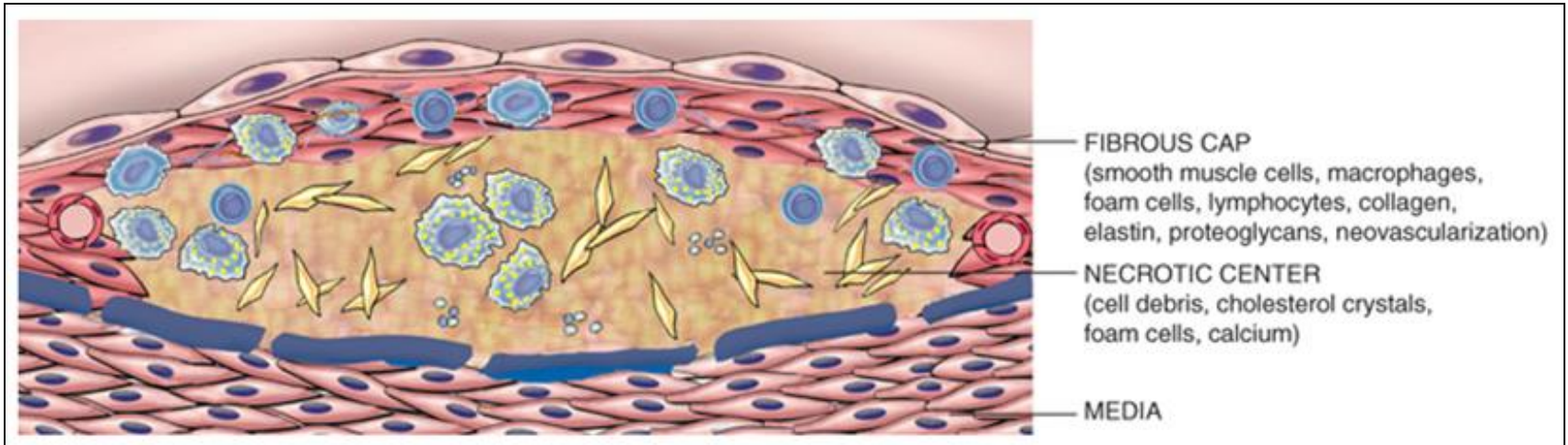
Endothelium, MΦ



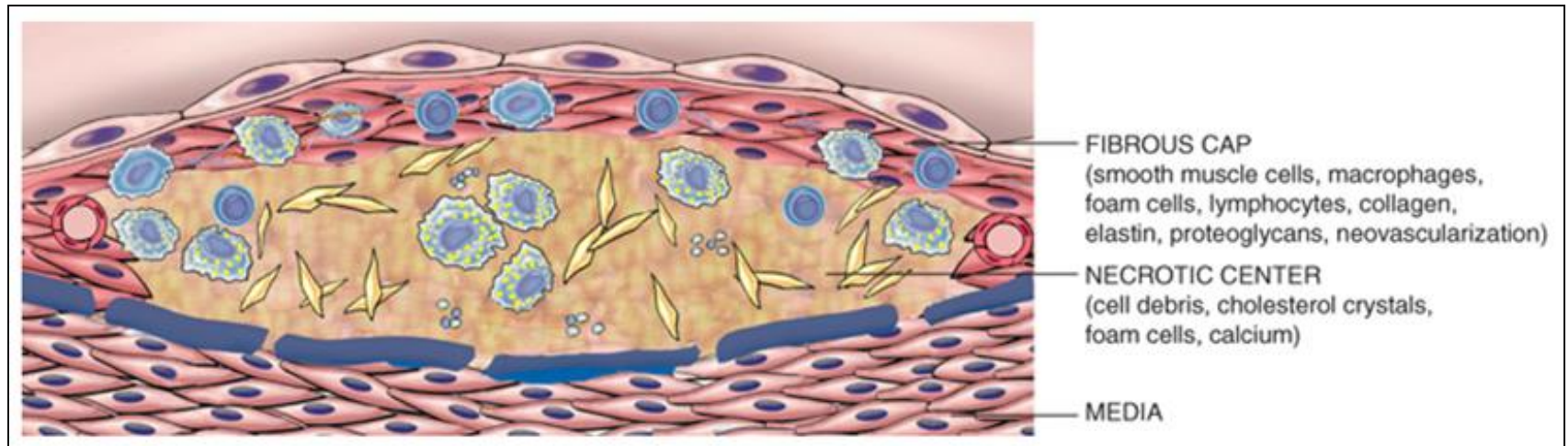
Lipid filled foam cells derived from MΦ and SMC form the **fatty streak**



## Atheromatous Plaque (continuous remodeling)

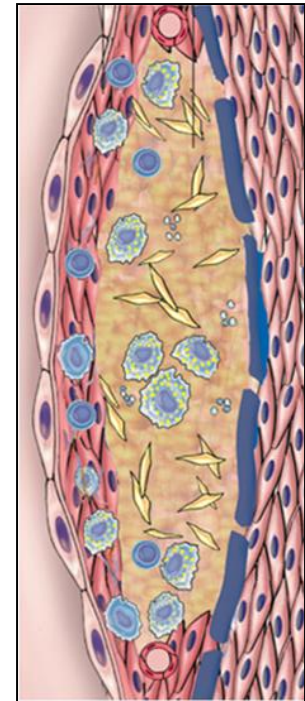
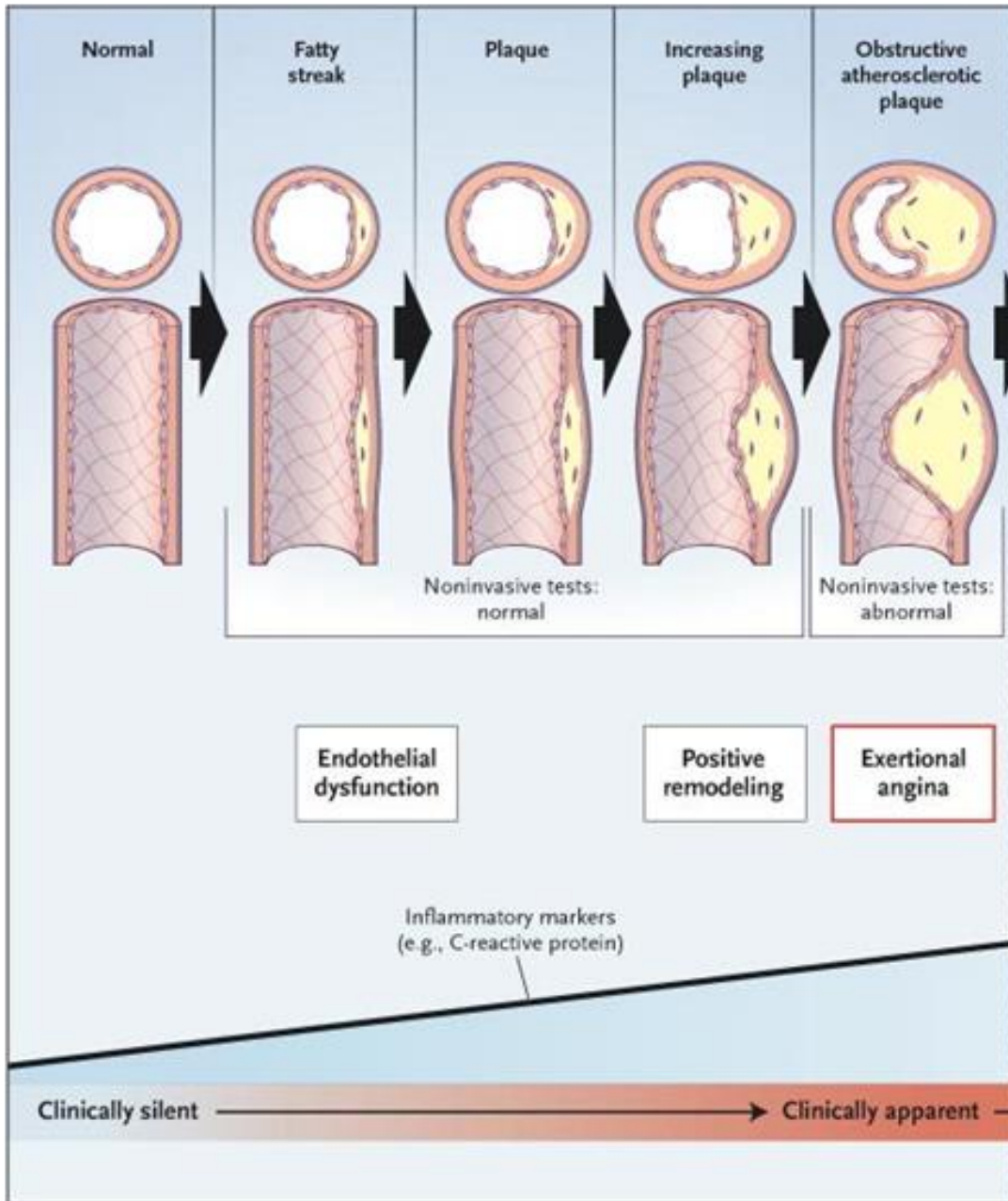


## Atheromatous Plaque (continuous remodeling)



Plaque stability depends on the **integrity of the fibrous cap**.

*Balance of Collagen Synthesis versus Degradation*



Our fatty streak has grown and remodeled.



Obstructive (Obliterative)

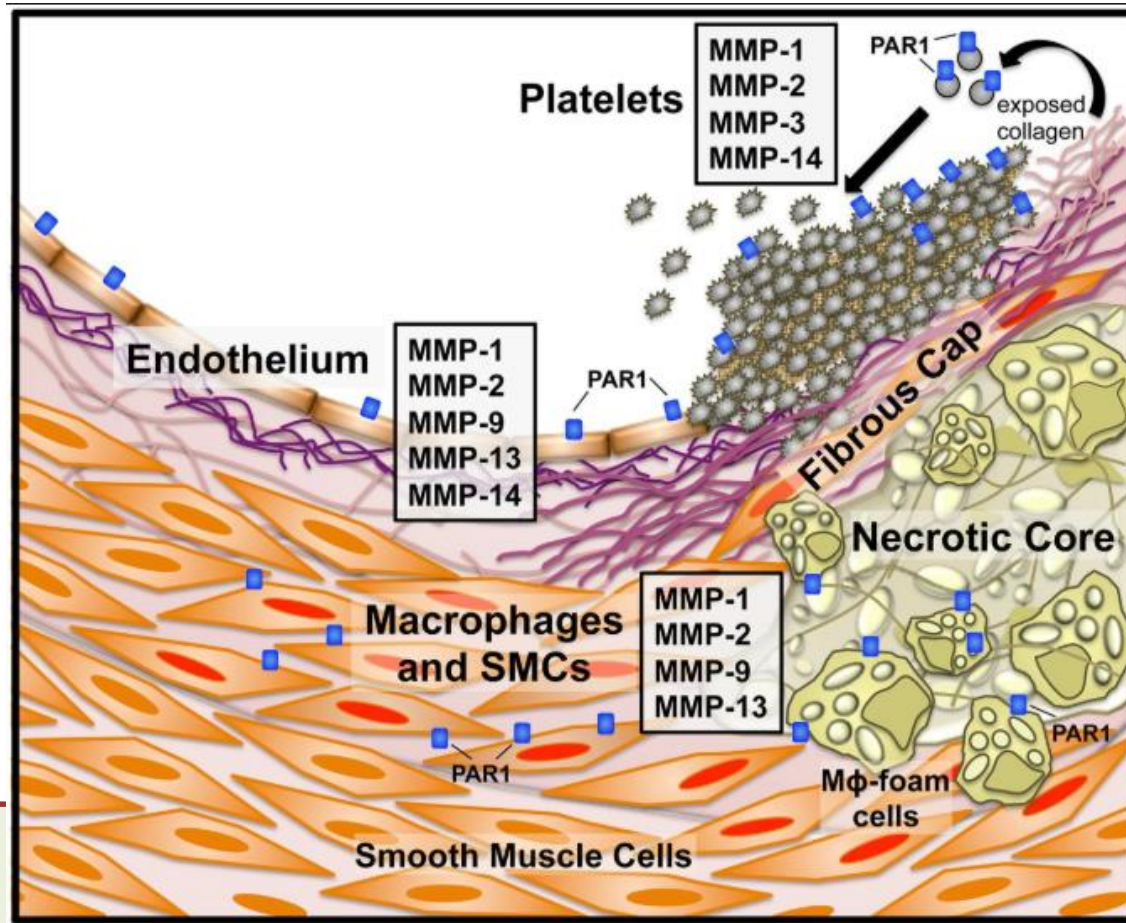
## Chest Pain: the Anginal Syndromes

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[www.12DaysinMarch.com](http://www.12DaysinMarch.com)

**Atherosclerotic Heart Disease:**  
Coronary Vessels, EKG Localization of STEMI and  
Complications/Derivatives for USMLE Step One



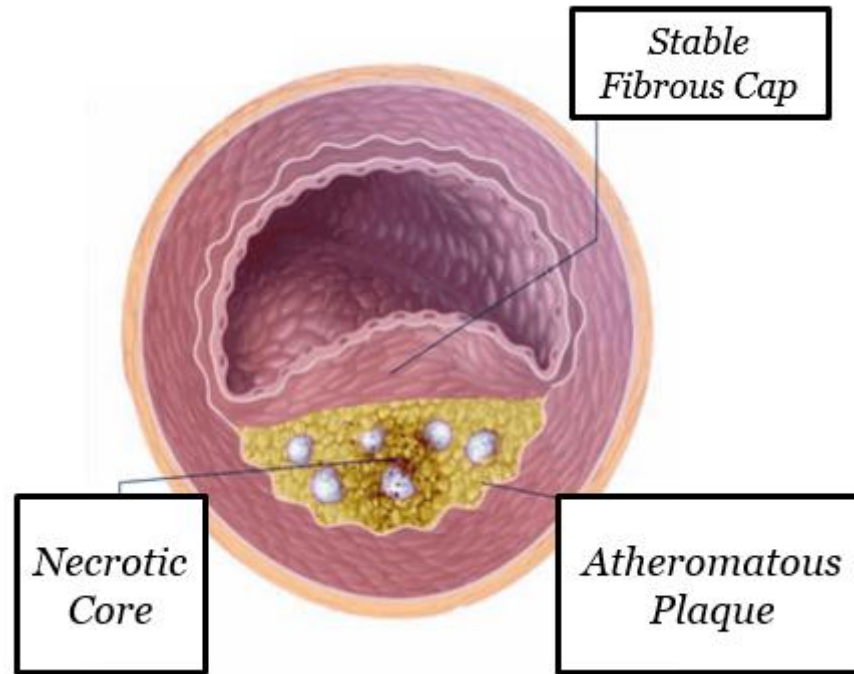
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**Metalloproteinases** secreted by M $\Phi$  destabilizes plaque integrity  $\rightarrow$  vulnerable plaque

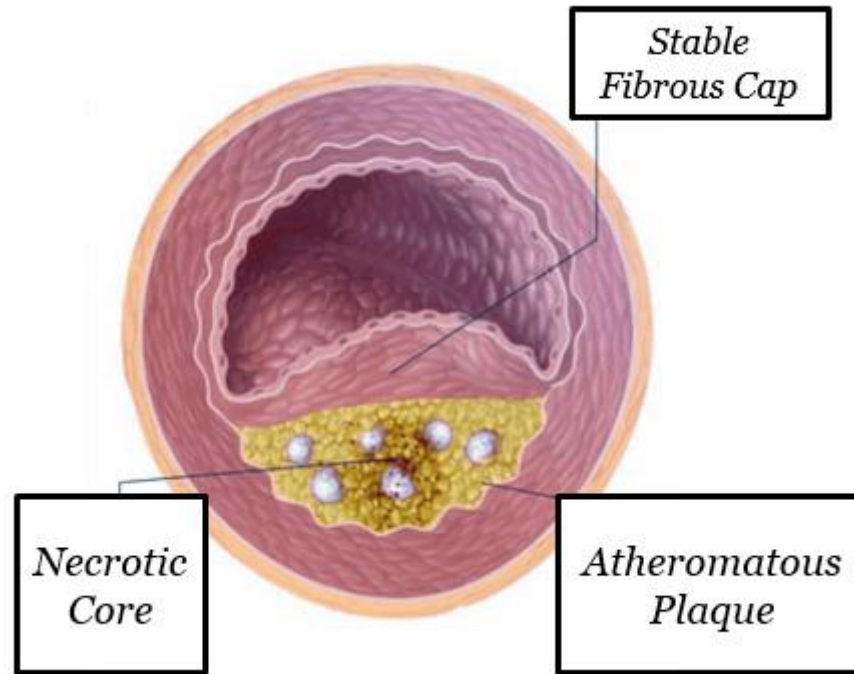
- Q. Stable plaque ruptures (EKG/troponins)...Which enzyme was the bad player?  
 A. Metalloproteinases





Which cell is responsible for synthesizing the fibrous cap?:

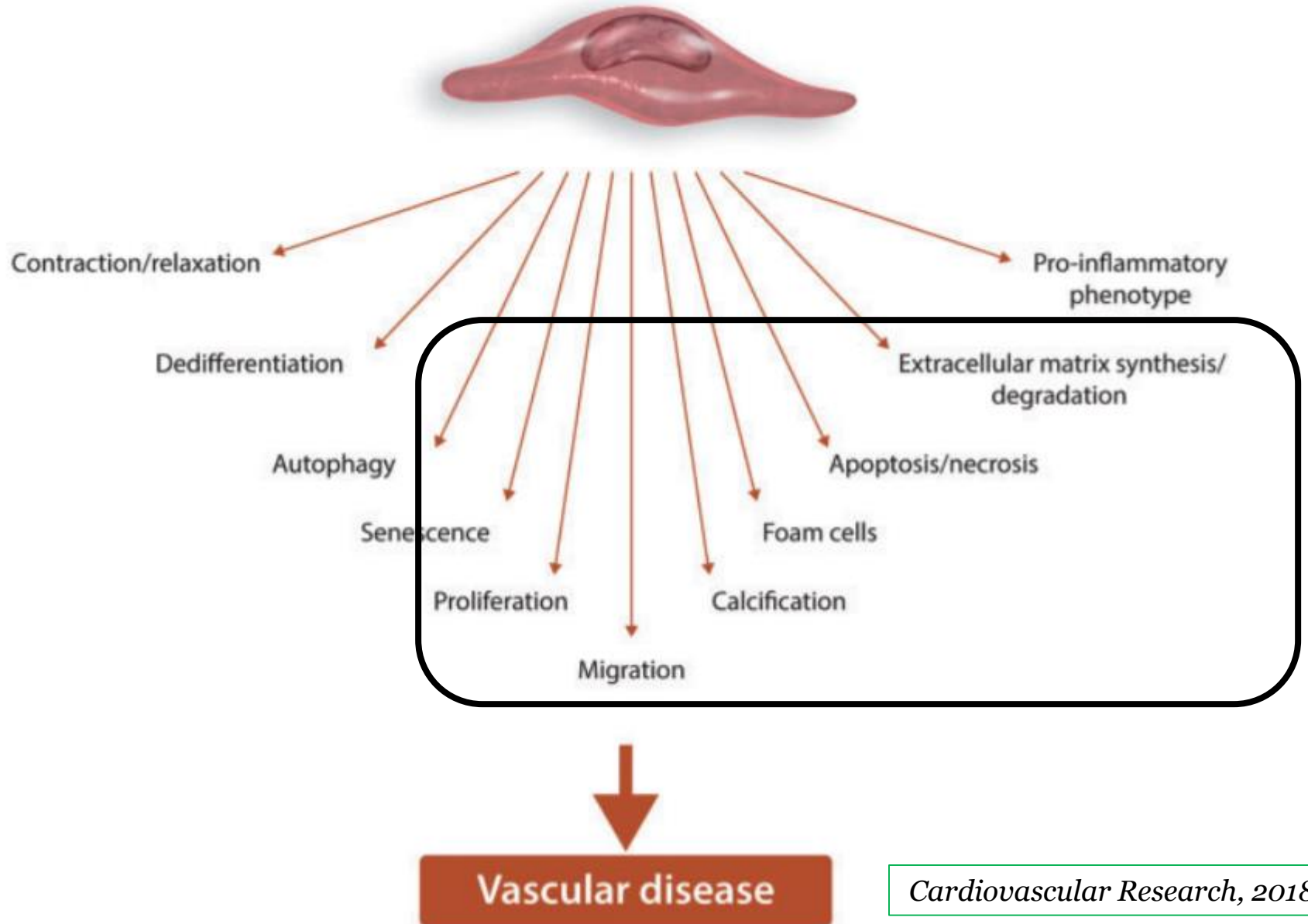
1. Interstitial Fibroblast
2. Macrophage
3. Endothelial cell
4. Smooth muscle cell



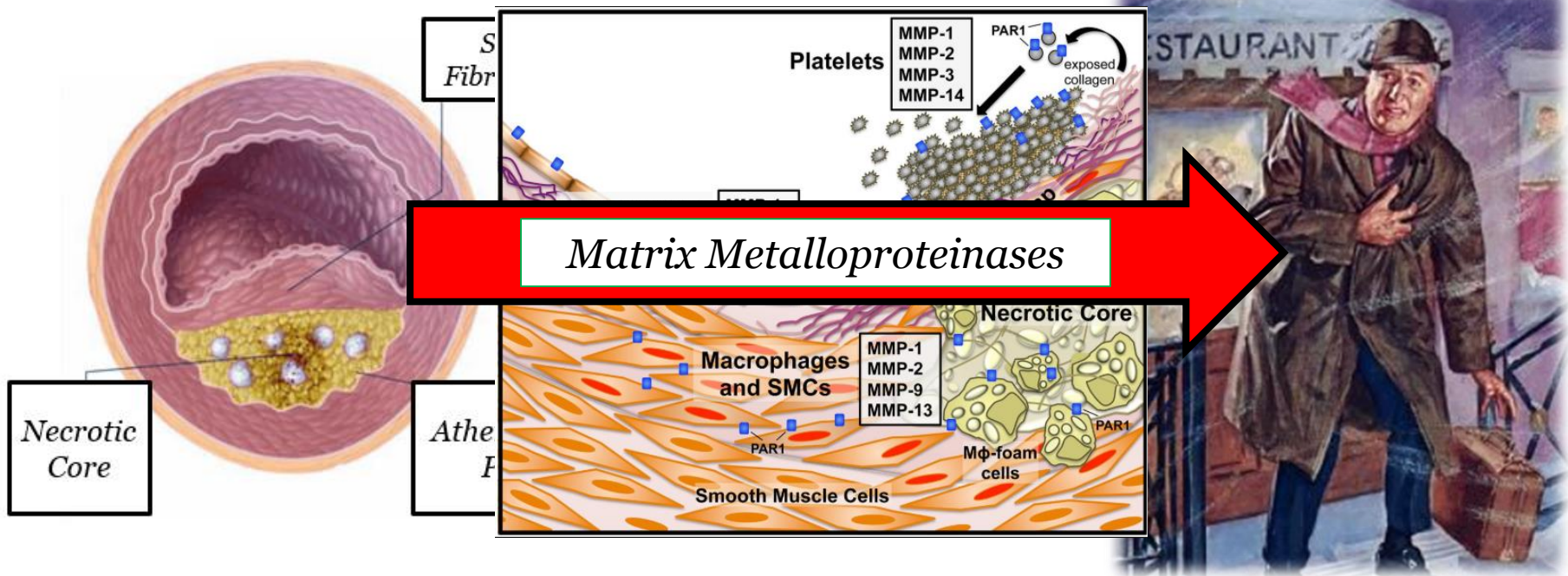
Which cell is responsible for synthesizing the fibrous cap?:

1. Interstitial Fibroblast
2. Macrophage
3. Endothelial cell
4. Smooth muscle cell

*FYI: Vascular Smooth Muscle Cell and Diverse Phenotypic Expression*



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