

# Rheumatoid Arthritis Autoantibodies in Interstitial Lung Disease in the Absence of Peripheral Arthritis

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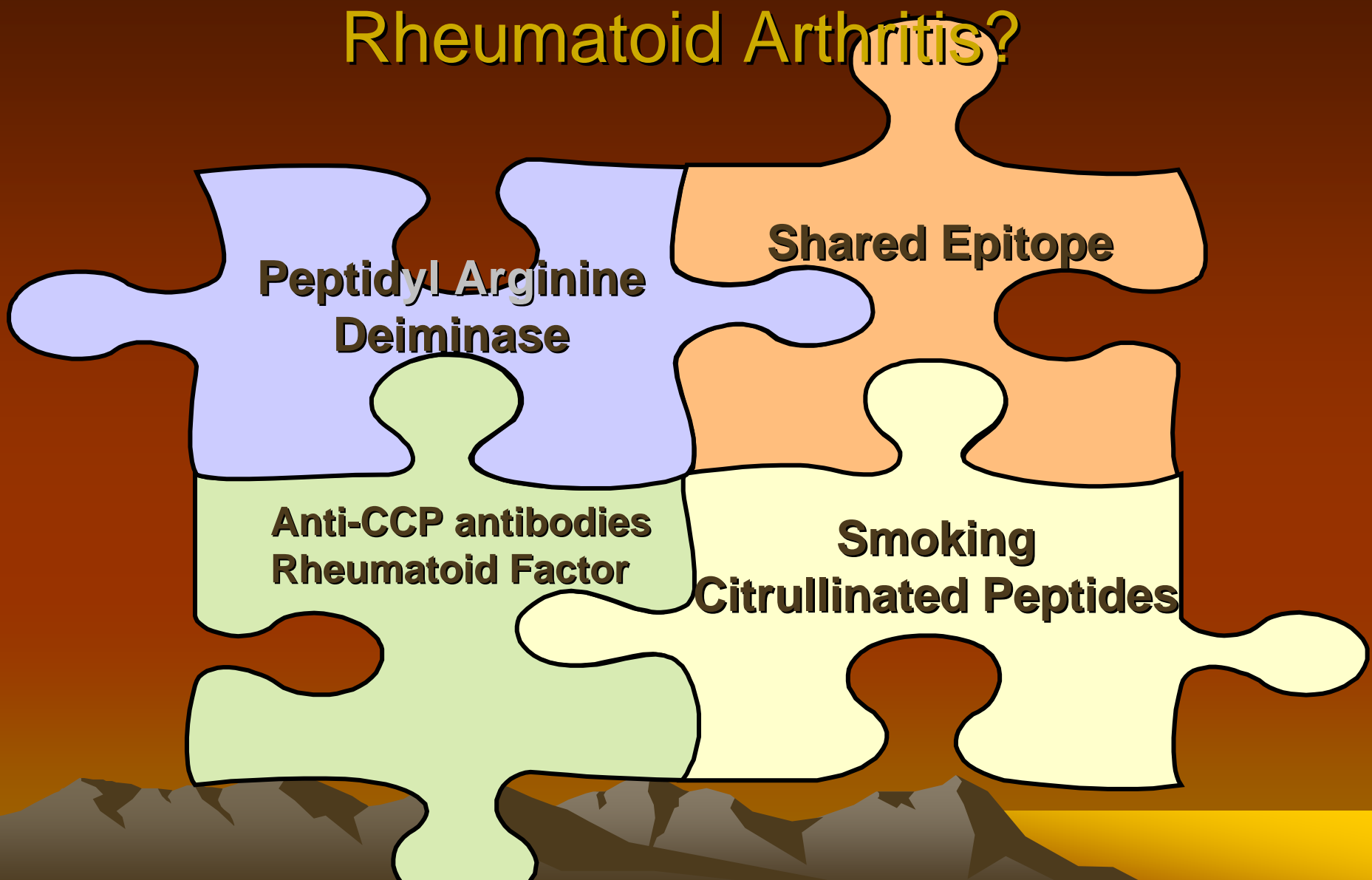
# How does it all fit together in Rheumatoid Arthritis?

**Peptidyl Arginine  
Deiminase**

**Shared Epitope**

**Anti-CCP antibodies  
Rheumatoid Factor**

**Smoking  
Citrullinated Peptides**



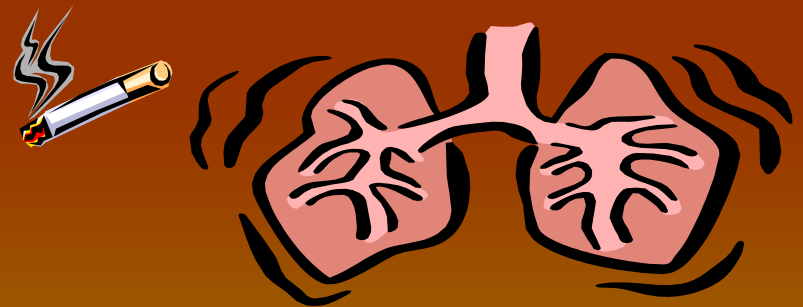
# Background

- Rheumatoid Arthritis is characterized by peripheral arthritis and by autoantibodies, including rheumatoid factor (RF) and antibodies directed against cyclic citrullinated peptides (anti-CCP).
- Rheumatoid Arthritis can involve the lungs in up to 58% of patients: pleural, ILD, nodules, small airway disease.
- The timing of development of lung disease in Rheumatoid Arthritis has not been clearly defined.



# Can Rheumatoid Arthritis Begin in the Lung?

- Autoantibodies can be detected years prior to diagnosis, it is probable that lung disease may also be present.
- Given the relationship of smoking, RF and Rheumatoid Lung disease, it is possible that the initial immune dysregulation begins in the lung.
- Brochoalveolar lavage cells from smokers bound antibodies to modified citrulline, no binding was seen in cells from non-smokers, suggesting smoking may induce deimination.<sup>1</sup>



1. Klareskog, L et al. A New Model for an Etiology of Rheumatoid Arthritis. Smoking May Trigger HLA-DR (Shared Epitope)- Restricted Immune Reactions to Autoantigens Modified by Citrullination. Arthritis Rheum 2006;54:53-61.

# RA autoimmunity and the Lung

- Description of cases of Interstitial Lung Disease with Rheumatoid Arthritis specific autoantibodies may lead to mechanistic research into the role of the lung in Rheumatoid Arthritis autoimmunity.



# National Jewish Chart Review

- Descriptive Case Series- Chart Review
- Aim to identify Anti-CCP and Rheumatoid Factor antibodies in patients with interstitial lung disease and no evidence of peripheral arthritis
- Record risk factors for Rheumatoid Arthritis
  - Smoking history
- Pathology
  - CT findings and Pathology



# Results

	Male	Female
<b>(6) RF+ Anti-CCP-</b>	<b>4</b>	<b>2</b>
<b>(5) RF+ Anti-CCP+</b>	<b>3</b>	<b>2</b>
<b>(18) RF+ Anti-CCP unknown</b>	<b>12</b>	<b>6</b>
<b>TOTAL</b>	<b>19</b>	<b>10</b>

# Results

	CT IPF	CT UIP	CT NSIP	CT DIP	
(6) RF+ Anti-CCP-	1	1	1		
(5) RF+ Anti-CCP+			1		
(18) RF+ Anti-CCP unknown	7	3	2	1	

# Conclusions

- Rheumatoid arthritis specific autoantibodies are present in patients with interstitial lung disease.



# Lung

SMOKING

# Synovium

Chronic  
Inflammation  
↑ Apoptosis

Inflammatory cells +  
Activation of PADI

Citrullinated Epitopes,  
Transport to draining  
Lymph Nodes

HLA DR4 presents  
Citrullinated Antigens  
Loss of tolerance

Antibodies  
to Citrullinated Antigens

Non-Antigen specific  
Inflammation  
Infection?

Inflammatory cells,  
Activation of PADI

Citrullinated antigens  
In the synovium

Synovial and cartilage damage  
Immune complex injury due to  
Mast cells, Neutrophils, FcR and  
Complement mediated mechanisms

# Future Directions

- Determine if smoking can up-regulate the expression of PADI4 in alveolar macrophages.
- Determine if smoking can increase deimination of proteins in alveolar macrophages and characterize the proteins deiminated.
- Determine if smoke exposure increases Anti-CCP binding to alveolar macrophages.

