NHS Foundation Trust

### DIFFERENCES IN FIBROPROLIFERATIVE HEALING IN EXOGENEOUS AND IDIOPATHIC ILDs. **ARE THERE ANY?**

**Fibrosing Interstitial Lung Diseases CPFS/WASOG/AIPO/ERS Conference** Prague, 19-21 June 2014

#### Luca Richeldi MD PhD

**Professor of Respiratory Medicine** Chair of Interstitial Lung Disease Honorary Consultant Physician

National Institute for Health Research

The NIHR Southampton Respiratory Biomedical Research Unit is funded by the National Institute for Health Research (NIHR) and is a partnership between University Hospital Southampton NHS Foundation Trust and the University of Southampton

I HAVE ABSOLUTELY **NO** IDEA AND PROBABLY NO ONE ELSE DOES FIBROPROLIFERATIVE HEALING















Mark Jones, University of Southampton



### American Thoracic Society Documents

#### An Official American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias

William D. Travis, Ulrich Costabel, David M. Hansell, Talmadge E. King, Jr., David A. Lynch, Andrew G. Nicholson, Christopher J. Ryerson, Jay H. Ryu, Moisés Selman, Athol U. Wells, Jurgen Behr, Demosthenes Bouros, Kevin K. Brown, Thomas V. Colby, Harold R. Collard, Carlos Robalo Cordeiro, Vincent Cottin, Bruno Crestani, Marjolein Drent, Rosalind F. Dudden, Jim Egan, Kevin Flaherty, Cory Hogaboam, Yoshikazu Inoue, Takeshi Johkoh, Dong Soon Kim, Masanori Kitaichi, James Loyd, Fernando J. Martinez, Jeffrey Myers, Shandra Protzko, Ganesh Raghu, Luca Richeldi, Nicola Sverzellati, Jeffrey Swigris, and Dominique Valeyre; on behalf of the ATS/ERS Committee on Idiopathic Interstitial Pneumonias



AJRCCM 2013; 188: 733-748









Im going to grow a hundred years old!"

#### ... and possibly she may-for the amazing strides of medical science have added years to life expectancy

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MELS Costlier



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The Cigarette Century. Allan M. Brandt, 2007



AJRCCM 2013; 188: 733-748

## Smoking-Related Interstitial Lung Diseases

Robert Vassallo, мD<sup>a,b</sup>, Jay H. Ryu, мD<sup>a,\*</sup>

#### KEYWORDS

- Smoking Interstitial lung disease
- Respiratory bronchiolitis
- Desquamative interstitial pneumonia
  Fibrosis
- Pulmonary Langerhans cell histiocytosis
- Acute eosinophilic pneumonia



Clin Chest Med 2012; 33: 165-78

#### **PROPOSED CLASSIFICATION OF SMOKING-RELATED ILDs**

**Group 1**: chronic ILDs that are very likely caused by cigarette smoking Respiratory bronchiolitis—associated ILD (RB-ILD) Desquamative interstitial pneumonia (DIP) Adult pulmonary Langerhans cell histiocytosis (PLCH)

Group 2: acute ILDs that may be precipitated by cigarette smoking Acute eosinophilic pneumonia (AEP) Pulmonary hemorrhage syndromes (PHS)

Group 3: ILDs that are statistically more prevalent in smokers Idiopathic pulmonary fibrosis (IPF) Rheumatoid arthritis—associated ILD (RA-ILD)

Group 4: ILDs that are less prevalent in smokers Hypersensitivity pneumonitis (HP) Sarcoidosis

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#### AT DIAGNOSIS

#### **3 MOS AFTER SMOKING CESSATION**



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Clin Chest Med 2012; 33: 165-78

### **IDIOPATHIC PULMONARY FIBROSIS**



King T, Pardo A and Selman M, Lancet 2011



## **Gene Discovery in Pulmonary Fibrosis**



Familial and Sporadic IPF **General Population OR=6.2** 34.1 Fold 5.3 Fold per allele P=0.00002 P=0.0003 MUC5B 5 Expression Relative Seibold. NEJM 2011; 364:1503 Variant WT Variant WT L IPF (N=203) Controls (N=139) **Courtesy David Schwartz** 

**Familial and Sporadic IPF** 







### **MUC5B** Variant has a Low Penetrance

#### **General Population**





**Courtesy David Schwartz** 

### **Genome Wide Association Study in IIP**



## GENE-ENVIRONMENT INTERACTION

# B B C NEWS HEALTH

7 March 2013 Last updated at 02:44 GMT



## Why do the Italians live longer than us?



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William D. Travis, Ulrich Costabel, David M. Hansell, Talmadge E. King, Jr., David A. Lynch, Andrew G. Nicholson, Christopher J. Ryerson, Jay H. Ryu, Moisés Selman, Athol U. Wells, Jurgen Behr, Demosthenes Bouros, Kevin K. Brown, Thomas V. Colby, Harold R. Collard, Carlos Robalo Cordeiro, Vincent Cottin, Bruno Crestani, Marjolein Drent, Rosalind F. Dudden, Jim Egan, Kevin Flaherty, Cory Hogaboam, Yoshikazu Inoue, Takeshi Johkoh, Dong Soon Kim, Masanori Kitaichi, James Loyd, Fernando J. Martinez, Jeffrey Myers, Shandra Protzko, Ganesh Raghu, Luca Richeldi, Nicola Sverzellati, Jeffrey Swigris, and Dominique Valeyre; on behalf of the ATS/ERS Committee on Idiopathic Interstitial Pneumonias

### REVISED ATS/ERS IIPs CLASSIFICATION: CATEGORIZATION OF MAJOR IIPs

CATEGORY	CLINICAL-RADIOLOGICAL- PATHOLOGICAL DX	ASSOCIATED MORPHOLOGIC PATTERNS
Chronic fibrosing IP	IPF	UIP
	I-NSIP	NSIP
Smoking-related IP	RB-ILD	RB
	DIP	DIP
Acute/Subacute IP	СОР	OP
	AIP	DAD

#### REVISED ATS/ERS IIPS CLASSIFICATION: CLASSIFICATION ACCORDING TO DISEASE BEHAVIOR - 1

<b>CLINICAL BEHAVIOR</b>	TREATMENT GOAL	MONITORING STRATEGY
<b>Reversible and self- limited</b> (e.g. RB-ILD)	Remove possible cause	Short-term (3-6 months) observation to confirm disease regression
<b>Reversible with risk of</b> <b>progression</b> (e.g. some NSIP, COP, DIP)	Initially for a response and then rationalize longer term therapy	Short-term observation to confirm response: long-term observation to ensure gains are preserved
Stable with residual disease (e.g. some NSIP)	Maintain status	Long-term observation to assess disease course

### REVISED ATS/ERS IIPS CLASSIFICATION: CLASSIFICATION ACCORDING TO DISEASE BEHAVIOR - 2

<b>CLINICAL BEHAVIOR</b>	TREATMENT GOAL	MONITORING STRATEGY
Progressive, irreversible with potential for stabilization (e.g. some NSIP)	To stabilize	Long-term (3-6 months) observation to assess disease course
Progressive, irreversible despite therapy (e.g. some NSIP, IPF)	To slow progression	Long-term observation to assess disease course and need for transplant or effective palliation



*"Bullshit is unavoidable whenever circumstances require someone to talk without knowing what he is talking about.* 

Thus the production of bullshit is stimulated whenever a person's obligations or opportunities to speak about some topic exceed his knowledge of the facts that are relevant to that topic."

Harry G. Frankfurt, On Bullshit. Princeton University Press 2005, page 63

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