

# Psoriasis

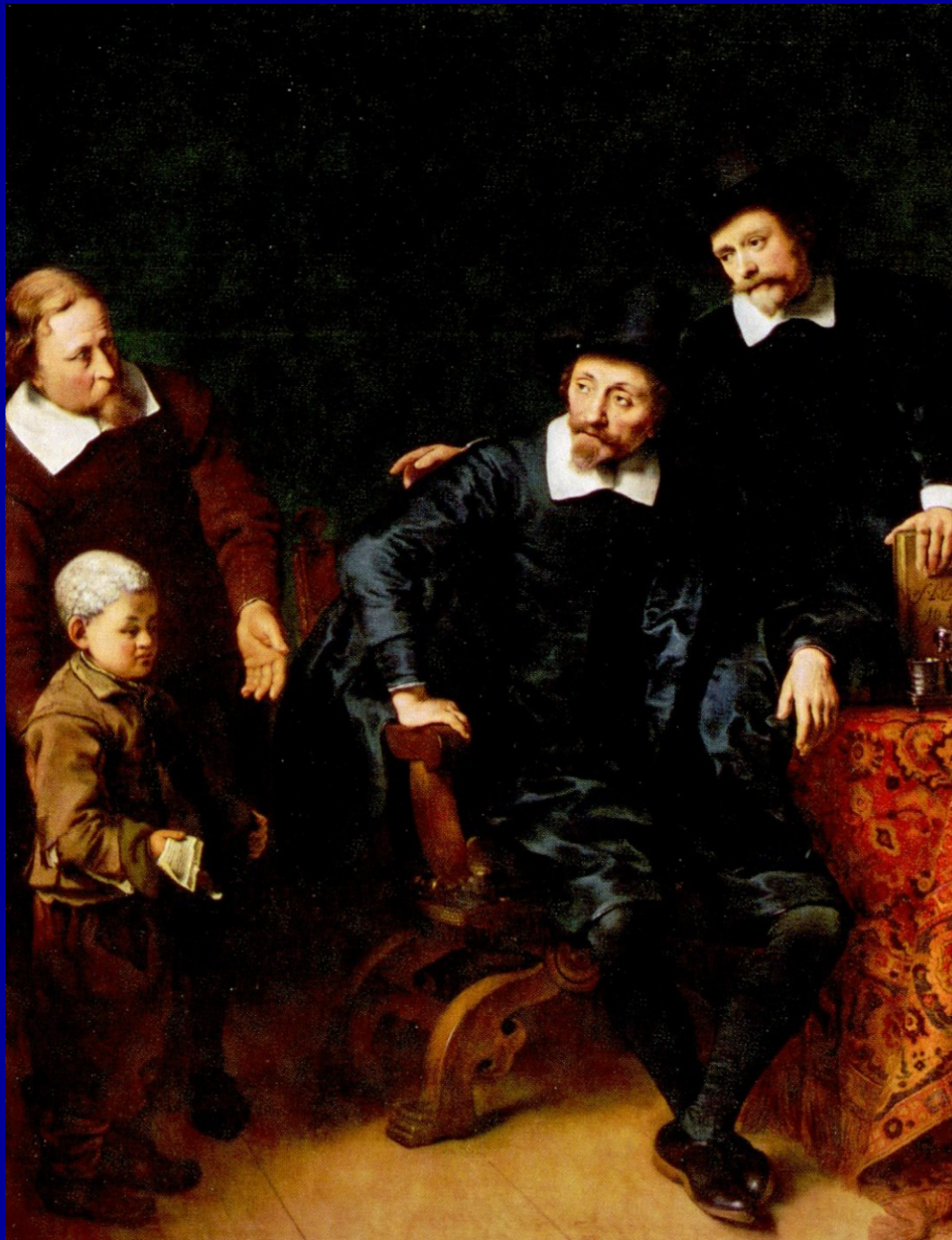
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Vladimír Vašků

I. dermatovenerologická klinika

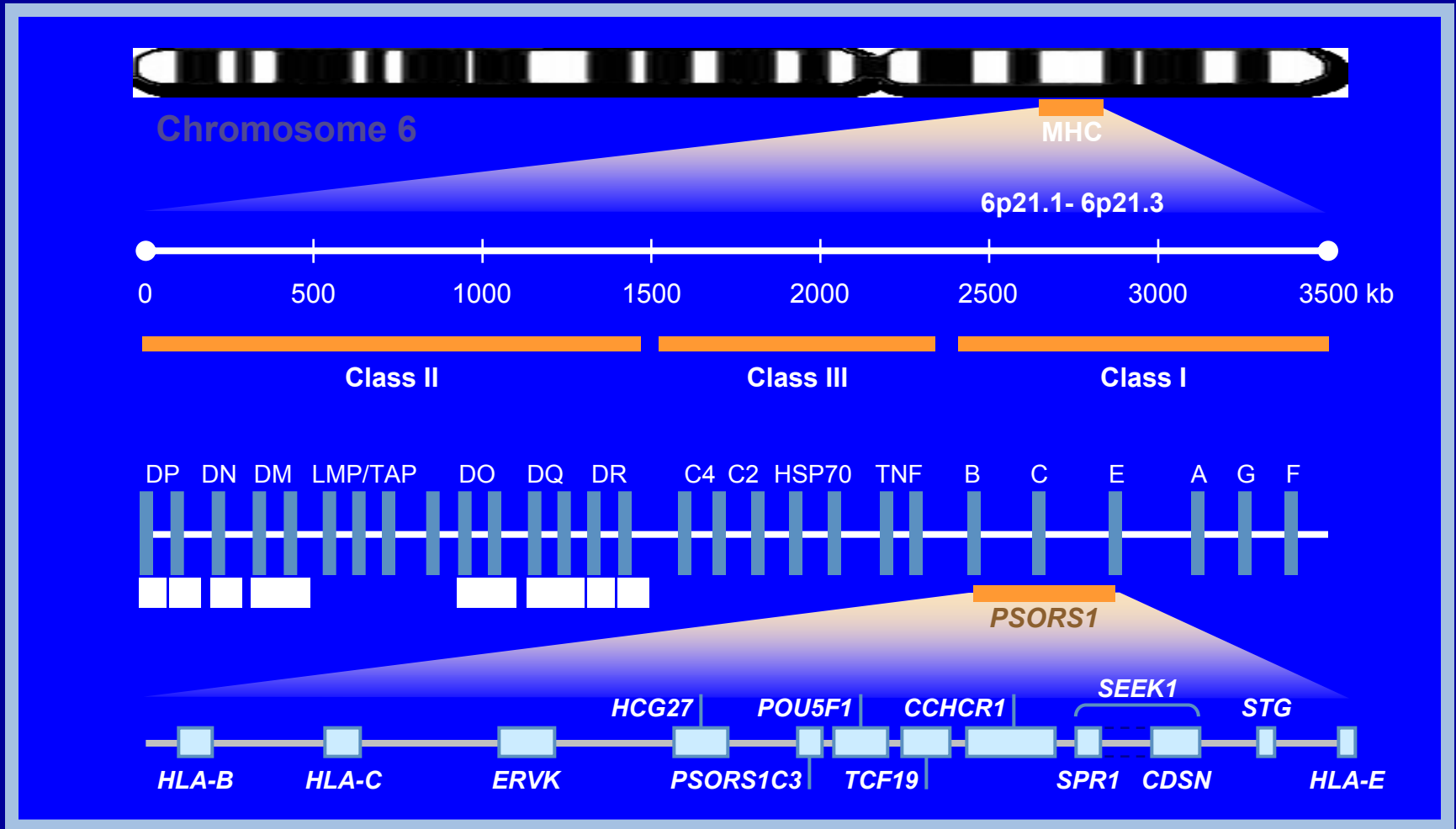
LF MU a FN u sv. Anny v Brně

Czech Republic

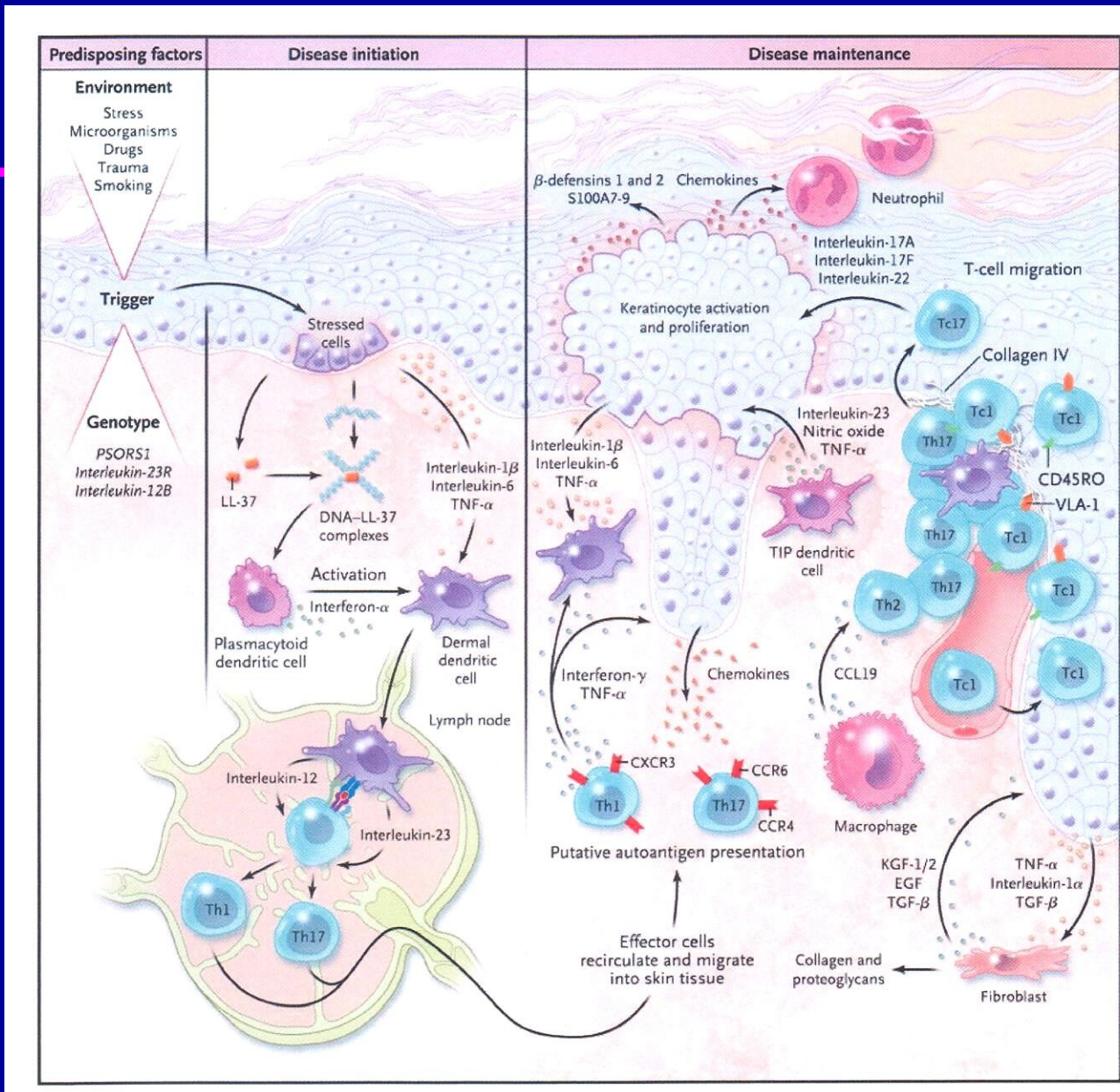


# PSORS1

Illustration adapted from Browne AM, Kere G. Nat Rev Immunol. 2005;5(9):699-711.



1. Trembath RC, et al. Hum Mol Genet. 1997;6(5):813-20.



# Psoriasis is a Complex Disease

## Characteristics

Multigenic predisposition  
(1% - 3% of Caucasian  
population affected)

Inflammatory  
disorder

Lifelong, chronic  
relapsing disease

Various clinical  
features

**Plaque-type psoriasis  
most common form**

### Palmoplantar<sup>1</sup>



### Plaque<sup>1</sup>



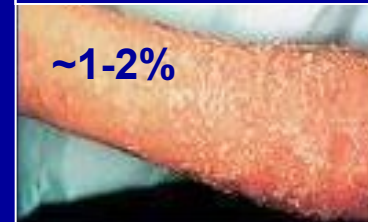
### Joints (PsA)<sup>2</sup>



### Erythrodermic<sup>1</sup>



### Pustular<sup>1</sup>



### Guttate<sup>1</sup>



### Inverse Psoriasis<sup>1</sup>



### Nail psoriasis<sup>3</sup>



<sup>1</sup>García-Diez A et al. *Dermatology*. 2008;216(2):137-151.

<sup>2</sup>Wilson FC et al. *Arthritis Rheum*. 2009;61:233-239.

<sup>3</sup>Griffiths CE et al. *Br J Dermatol*. 2007;156(2):258-262.

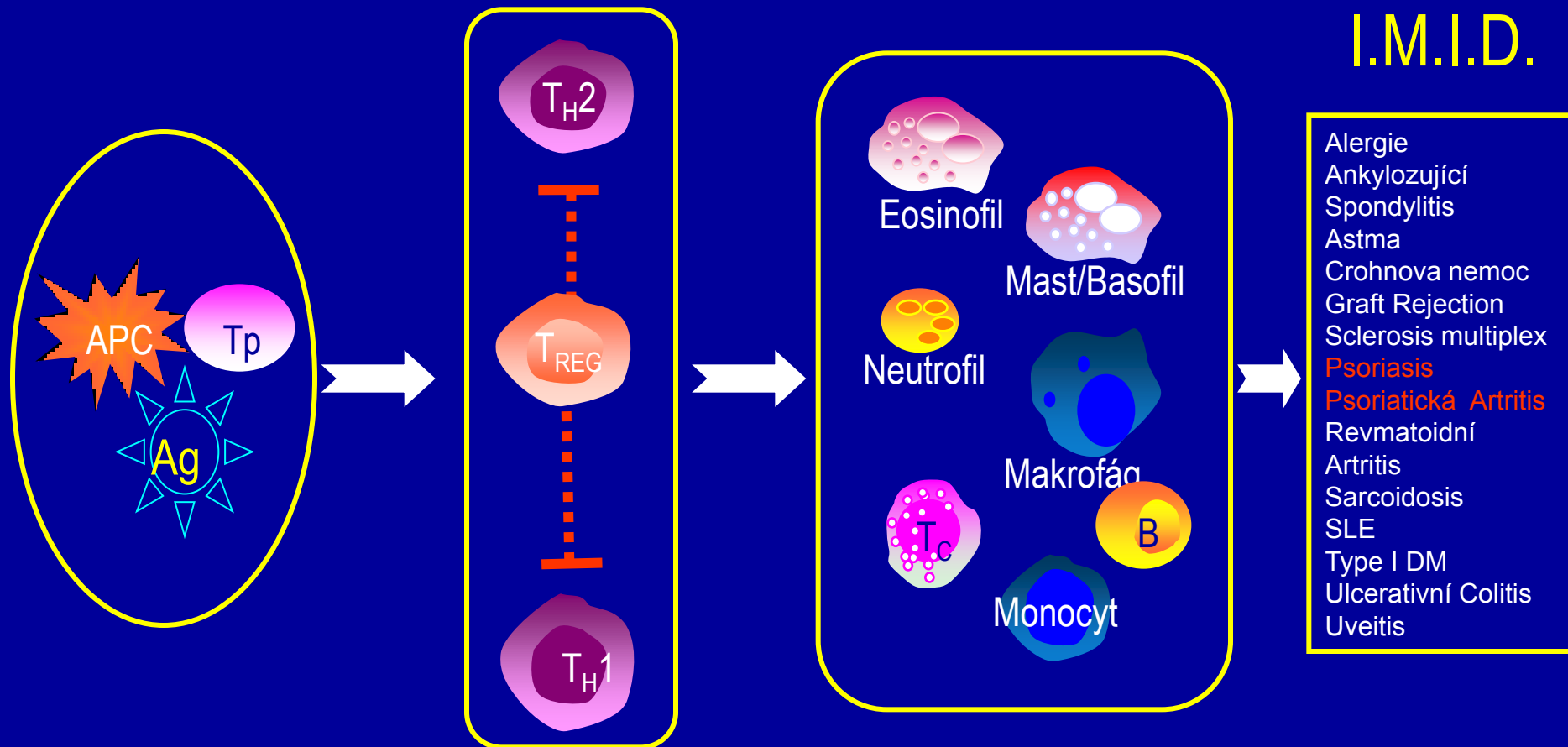
# Imunobiologie IMID („immune mediated inflammatory diseases“)

Senzitizace

Vývoj patogenních T-buněk  
Nerovnováha efektor/ supresor

Místní zánět

Tkáňové poškození  
Fibróza



# Psoriasis Demography Czech Republic

Severity	%	Prevalence 2%
mild to moderate	75	153000
moderate to severe	25	51000
severe	15	30600

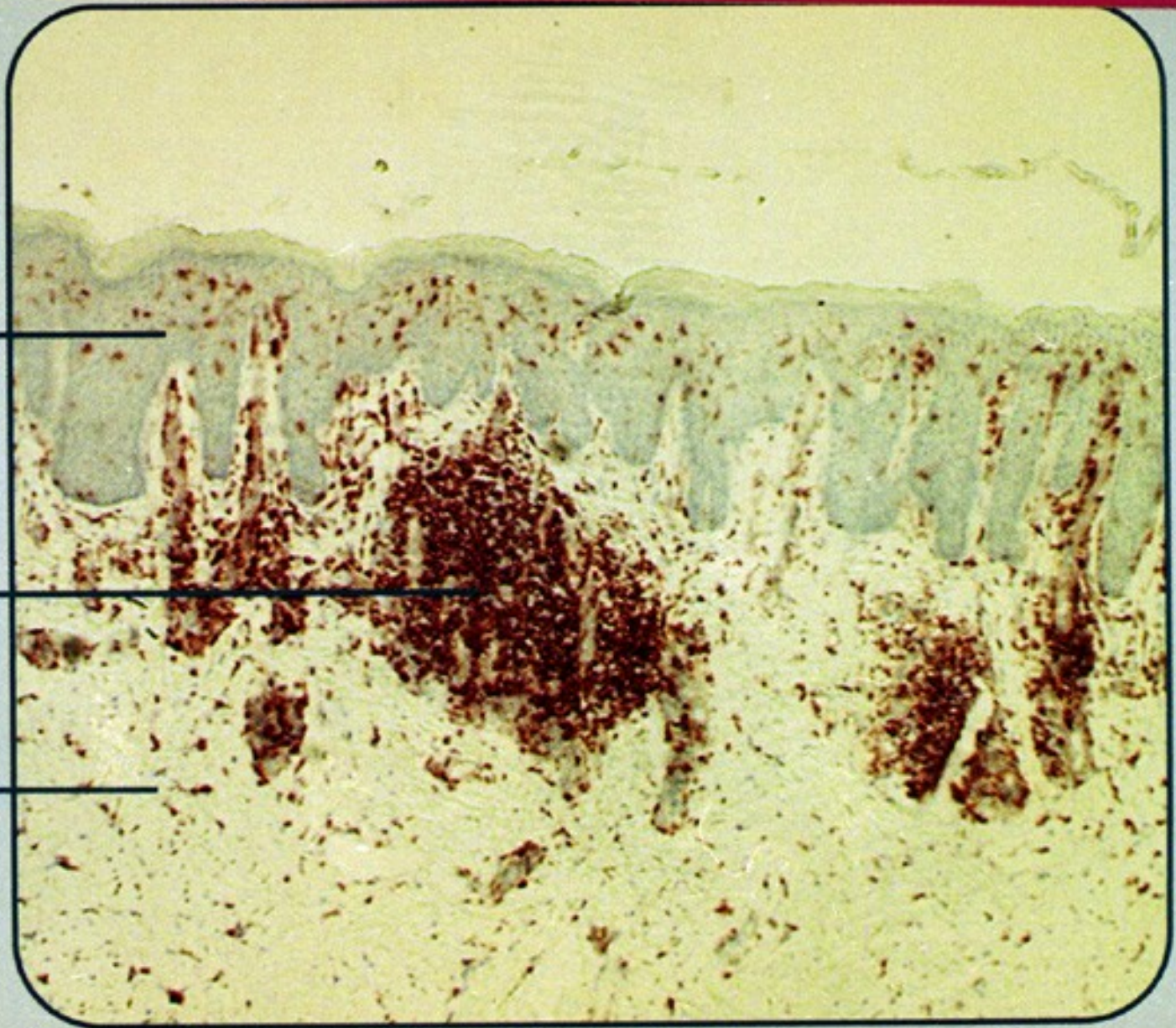
Epidermis



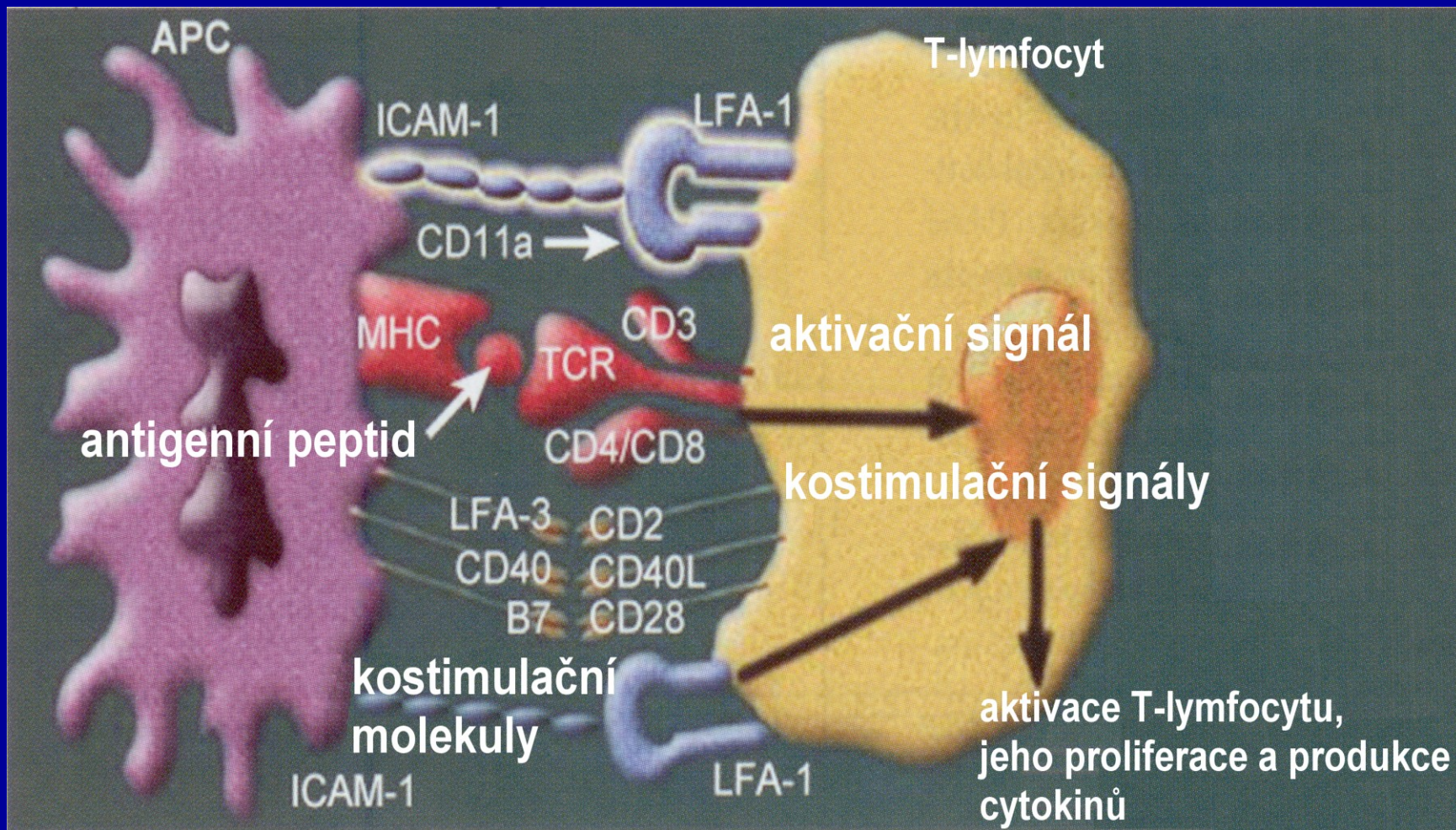
CD4+ T cell



Dermis



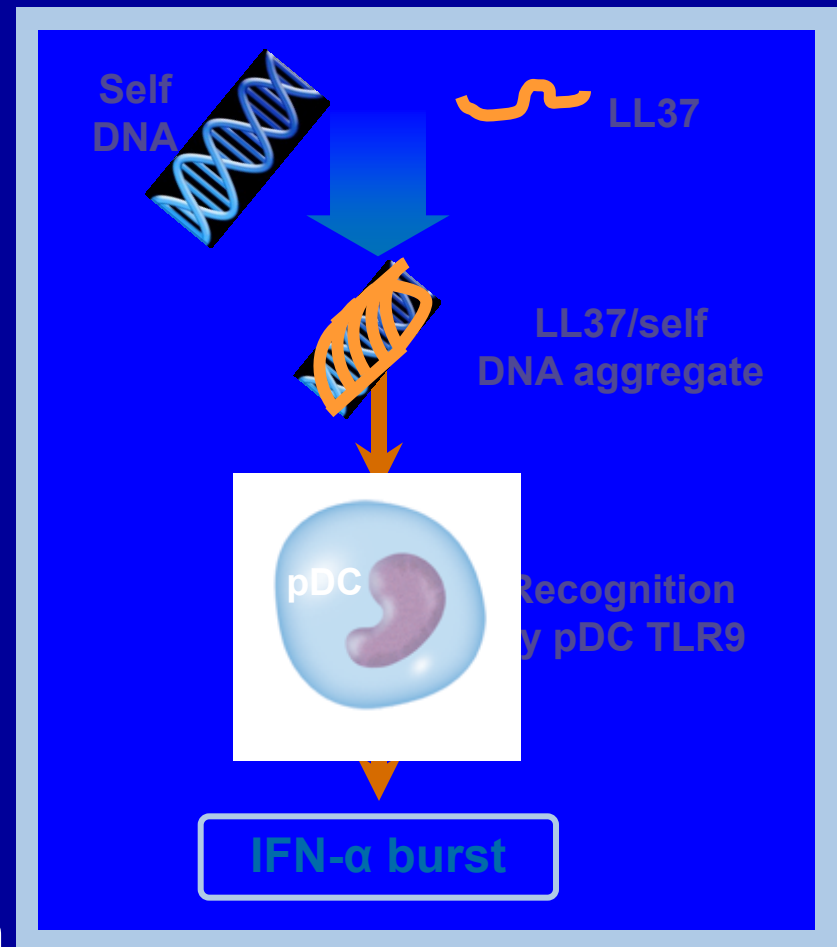




Podle Gottliebové, 2004

# Plasmacytoid Dendritic Cell Activation and Initiate Psoriasis <sup>1</sup>

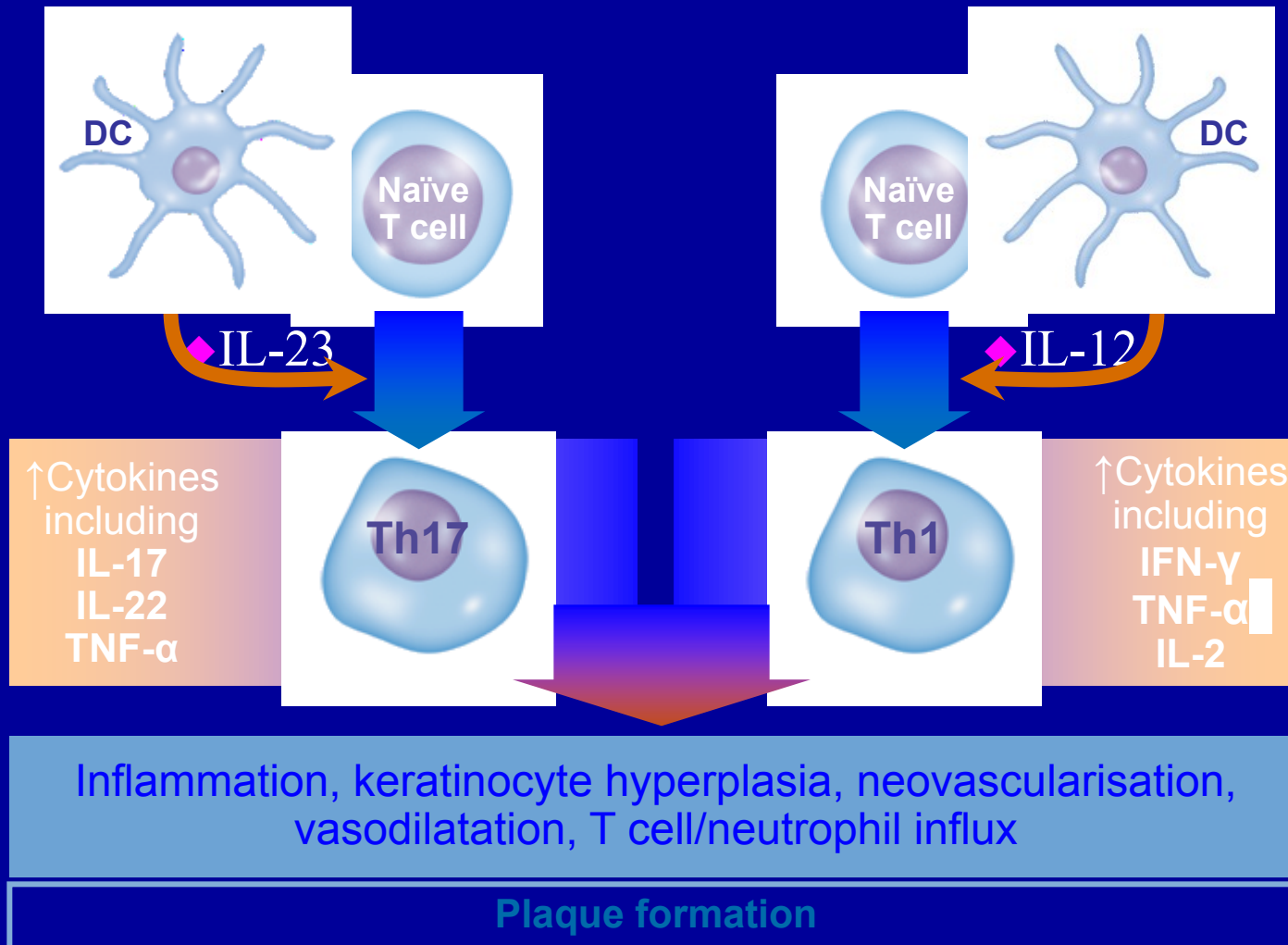
- pDCs use Toll-like receptor (TLR)7 and TLR9 to recognise viral/microbial nucleic acids in endosomal compartments
- The antimicrobial peptide LL37, a cathelicidin overexpressed in psoriatic skin, forms an



◆ 1. Lande R, et al. Nature. 2007; 449: 564-91

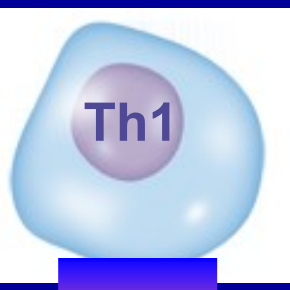
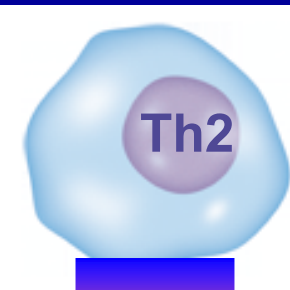




# helper

## Environment in Psoriasis<sup>1,2</sup>



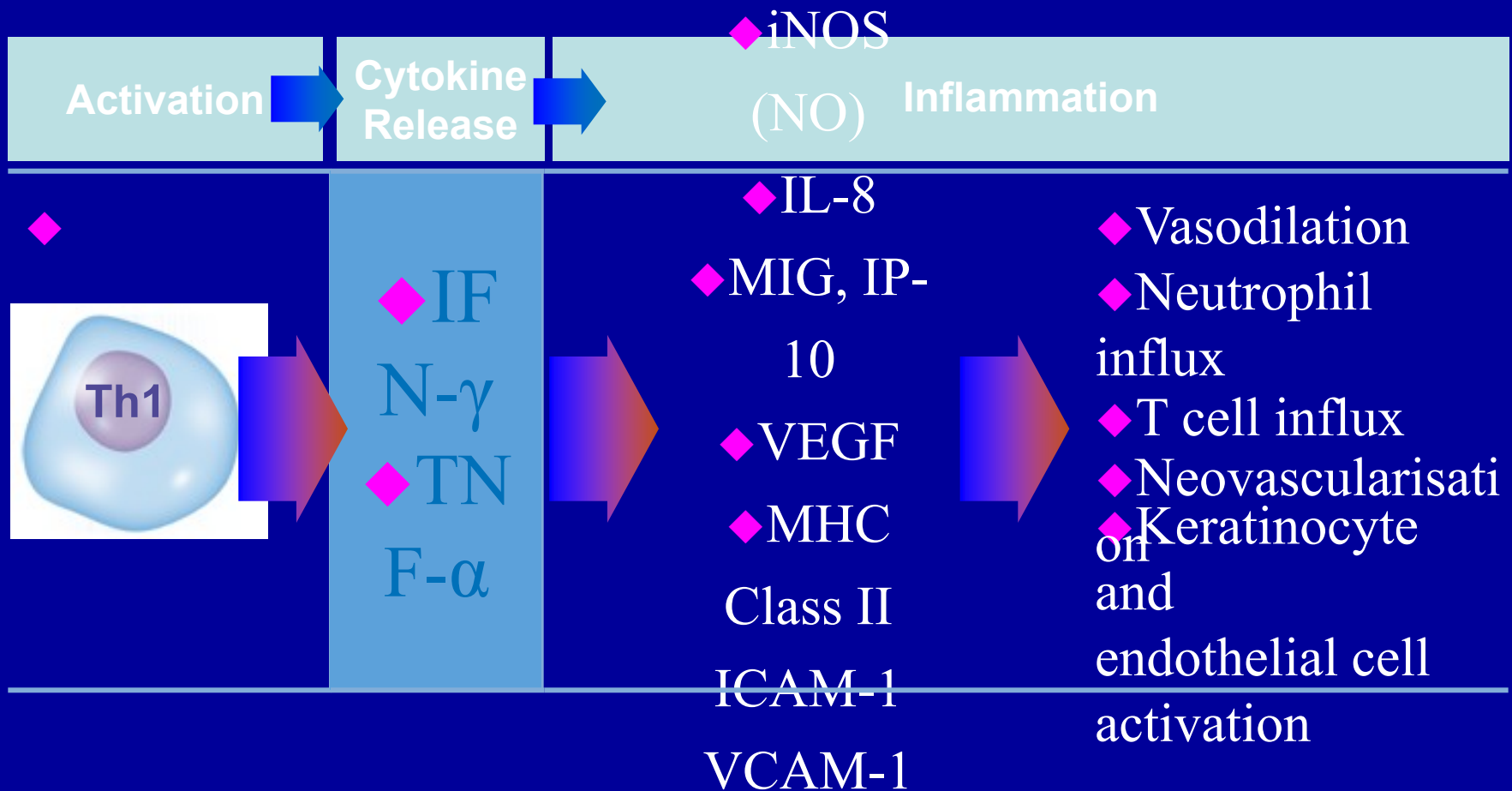
# Plaques:

## Th1 and Th17<sup>1,2</sup>

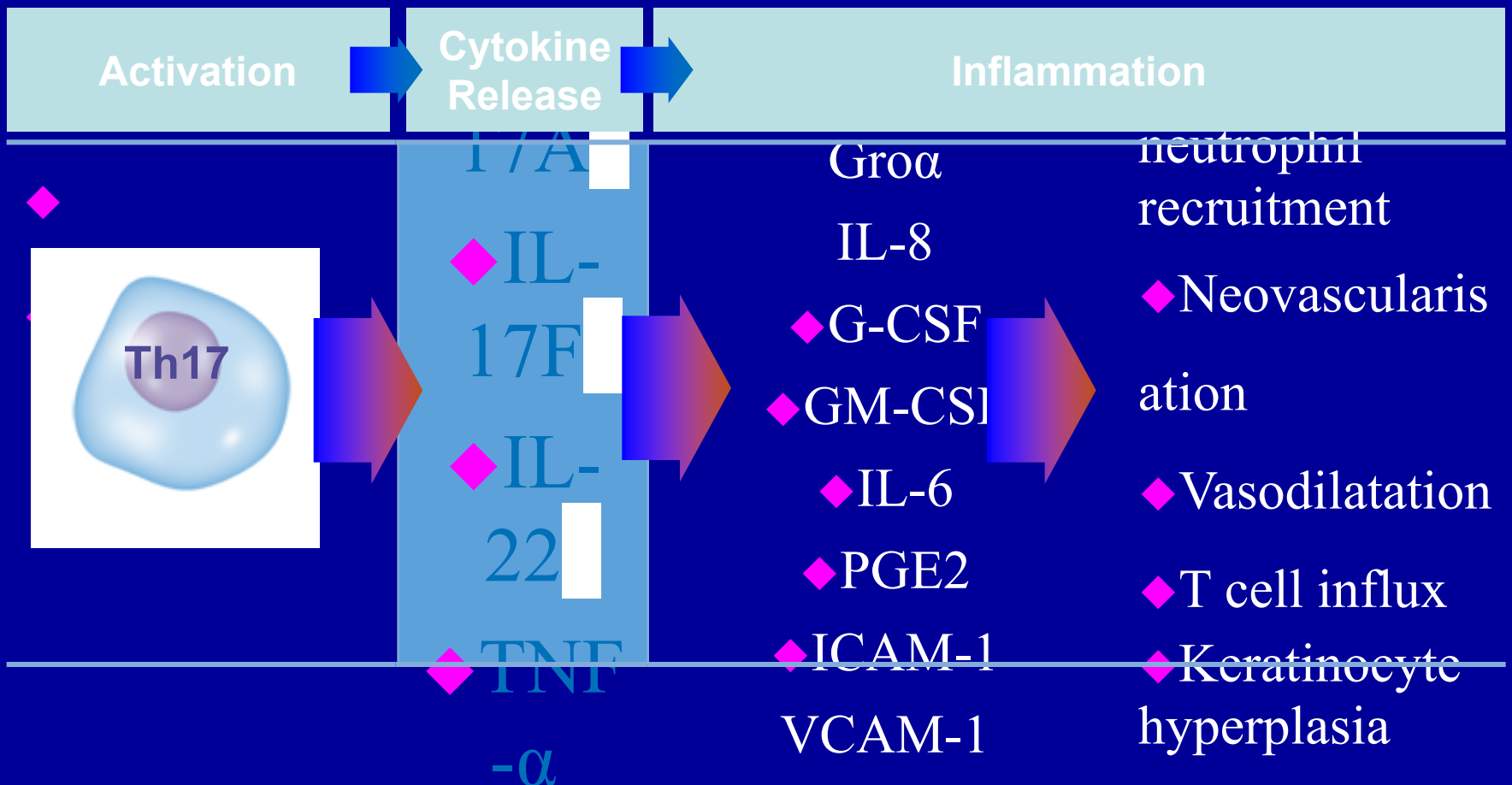
◆ Subset				
◆ Defining Cytokines <sup>3-5</sup>	◆ IFN- 	◆ IL-4	◆ IL-17 ◆ IL-22	◆ IL-10 ◆ TGF- 
◆ Found in psoriatic plaque <sup>6</sup>	◆ Yes	◆ No	◆ Yes	◆ Low level

- ◆ 1. Austin LM, et al. *J Invest Dermatol.* 1999;113:752-9. 2. Sabat R, et al. *Exp Dermatol.* 2007;16:779-98. 3. Janeway CA, et al. *Immunobiology.* 5th ed. New York: Garland; 2001. 4. Wilson NJ, et al. *Nat Immunol.* 2007;8(9):950-7. 5. Kagen MH, et al. *Ernst Schering Res Found Workshop.* 2006(56):193-209. 6. Lowes MA, et al. *J Invest Dermatol.* 2008. Epub 2008 Jan 17.

# Inflammatory Processes in the Psoriatic Plaque

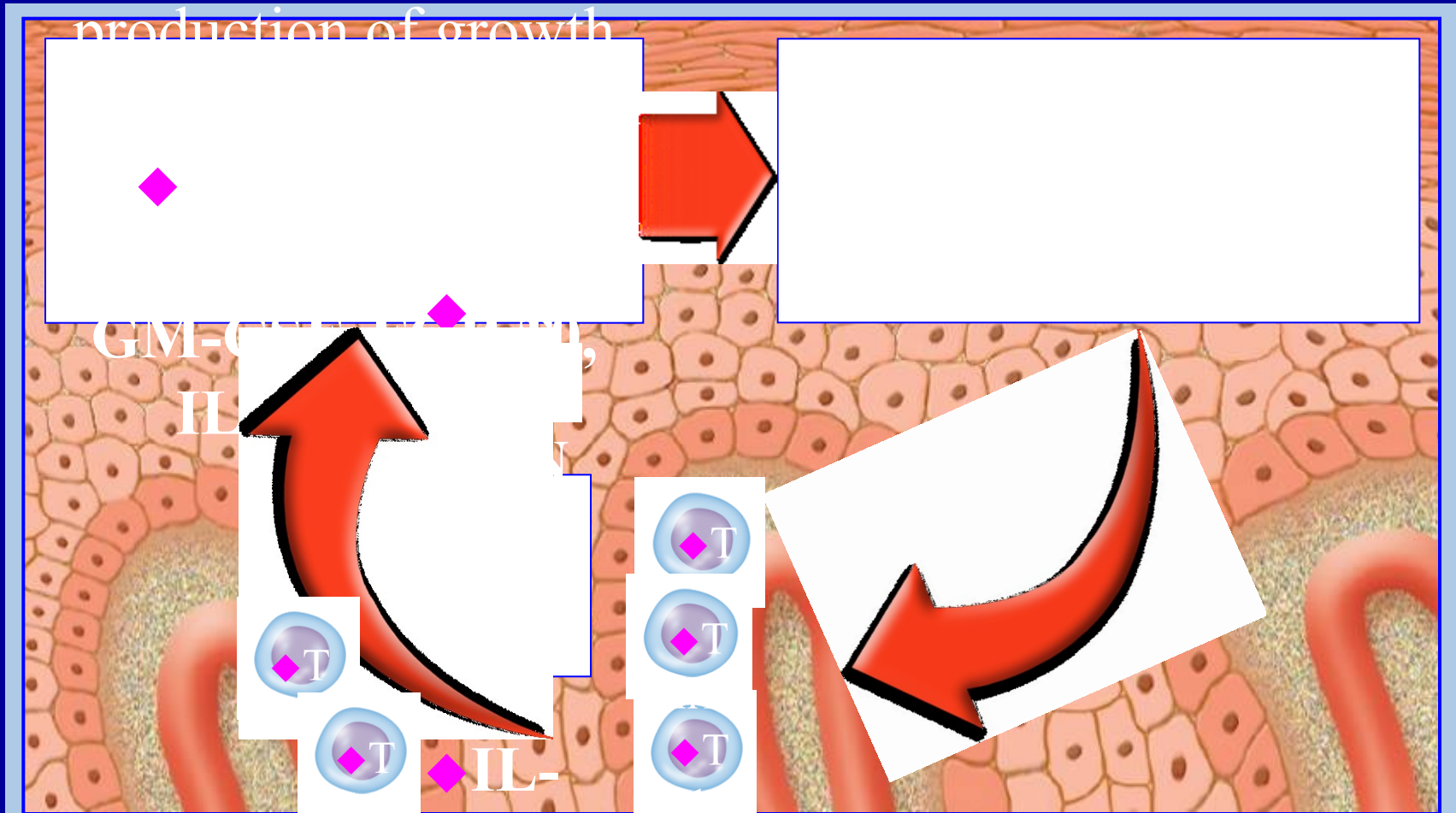


# Inflammation and Keratinocyte Hyperplasia in Psoriatic Plaque



# T-cell Cytokines Stimulate Keratinocyte Hyperplasia<sup>1,2</sup>

## ◆ Dysregulated KC



◆ 1. Albanesi C, et al. Clin Dermatol. 2007; 25:581-8. 2. Weinstein GD et al. J Invest Dermatol. 1985; 85:579-83.

# and Epidermal Hyperplasia: the Vicious Cycle of Psoriasis

- Dendritic cells, lymphocytes, and keratinocytes interact in a "vicious cycle" to establish and perpetuate the inflammatory phenotype

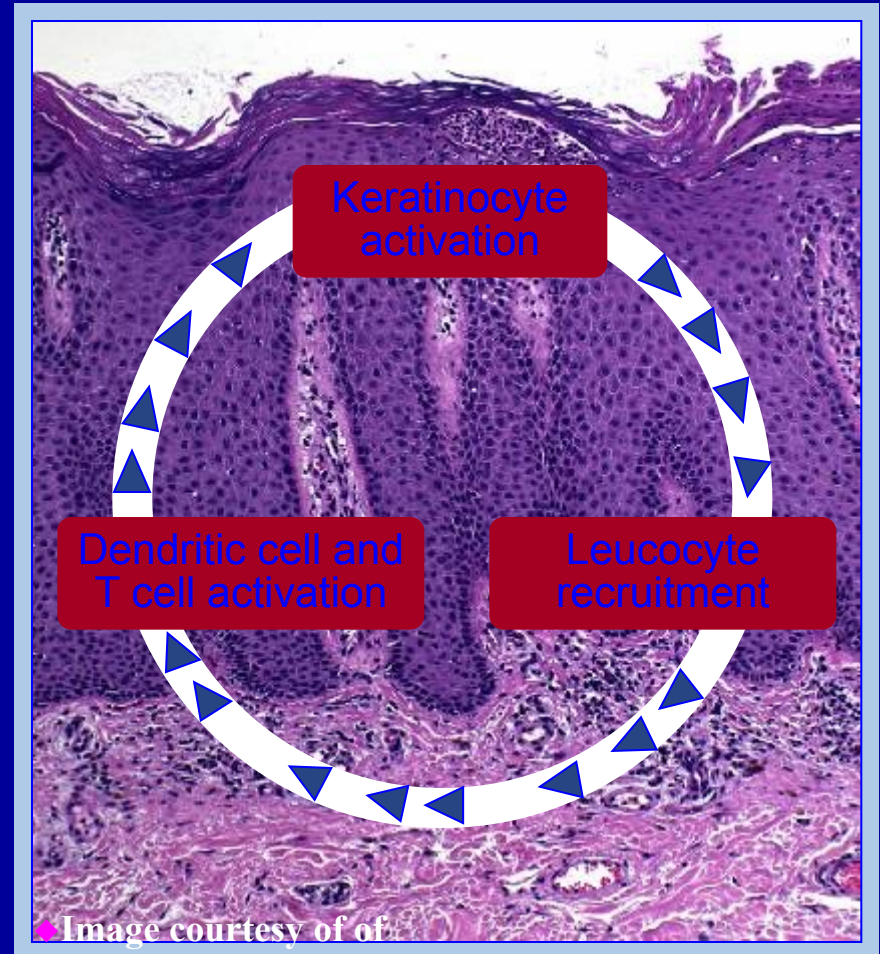
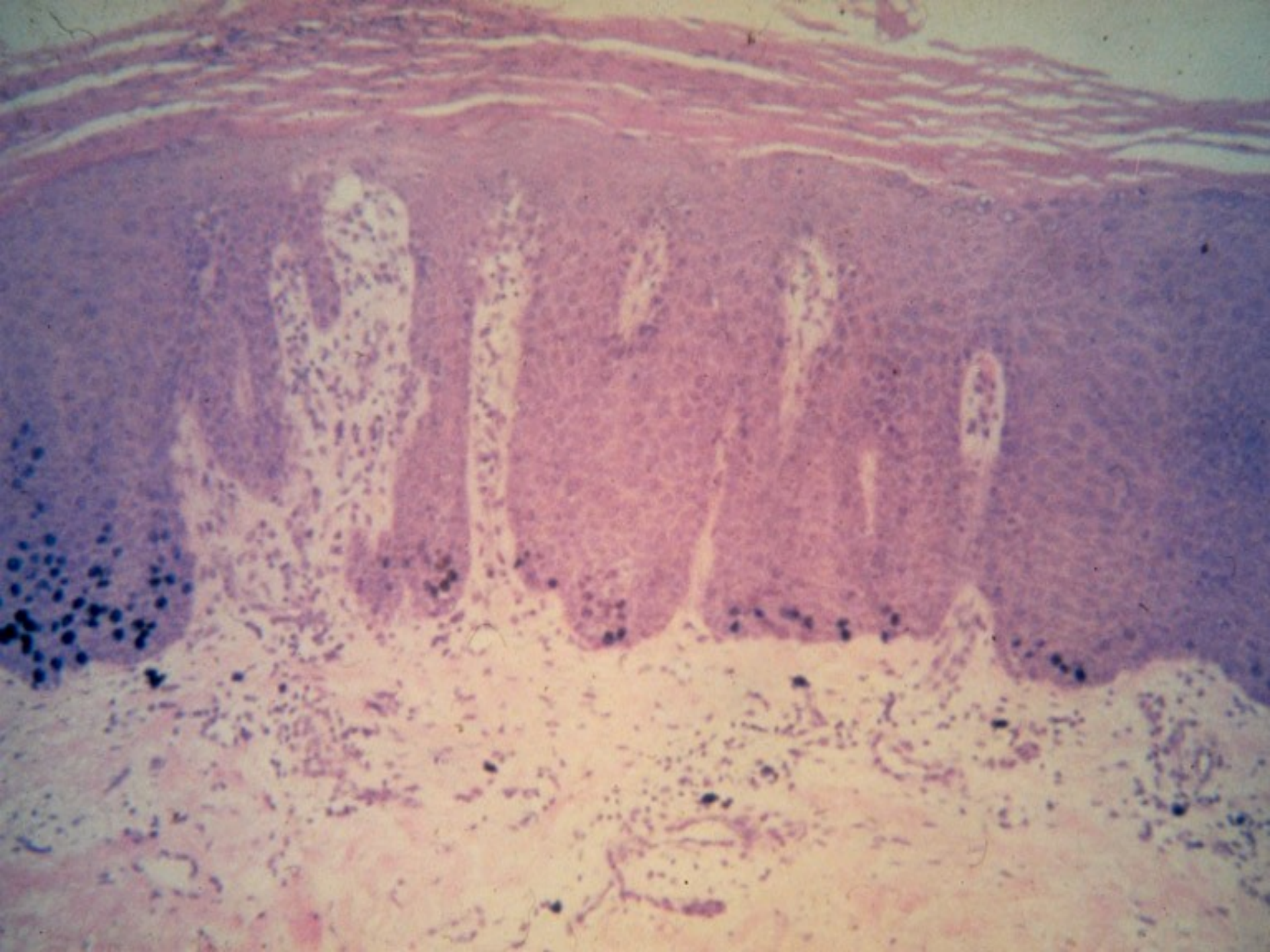


Image courtesy of

Professor J Prinz.







0274

10KV

X2,500

10µm

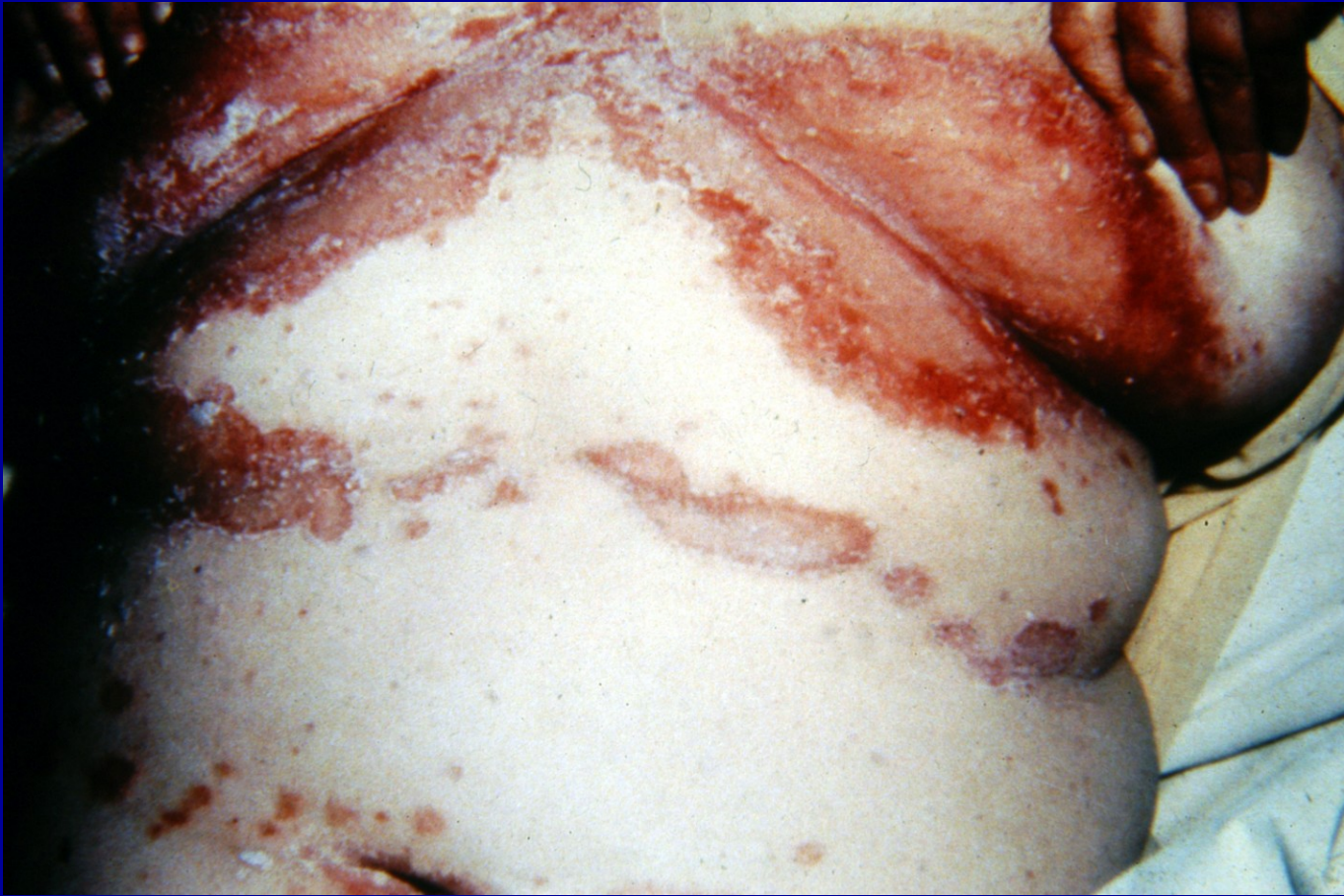
WD 9.1













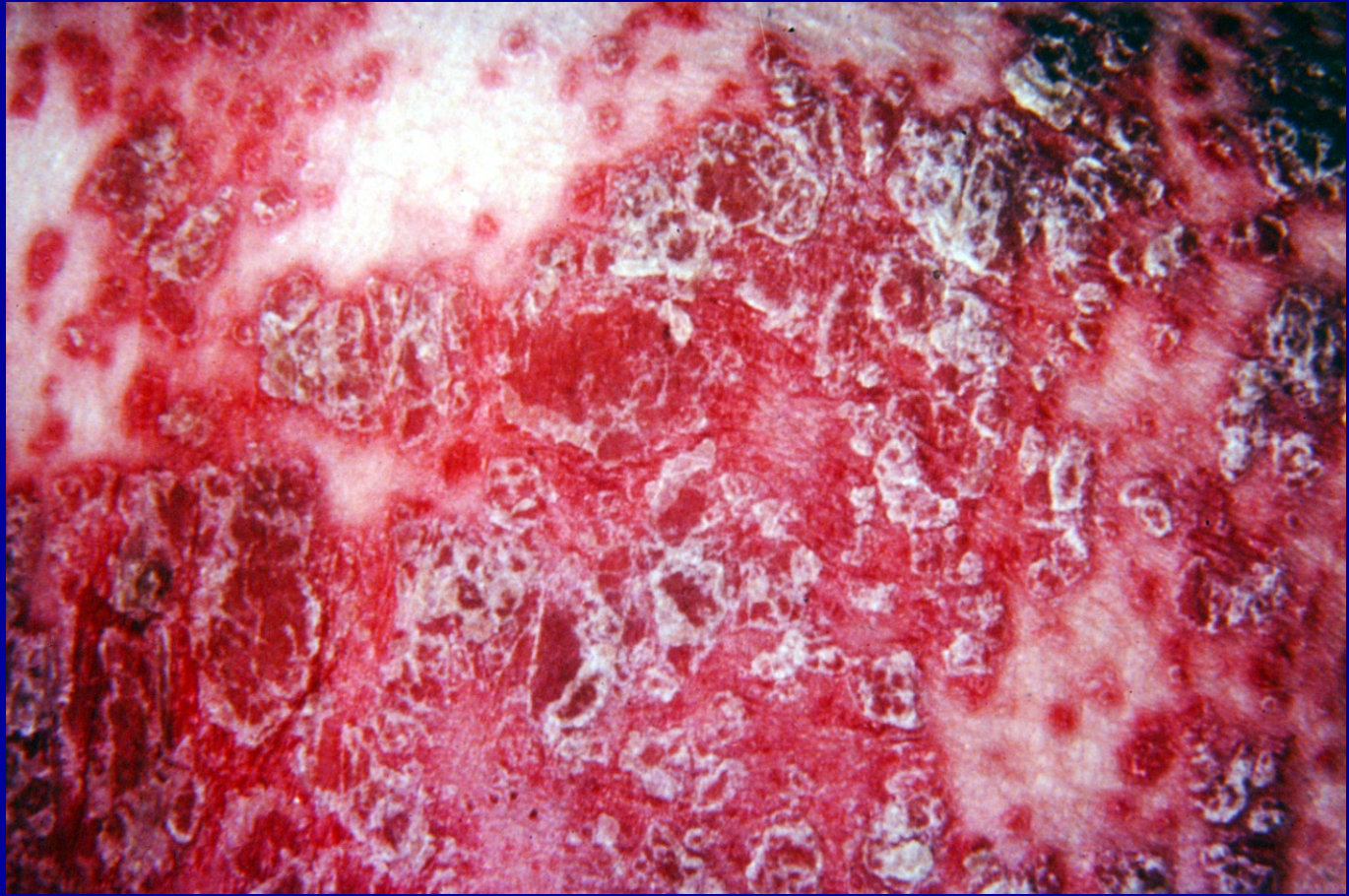






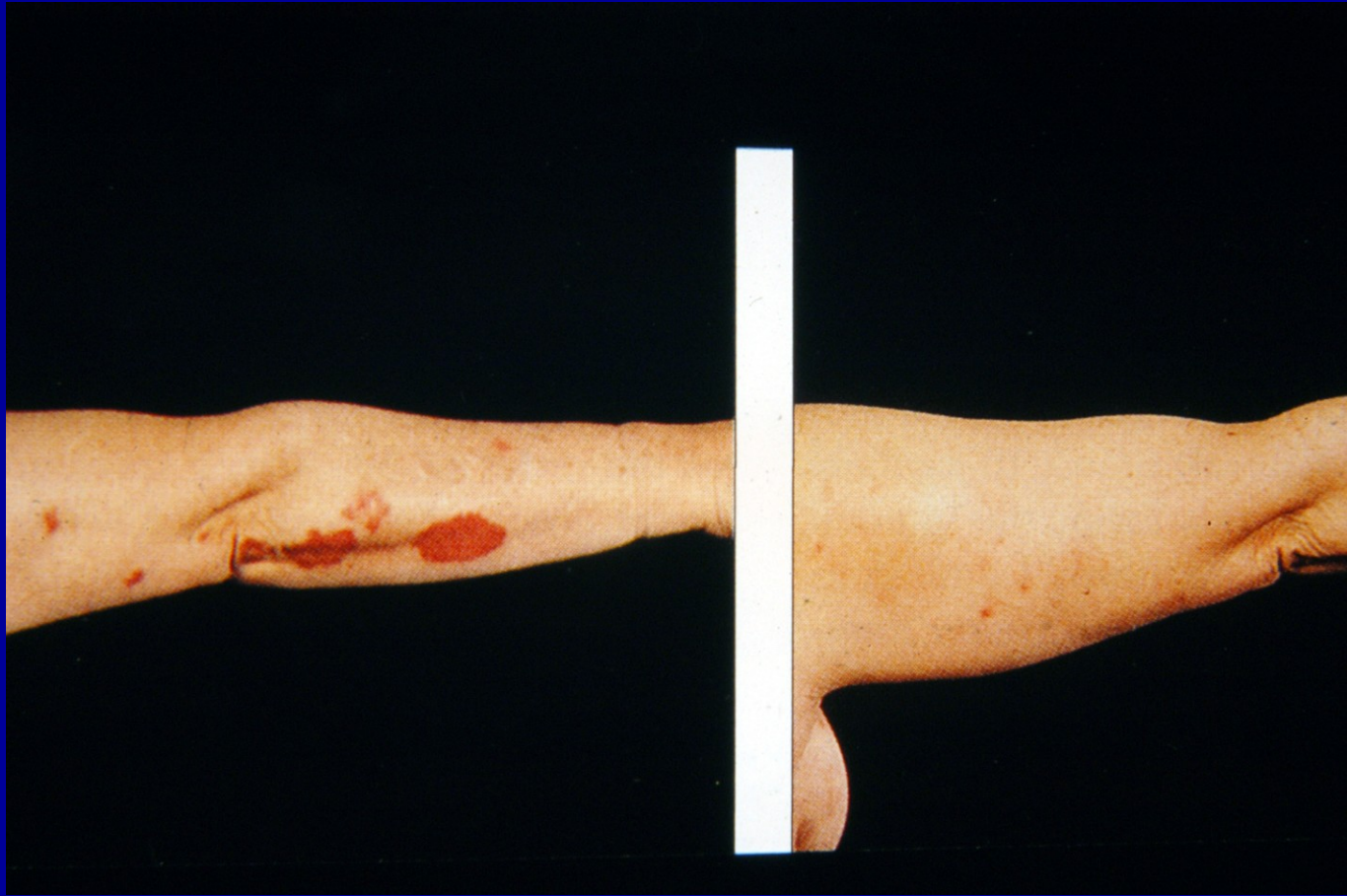






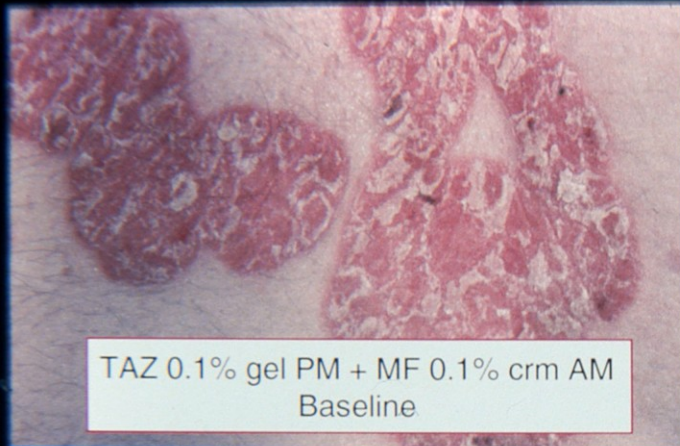








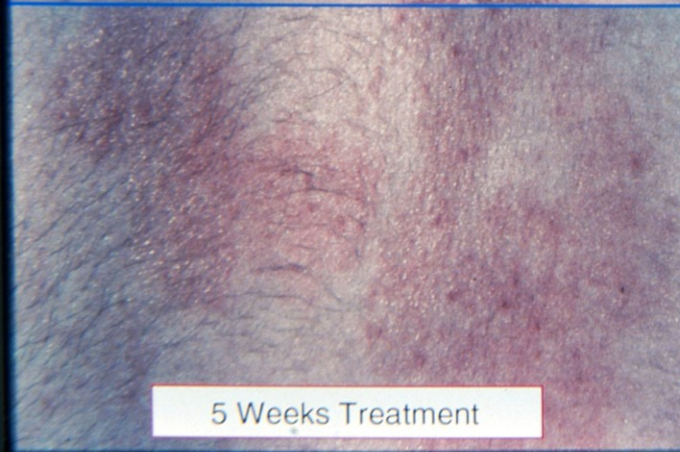




TAZ 0.1% gel PM + MF 0.1% crm AM  
Baseline



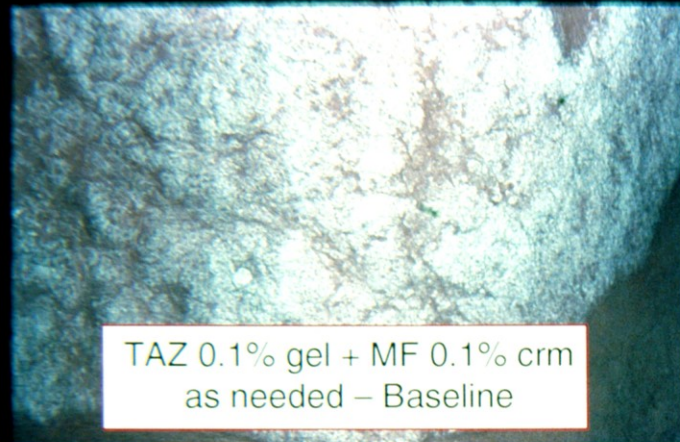
2 Weeks Treatment



5 Weeks Treatment



19 Weeks No Treatment



TAZ 0.1% gel + MF 0.1% crm  
as needed – Baseline



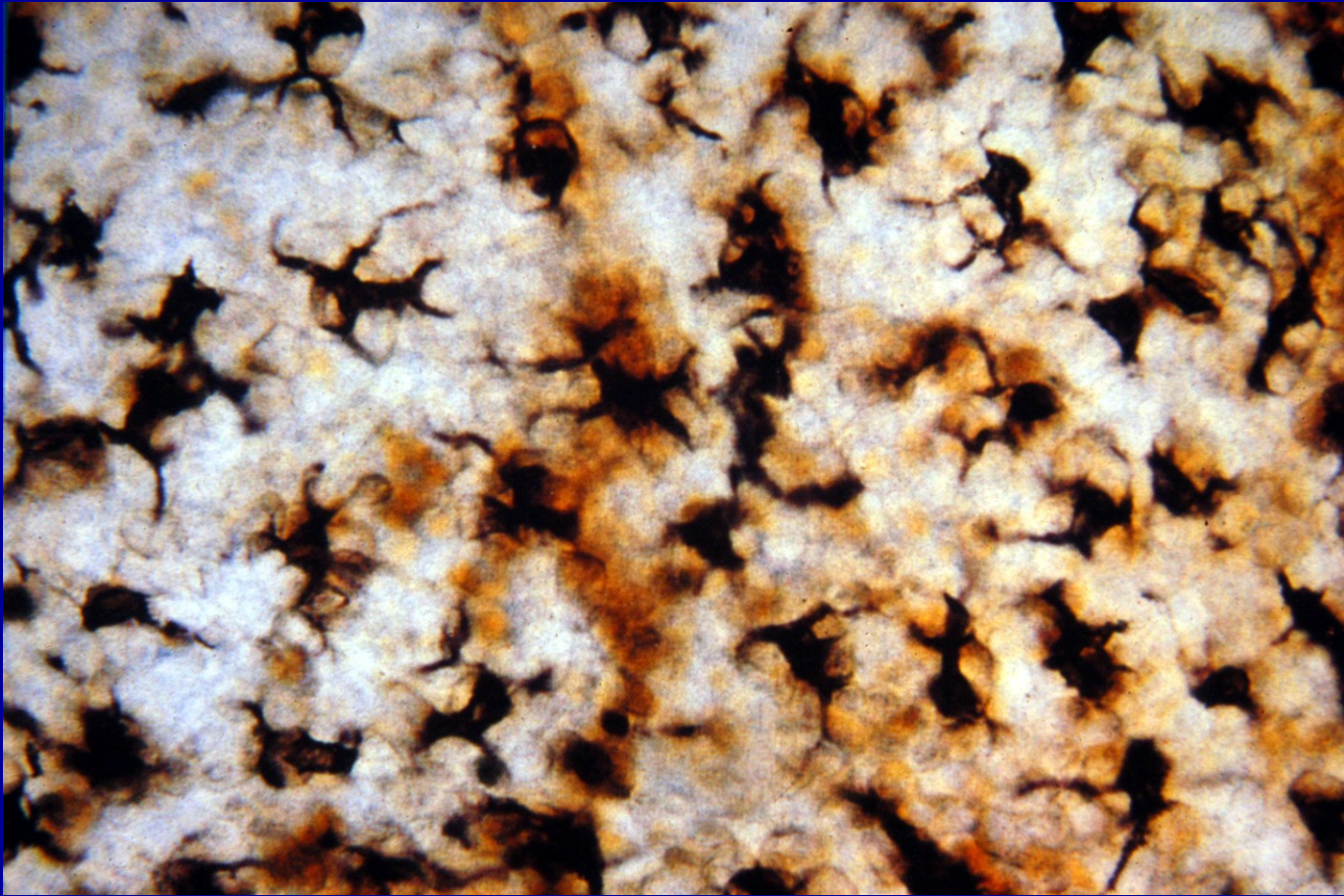
2 Weeks Treatment

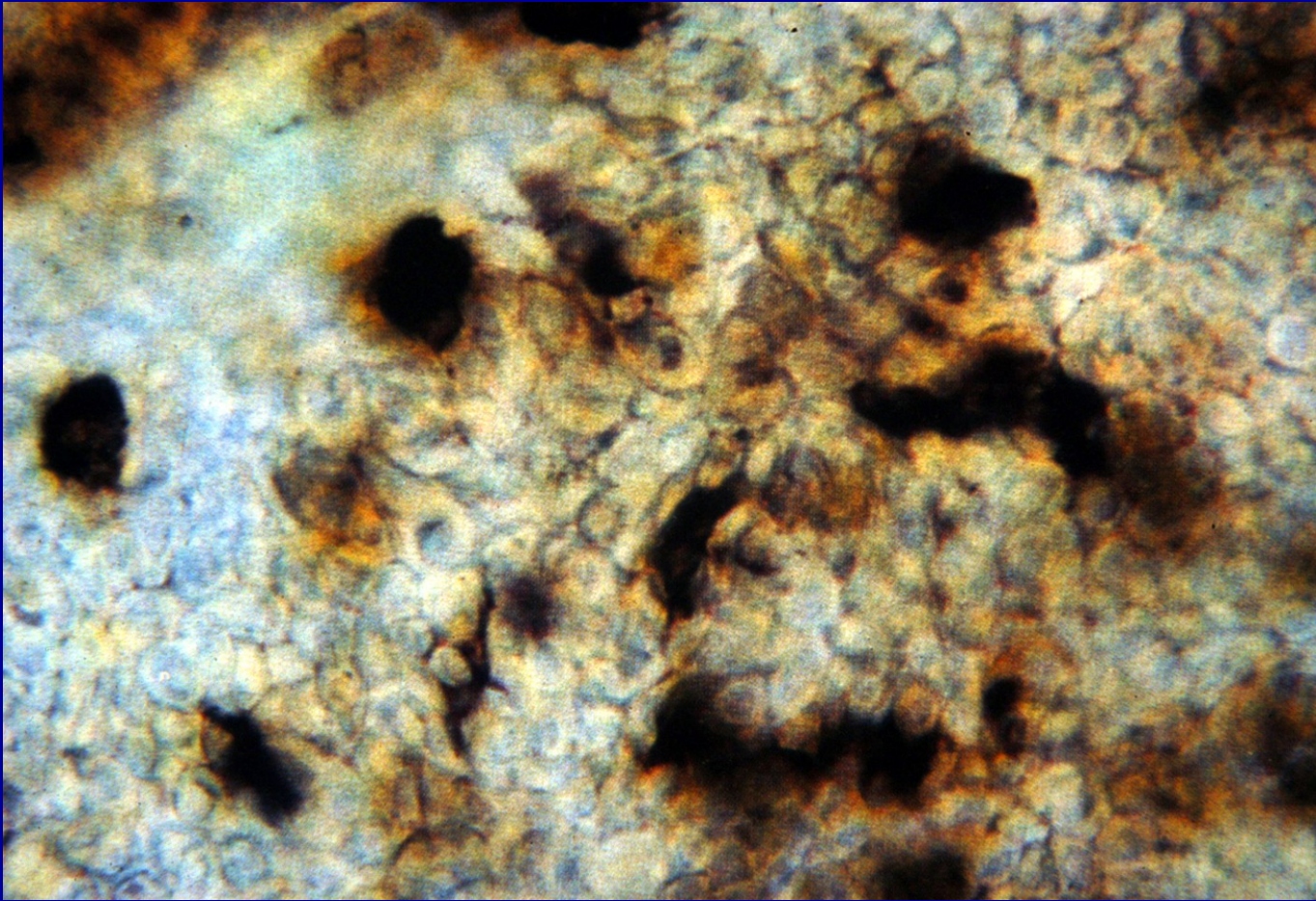


13 Weeks Treatment



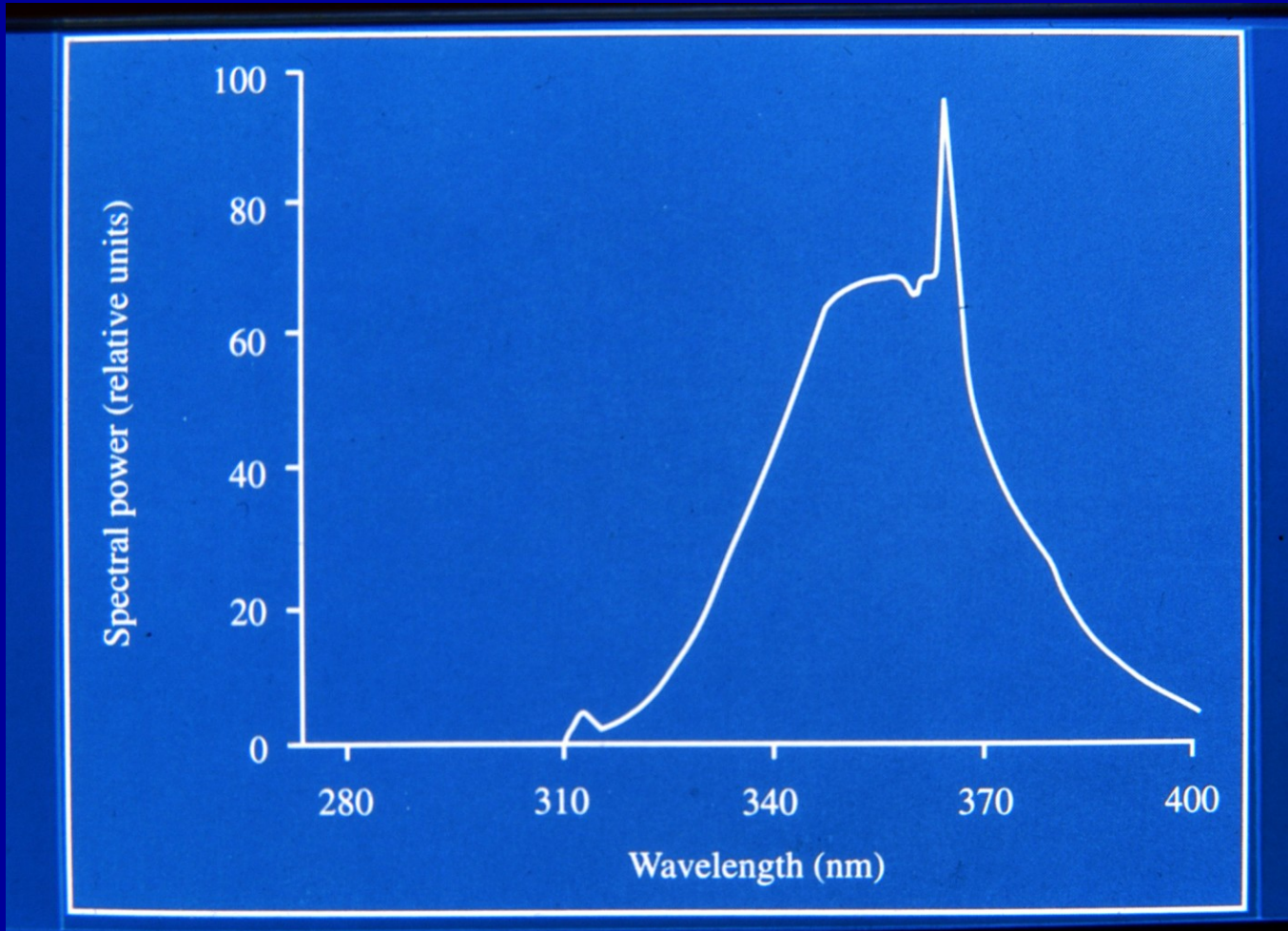
8 Weeks No Treatment



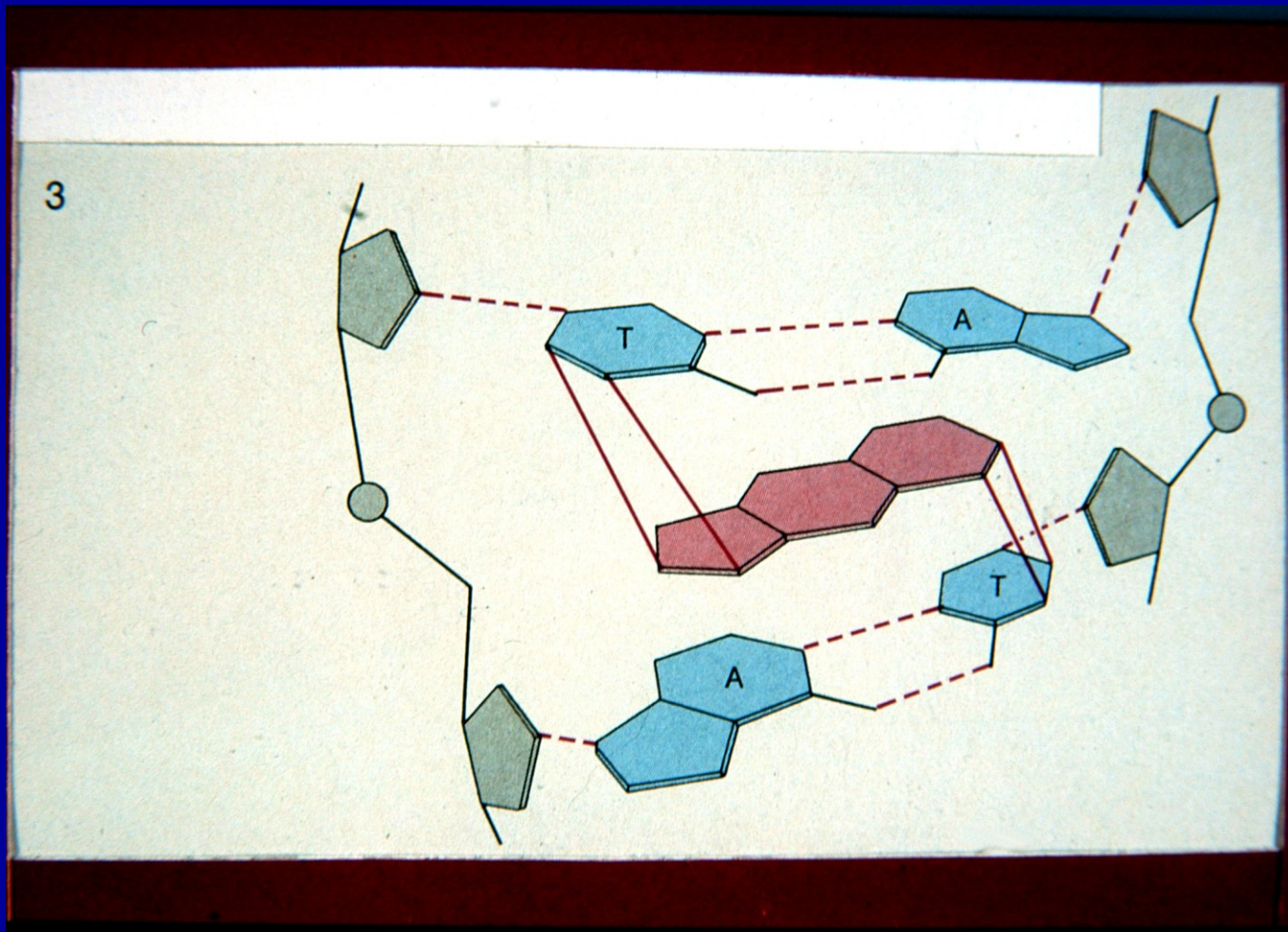




# Fotochemoterapie - PUVA



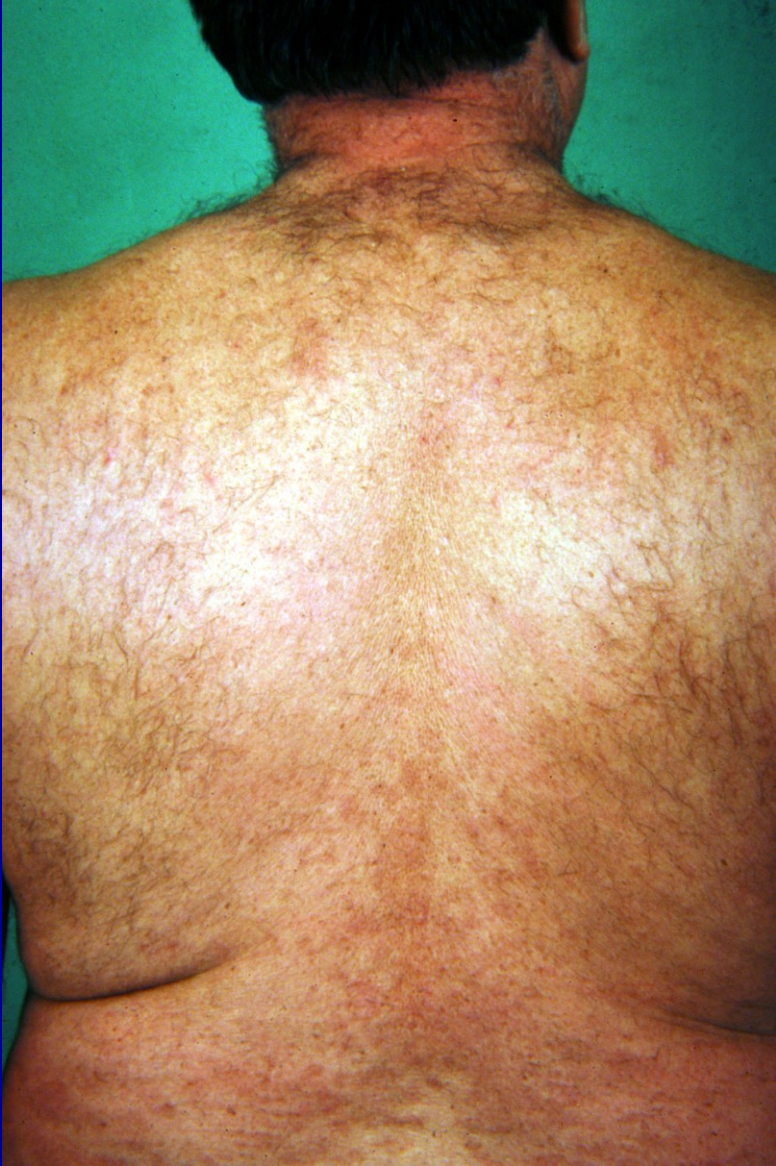
# Fotochemoterapie - PUVA

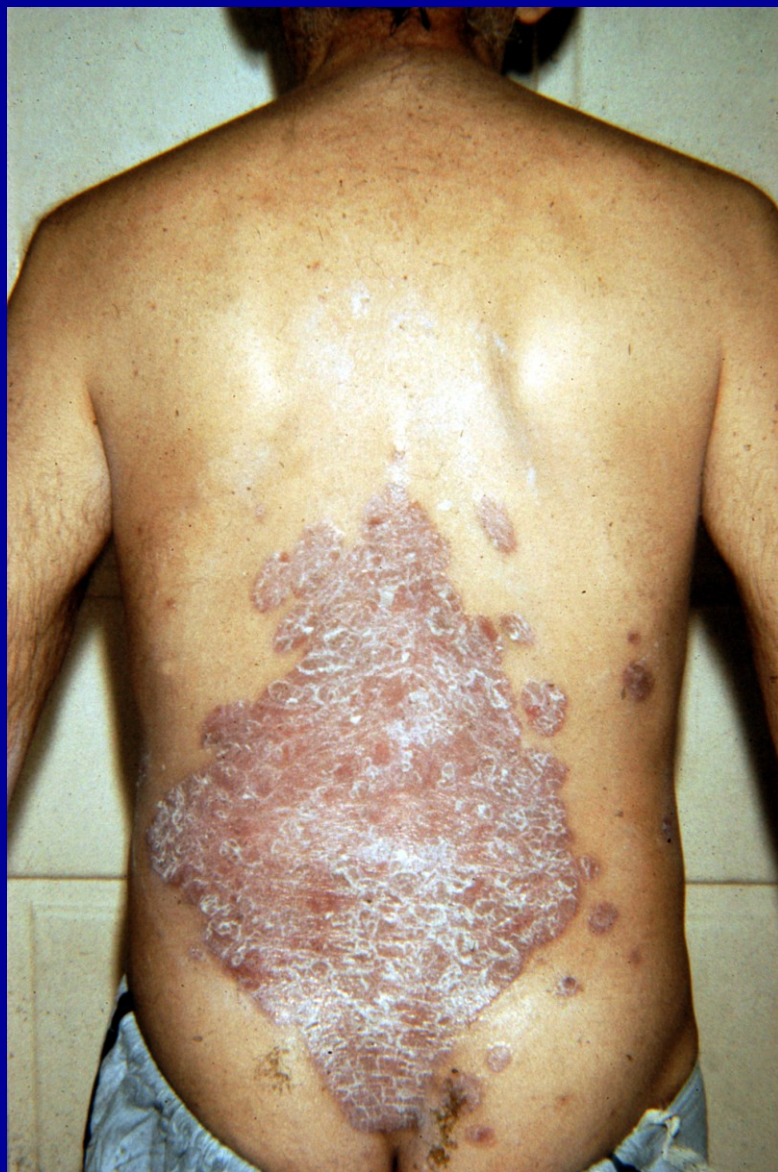






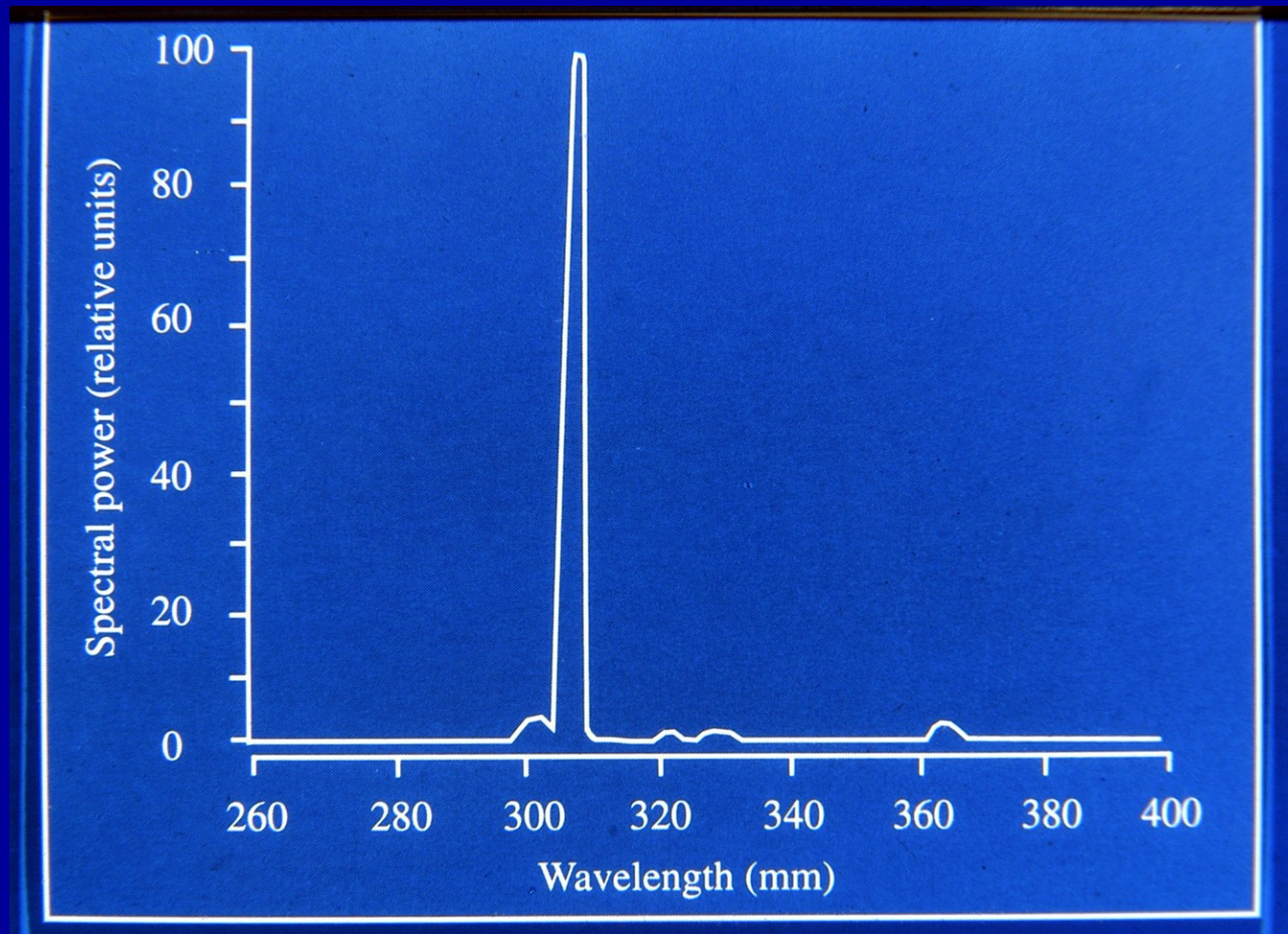








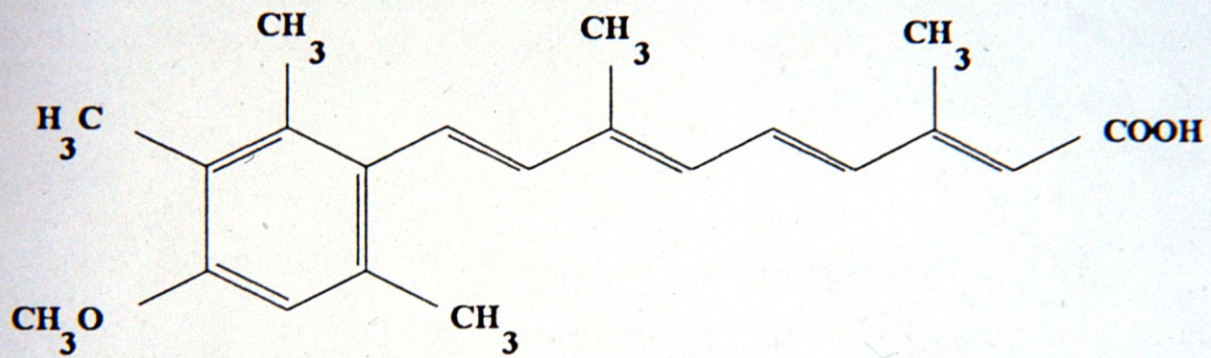
# UVB – „Narrow band lamp“

























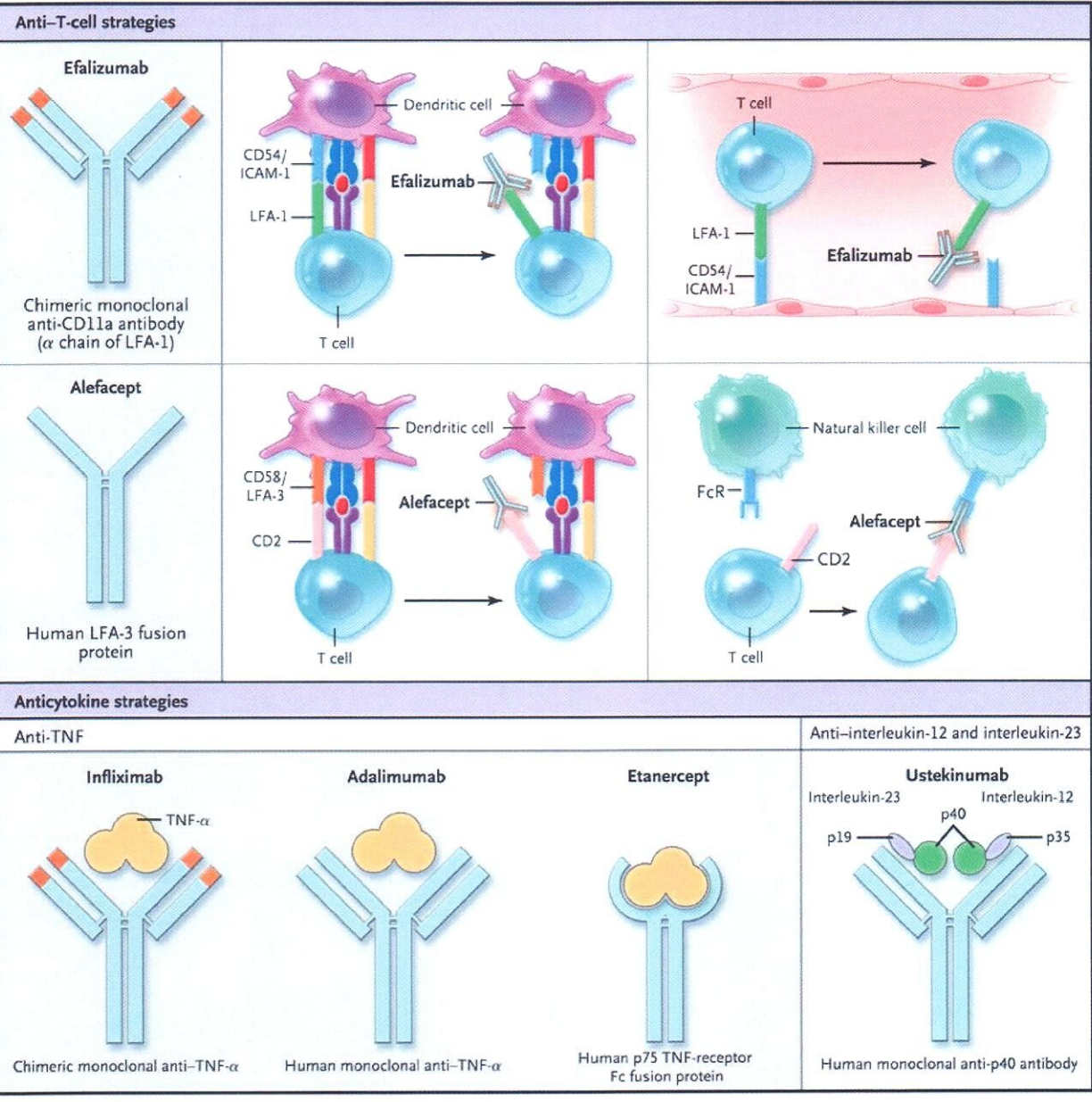




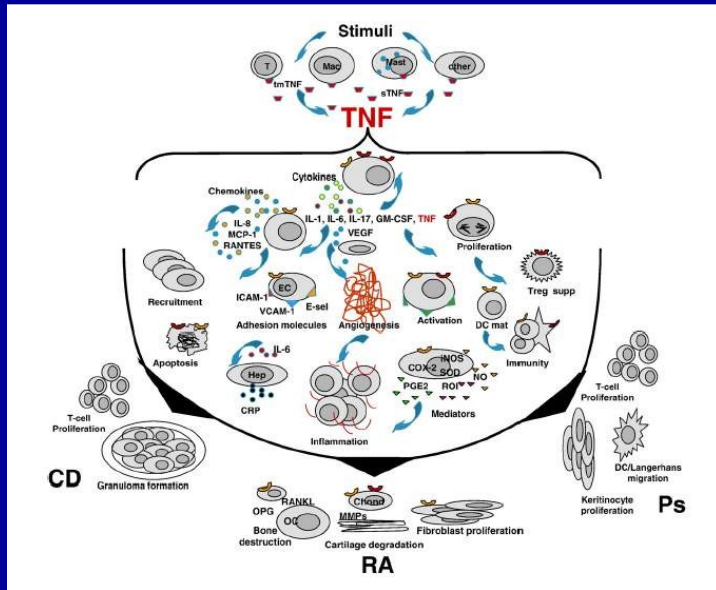








# Tumor Necrosis Factor-Alpha (TNF- $\alpha$ )



- ◆ A cytokine and major mediator of inflammation.
- ◆ Primarily produced by macrophages, but also by T cells, NK cells and mast cells.
- ◆ Both soluble and membrane-bound forms of TNF- $\alpha$  have biologic activity.

# The future in the biological treatment

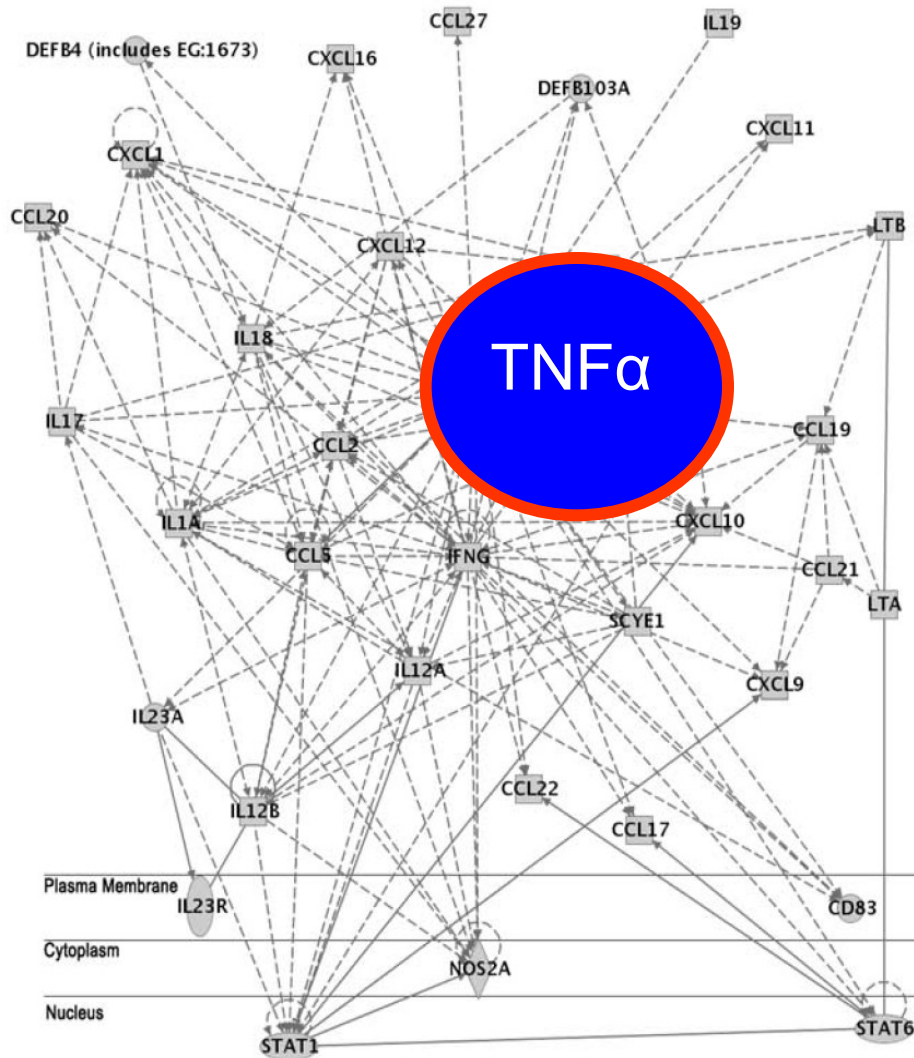
→ Prognostic biomarkers

→ Personalized medicine

→ New molecules

→ Wide knowledge of genetic background of psoriasis

# TNF $\alpha$ Plays a Central Role in the Pathogenesis of Psoriasis



Genes and Immunity (2007) 8, 1–12  
© 2007 Nature Publishing Group All rights reserved 1466-4879/07 \$30.00  
www.nature.com/gene

## REVIEW

### *Psoriasis: genetic associations and immune system changes*

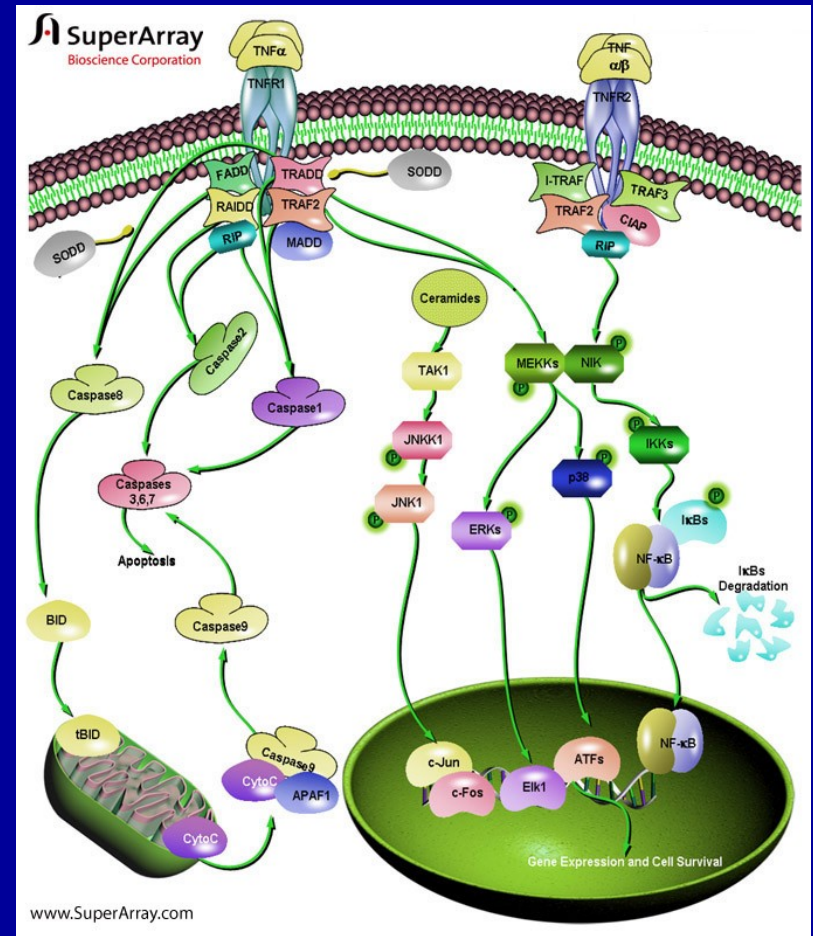
Y Liu<sup>1</sup>, JG Krueger<sup>2</sup> and AM Bowcock<sup>1,3</sup>

<sup>1</sup>Department of Genetics, Washington University School of Medicine, St Louis, MO, USA; <sup>2</sup>Laboratory for Investigative Dermatology, The Rockefeller University, New York, NY, USA and <sup>3</sup>Departments of Pediatrics and Medicine, Washington University School of Medicine, St Louis, MO, USA



# TNF

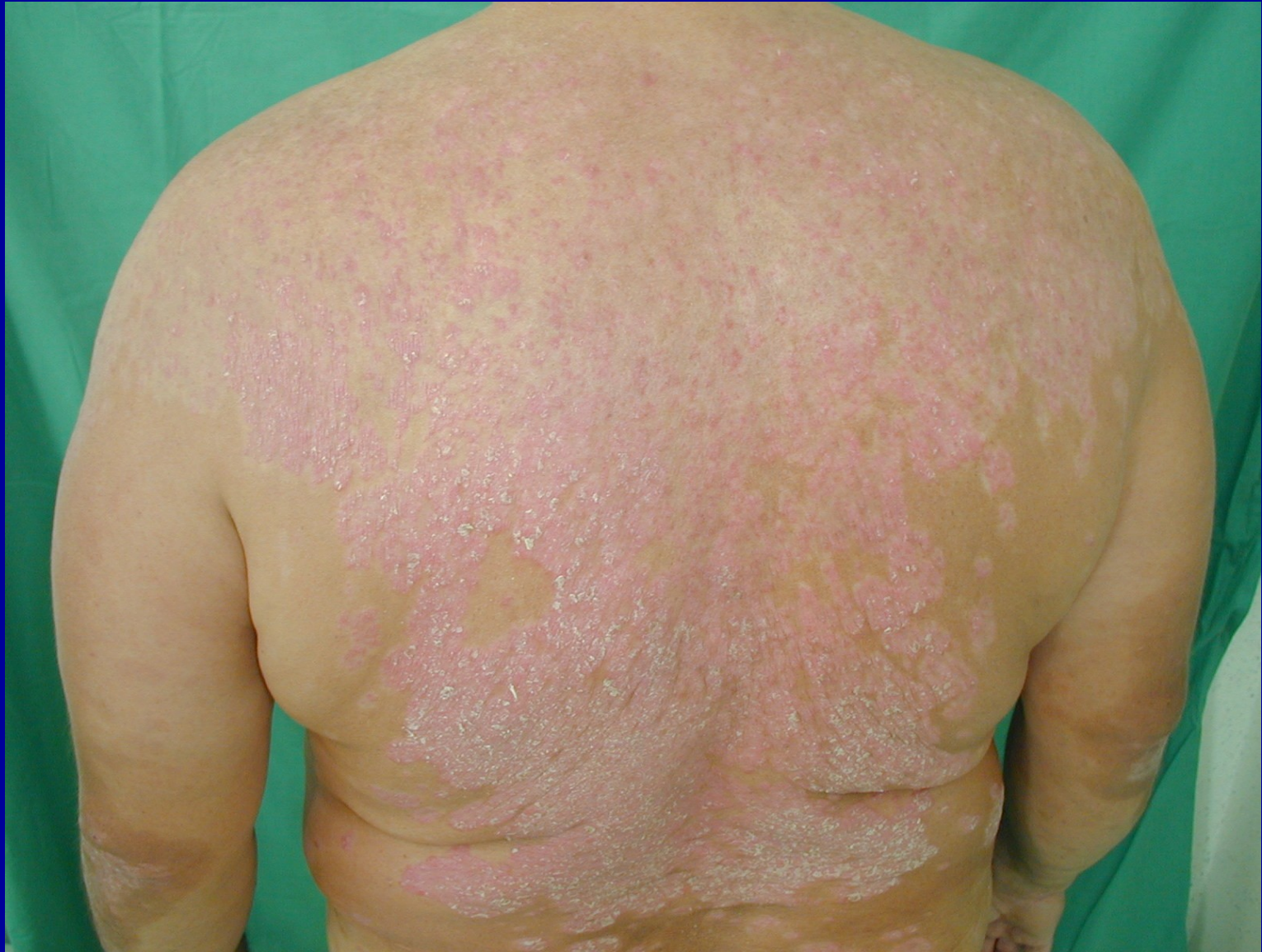
Multifunctional proinflammatory cytokine



# Před léčbou



# Před léčbou



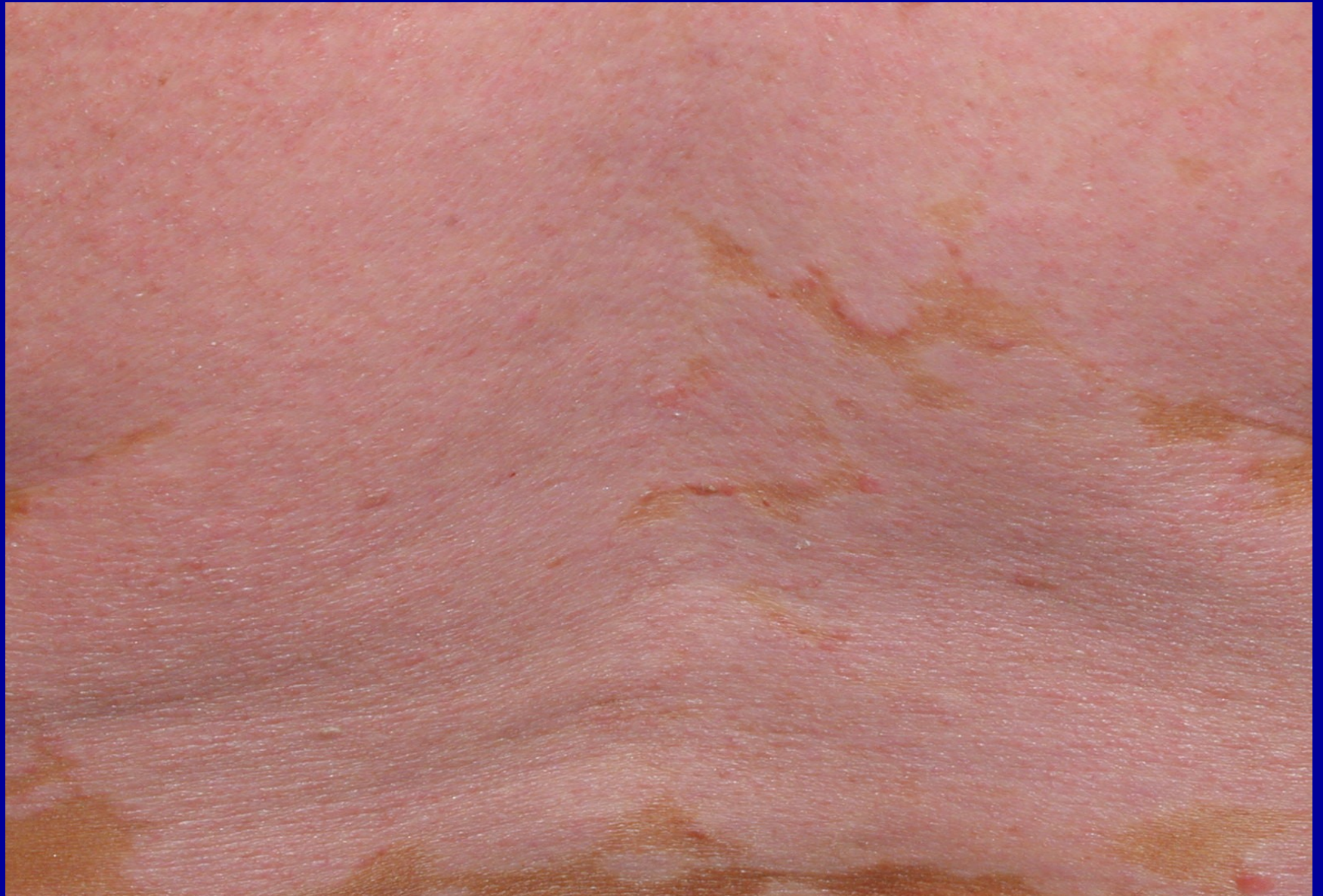
# Před léčbou



**Po 4 týdnech léčby**



**Po 4 týdnech léčby**



# Po 24 týdnech léčby



**Po 24 týdnech léčby**





# Před léčbou



**Po 4 týdnech léčby**



**Po 24 týdnech léčby**





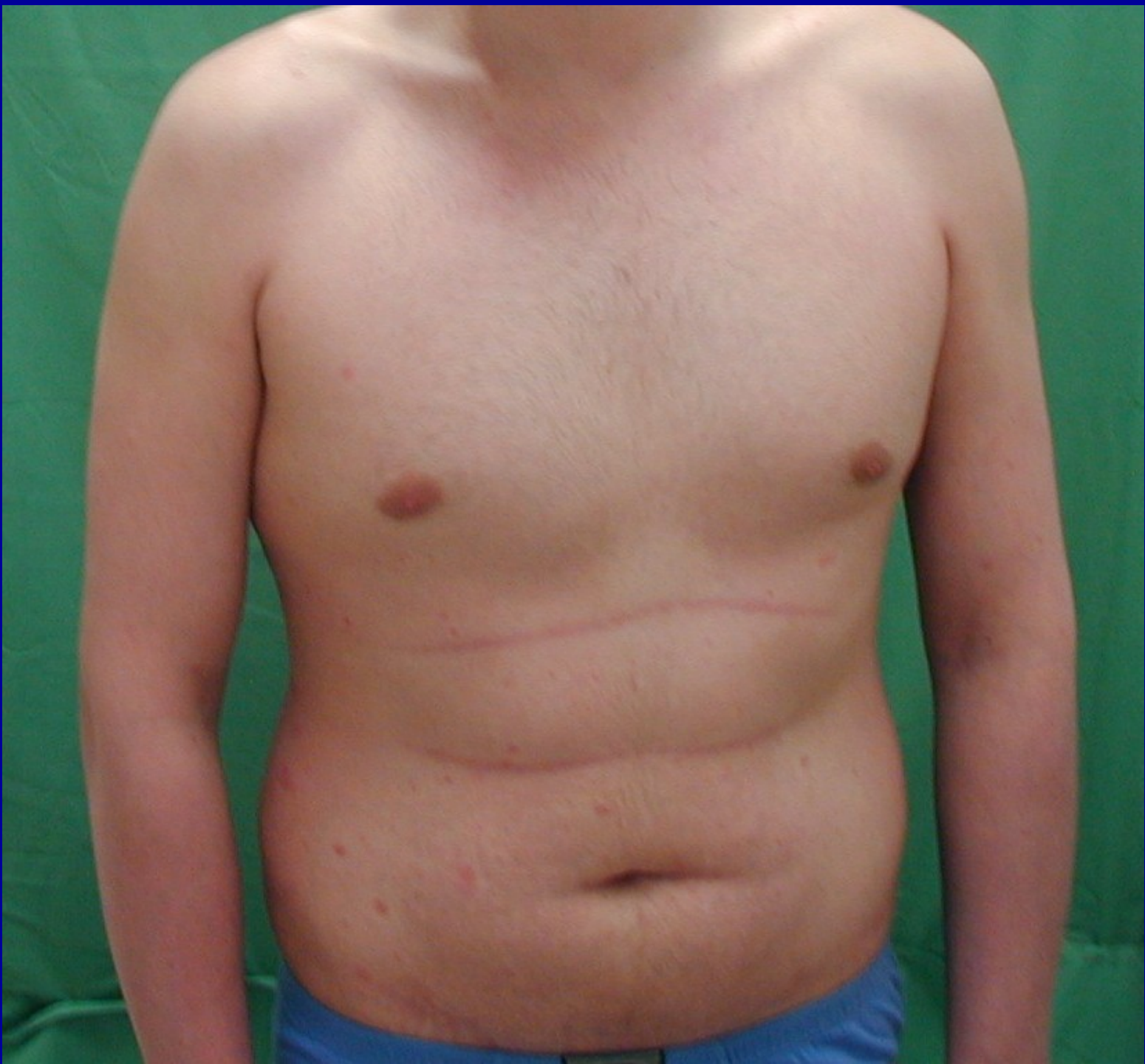


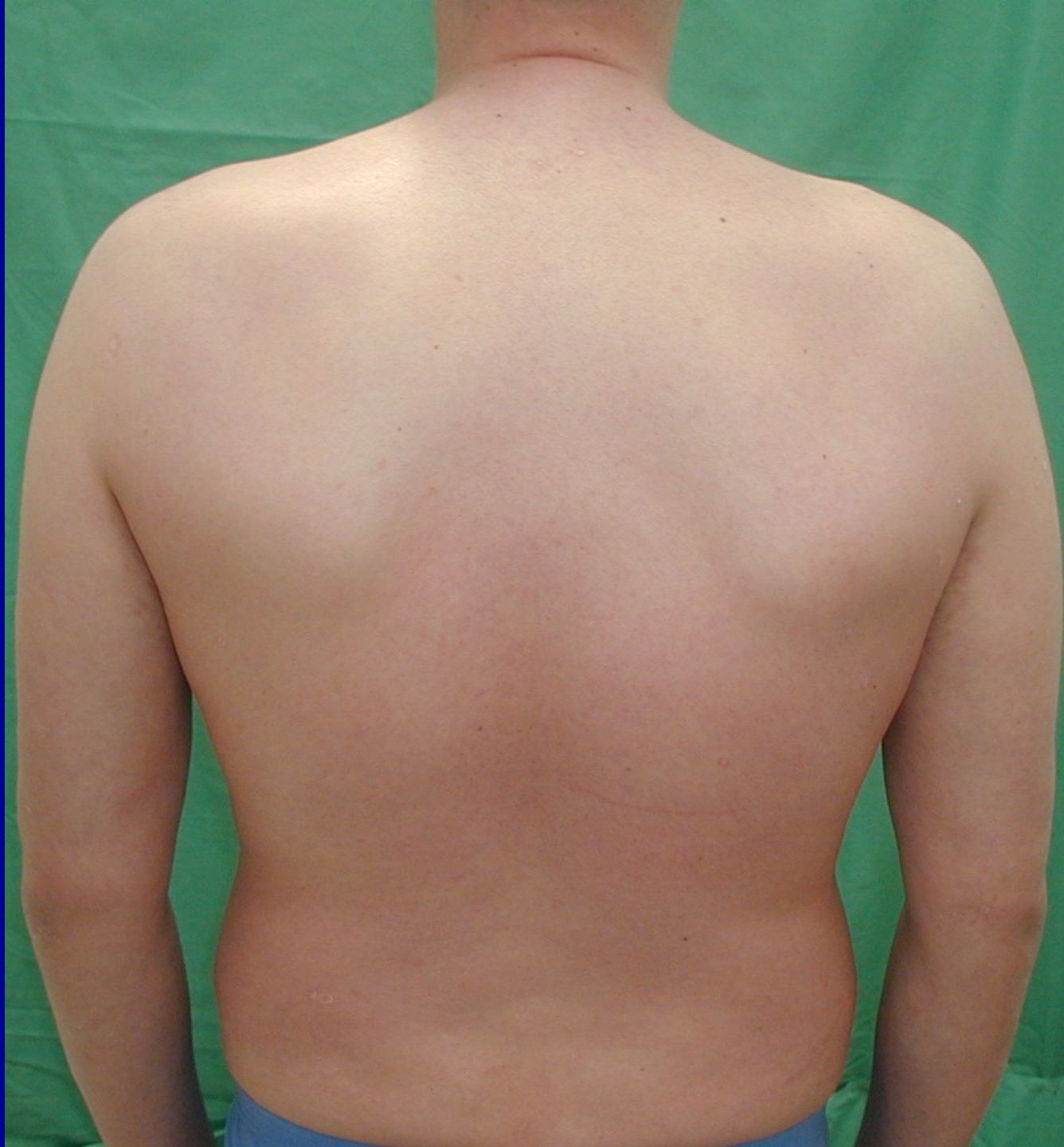
















Buchdruckerei  
MAHKUS KRAL