

# **Immunogenetics**

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## LABORATORY OF IMMUNOGENOMICS AND IMMUNOPROTEO

6 I.P. Pavlova St., 77520, Olomouc, CZ  
phone: +420 58 5632771, fax: +420 58 5415116[About us](#)[Staff](#)[Collaborators](#)[Publications](#)[Posters](#)[Grants](#)[Facilities](#)[News](#)[For students](#)[Outdoor](#)[Location](#)[Files & Links](#)**New!!! Research Fellowships at Palacky University ([flyer here](#))****New!!! 2011 Doktorské (Ph.D.) studium v LIGP/Doctoral study (Ph.D.) in LIPG (****New!!! New grant projects approved and our grant project nominated for the Prize**

The mission of Laboratory of Immunogenomics and Immunoproteomics is to explore situations and in pathogenesis of complex disease with immune component. We aim a susceptibility/protection genes and also search for genes modifying disease remission/progression. The underlying mechanisms, expression of revealed genes is explored at mRNA and protein level by up-to-date technologies such as real time PCR and SELDI-TOF mass spectrometry. Dept. of Immunology, Palacky University Faculty of Medicine and to the Tissue Typing Unit, Olomouc, participates in a number of collaborations on international and local level and receives grants from various international funding bodies, and partially also by the Rector of the Palacky University.

We would be happy if our pieces of work on particular genes, proteins and their complexes will contribute to better understanding of immune system in health and disease within the „Systems Biology“ concept. Systems Biology is a systems-oriented approach to study the organism as an integrated and interacting network of genes, proteins and biochemical pathways. In this interpretation, “the immune system is not the result of a single mechanism or gene. Rather, it is the result of many genes, proteins, mechanisms and the organism’s external environment, produce immune response to various diseases”.

For more about **Systems Biology: the 21 st Century Science** see: <http://www.systemsbiology.org>

## **Area of immunogenetics**

**study of genes coding for molecules of the immune system**

- analysis of polymorphisms in these genes
- **evaluation of functional relevance of immune gene polymorphisms in health and diseases**

# Immunogenetics of complex disease

What areas we and our collaborators chose in Olomouc?

1. Diffuse Lung Disease, sarcoidosis, IPF
2. Hematopoietic Stem Cell Transplantation  
(non-HLA genes)
3. Complications of joint replacements
4. Coronary atherosclerosis  
(*PGx after coronary stenting, AF*)

# **Immunogenetics of sarcoidosis**

## *with Respiratory Medicine*

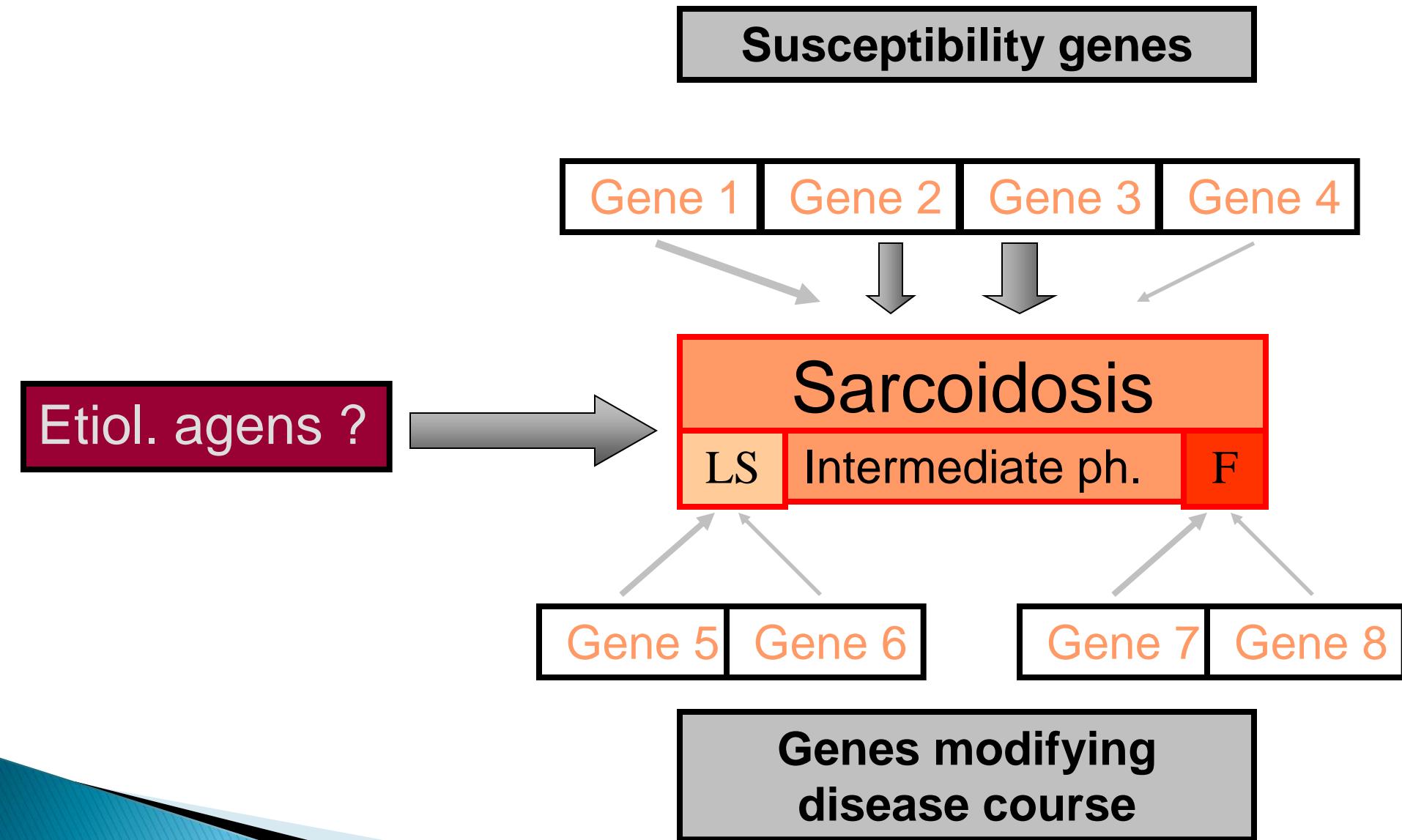
### **Prof. V. Kolek**

Heterogeneous phenotype and prognosis  
“extreme”, polarised forms of disease

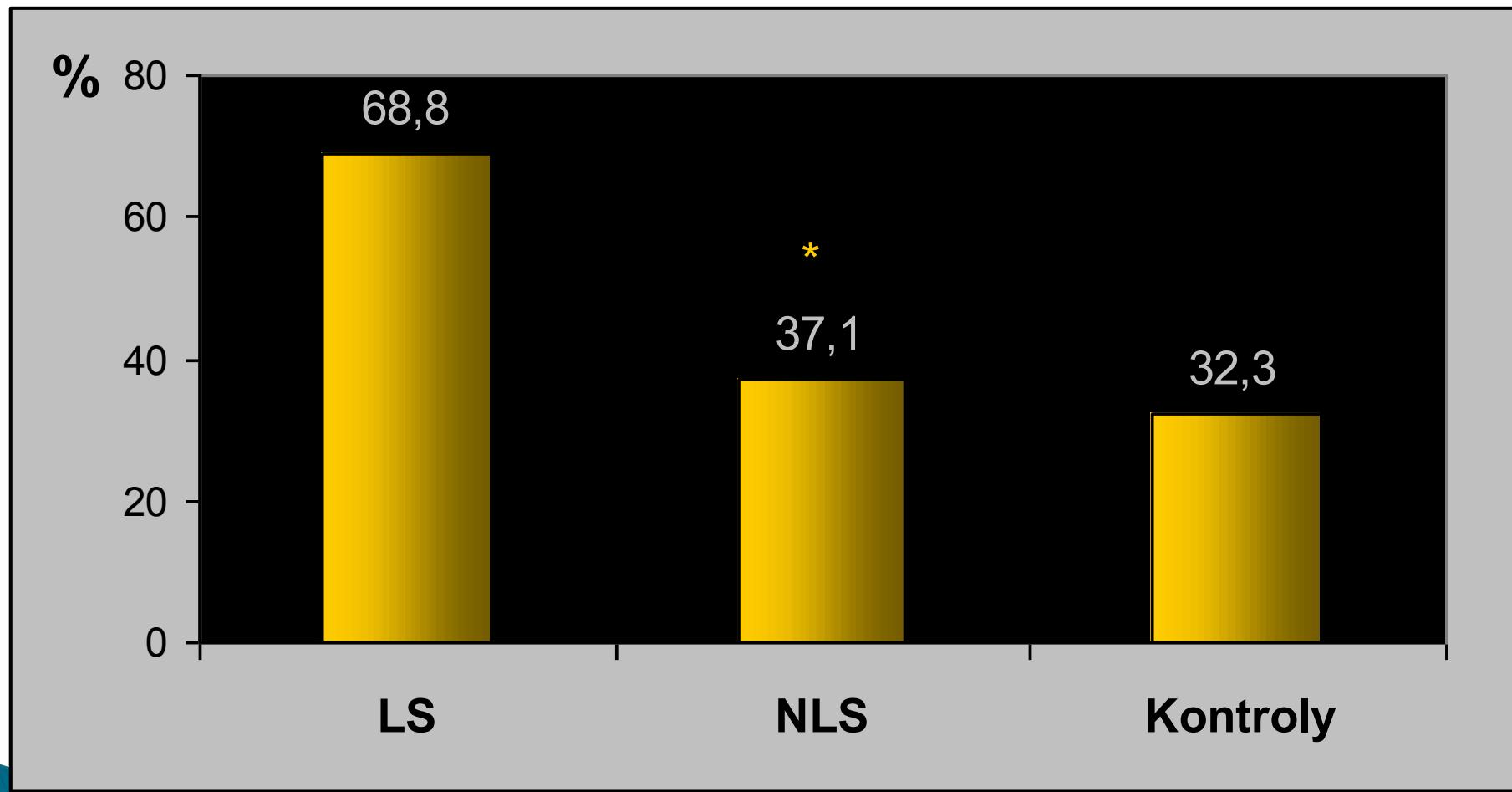
**Acute:** Löfgren syndrome

**Chronic:** progression-fibrosis

# Sarcoidosis - “*polygenic*” predisposition

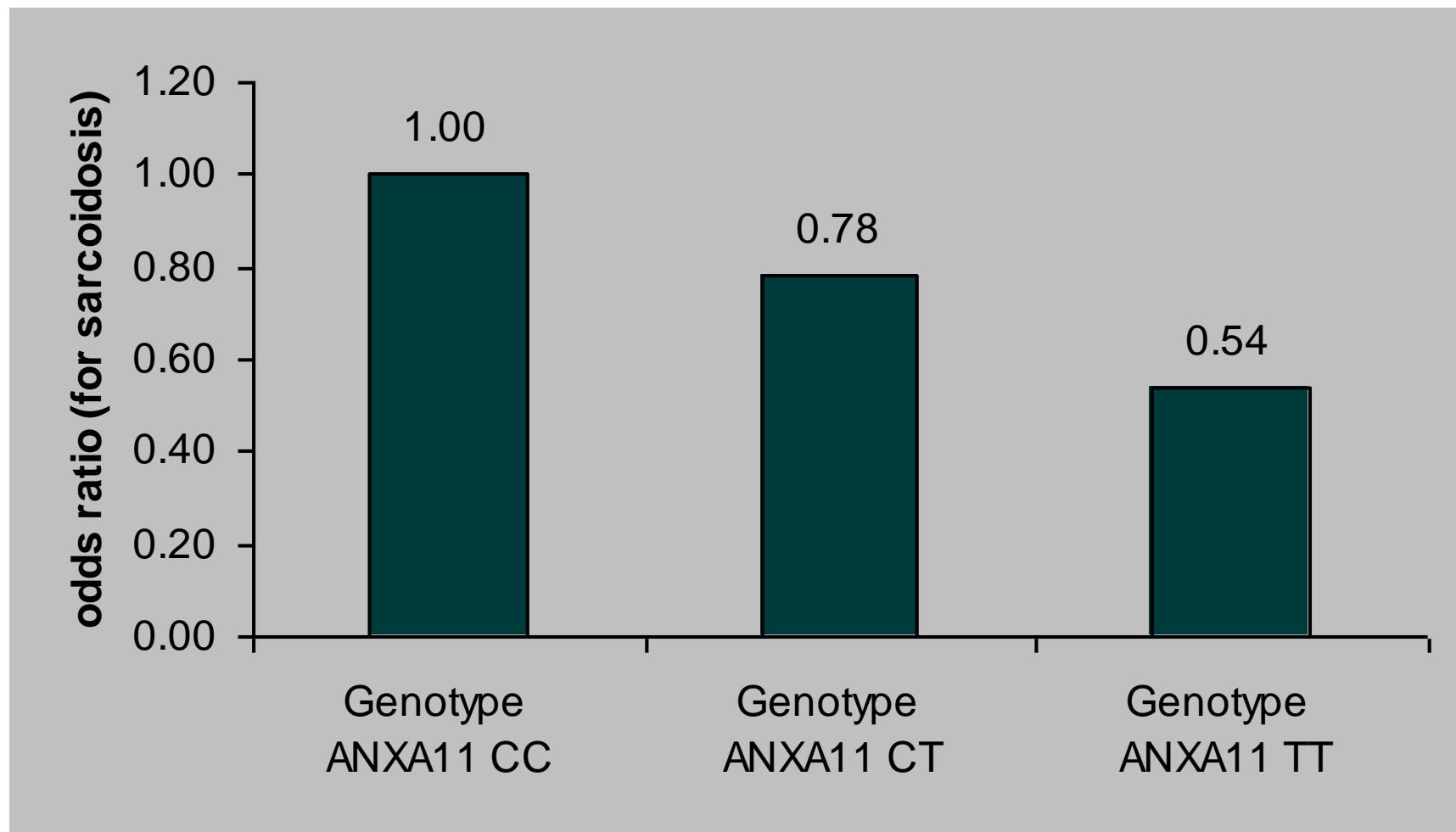


# TNF-308\*A allele in sarcoidosis patients according to presence / absence of Löfgren syndrome (LS)



\* LS vs. NLS: P=0.038, odds ratio (OR)=3.73

# Susceptibility to sarcoidosis depends on copy number of *ANXA11* rs1049550\*T allele („gene-dose effect“)



# Publications - Respiratory

- 1. Chemokines in „polar“ forms of sarcoidosis**  
*(Clinical Exp. Immunol. 2009)*
- 2. Annexin as a protective gene in sarcoidosis**  
*(Genes and Immunity 2011)*
- 3. T-bet expression in sarcoid** *(Eur. Respir. J. 2011)*
- 4. miRNA in lung disease**  
*(Respiratory Research 2010, Scand. J. Immunol. 2011)*

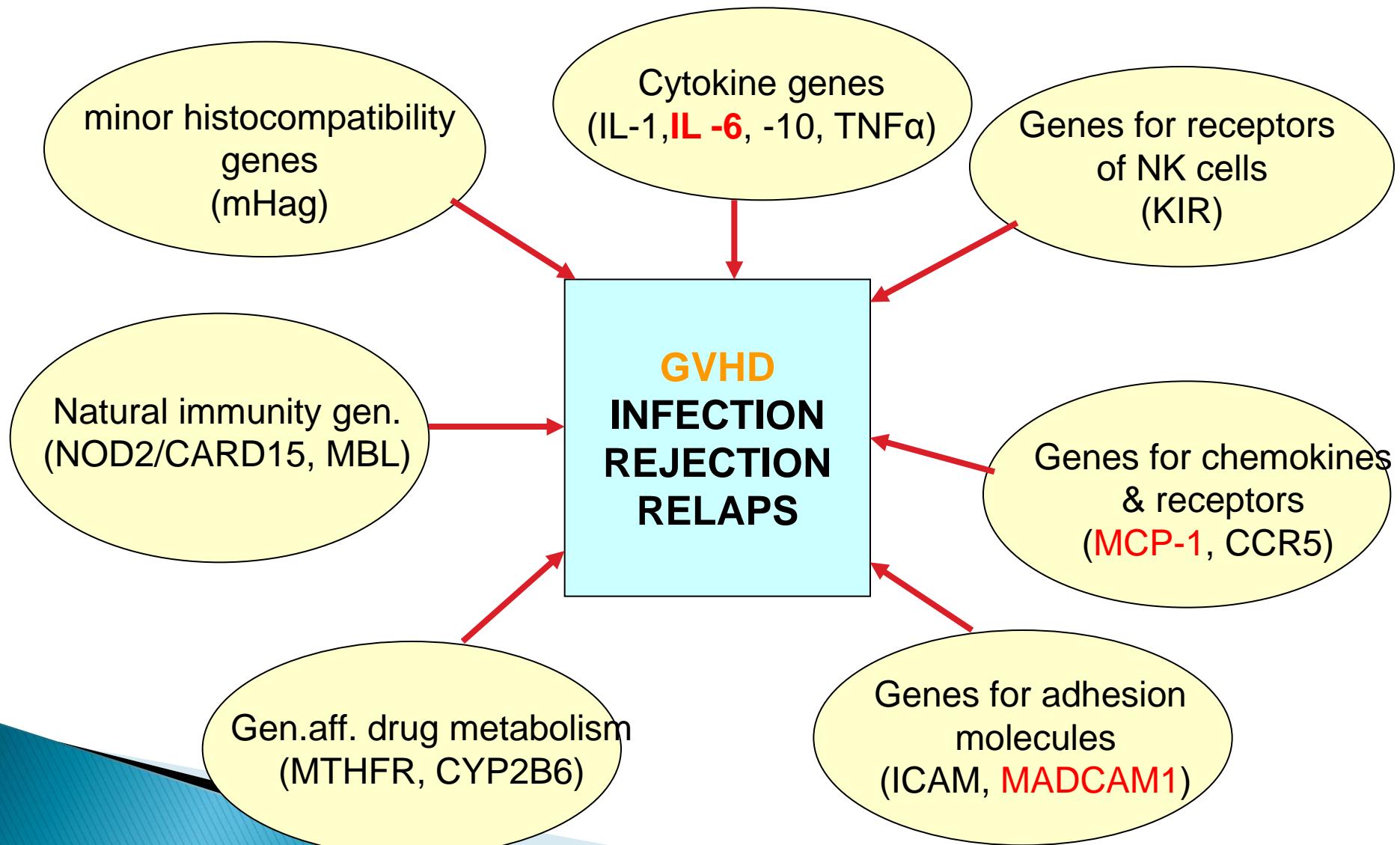
# **Immunogenetics of hematopoietic stem cell transplantation**

*with Hematooncology*

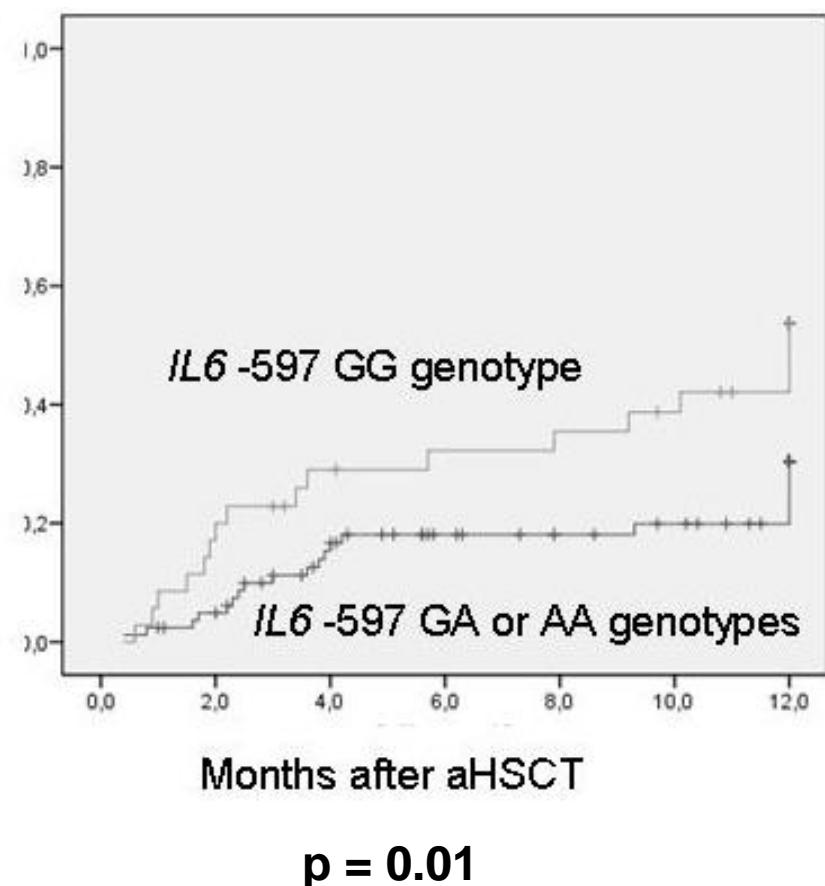
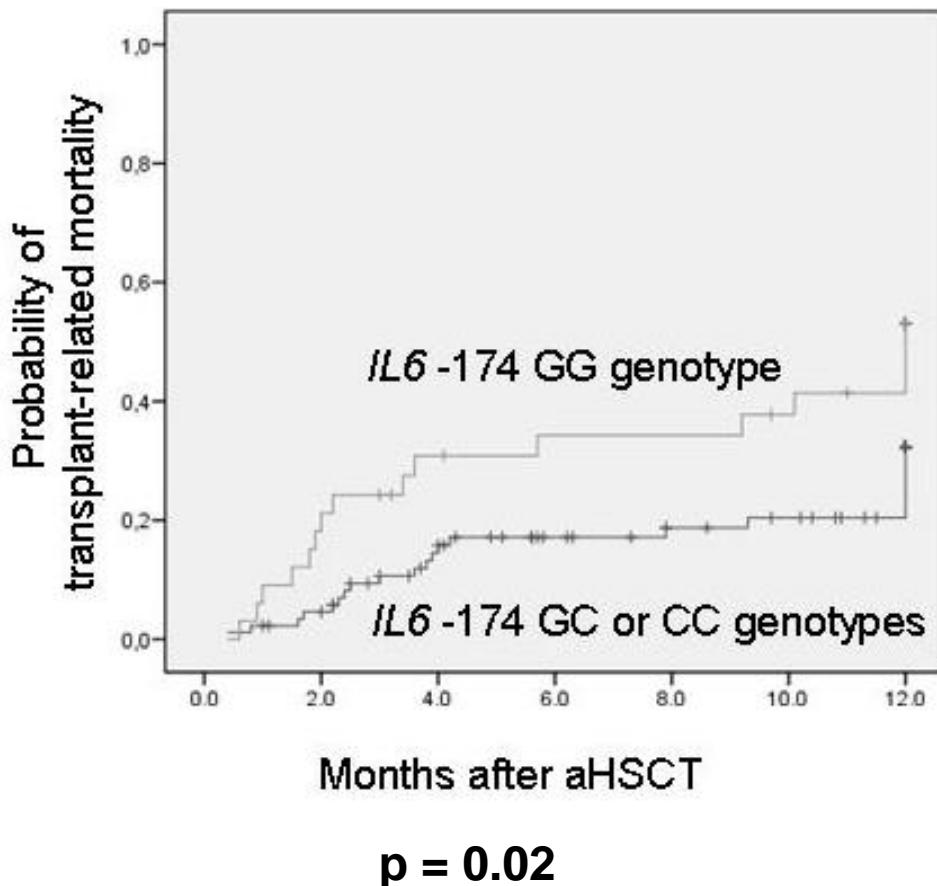
*Prof. K. Indrak*

Non-HLA factors and GvHD

# Complications of aHSCT & nonHLA genes



# ***IL6*-174 / -597 genotypes and TRM**



Ambruzova Z et al, **Bone Marrow Transplant** 2009;44(4):227-35

# **Immunogenetics of complications of joint replacements**

*with Orthopaedics*  
**Assoc. Prof. J. Gallo**

Patient 1

Patient 2

Implantation of prosthesis

Exposition to wear particles

Gene 1 !

Gene 2 !

Gene 3

Gene 4 !

Gene 1

Gene 2 !

Gene 3

Gene 4

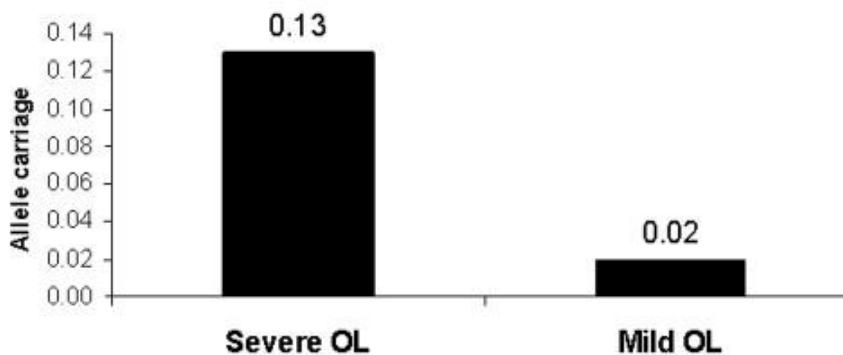
High genetic risk

Low genetic risk

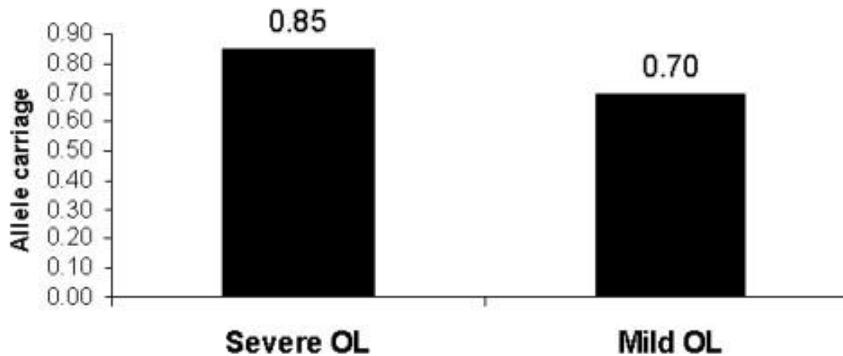
Prosthesis failure

Prosthesis tolerance

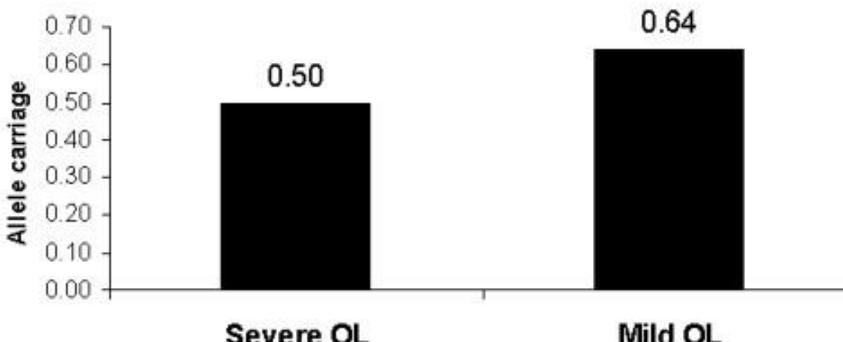
### A) *TNF*-238\*A allele carriage



### B) *IL6*-174\*G allele carriage



### C) *IL2*-330\*G allele carriage



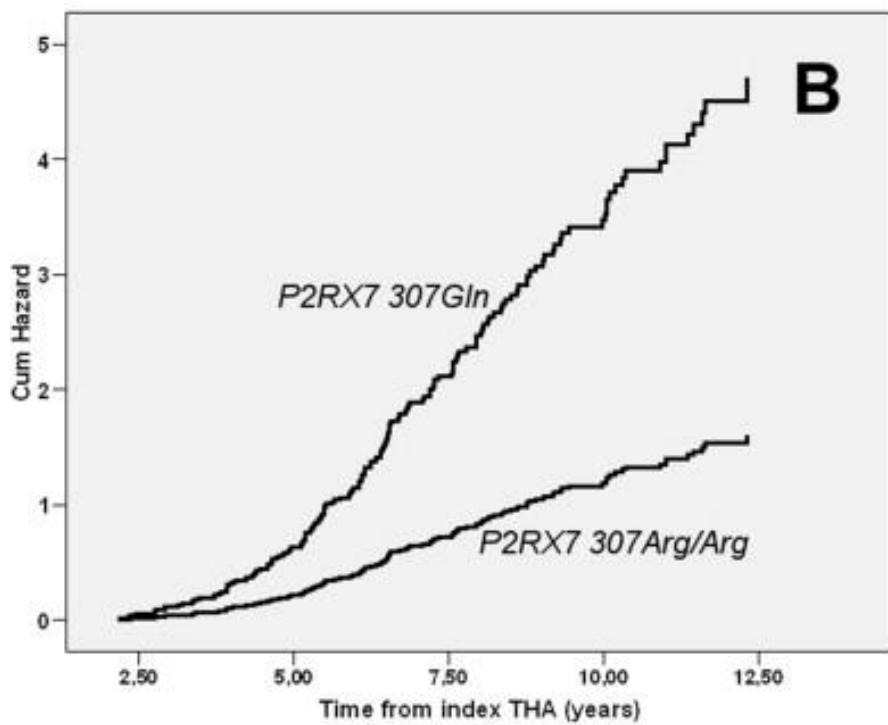
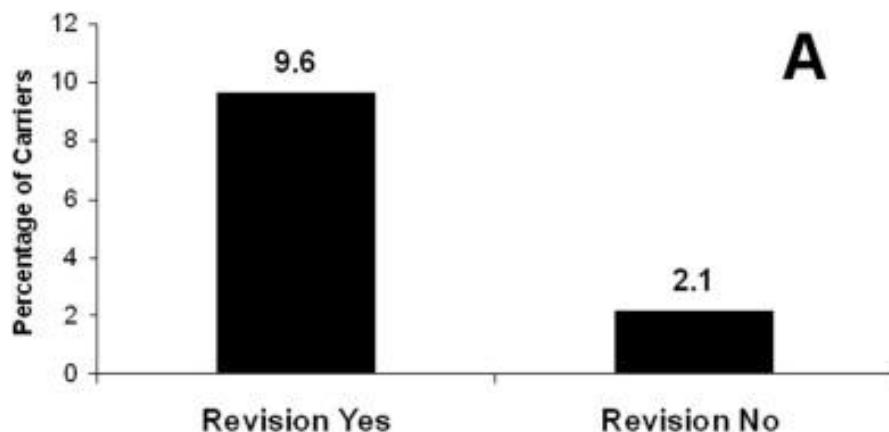
**Carriers of *TNF*-238\*A (A), *IL6*-174\*G (B) a *IL2*-330\*G (C) in patients with severe and mild osteolysis**

*TNF*-238\*A:  $p = 0.005$ , OR = 6.59

*IL6*-174\*G:  $p = 0.007$ , OR = 2.51

*IL2*-330\*G:  $p = 0.043$ , OR = 0.55

Gallo J, Mrazek F, Petrek M.  
**BMC Med Genet.** 2009 Oct 27;10:109.



(A) Carriers of loss of function variant s of *P2RX7* genes in patients with/without revision

(B) Cumulative risk of prosthesis revision in carriers (*P2RX7* 307Gln) vs. noncarriers (*P2RX7* 307Arg/Arg) of loss of function variant *P2RX7* 307Gln ( $p = 0.019$ ).

Mrazek F, Gallo J, Stahelova A, Petrek M.  
*Hum Immunol.* 2010 Feb;71(2):201-5.

# “In what we trust”

Plan / clinical phase

**Disease phenotype**

Population background

**Statistical power**

Genotyping, analysis,  
interpretation

Accurate genotyping  
Adequate statistical analysis  
Linkage disequilibrium

Verification phase

**Replication** of results  
Functional studies

Disease

# **Immunogenetics of atherosclerosis**

*with Internal Medicine I*

*Doz. Dr. M. Taborsky*

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E Kriegova, R Fillerova, T Tomankova, B Hutyrova, F Mrazek, T Tichy, V Kolek, R M du Bois and I Up-regulated In Pulmonary Sarcoidosis. Eur. Respir. J., IF 5,01 (1st revision submitted 20th October 2010)

## Accepted / In press:

Irina P Tereshchenko, Jana Petrkova, Mikhail I. Voevoda, Milos Taborsky, Zdenka Navratilova, Aida Frantisek Mrazek, and Martin Petrek. [CCL5/RANTES gene polymorphisms in Slavonic patients with Inflammation. Received 30 November 2010; Accepted 27 January 2011.](#)

## Published:

[Popa OM, Popa L, Dutescu MI, Bojinca M, Bojinca V, Ciofu C, Bara C, Mrazek F, Petrek M.](#) HLA arthritis in Romanian population. *Tissue Antigens*. 2011 Apr;77(4):325-328. doi: 10.1111/j.1399-0039.2011.01930.x

[Tomankova T, Petrek M, Kriegova E.](#) Involvement of microRNAs in physiological and pathological processes. *Postepy Med Klin*. 2011 Mar;23(1):159. [Epub ahead of print] (IF 3.13) [Open Access](#)

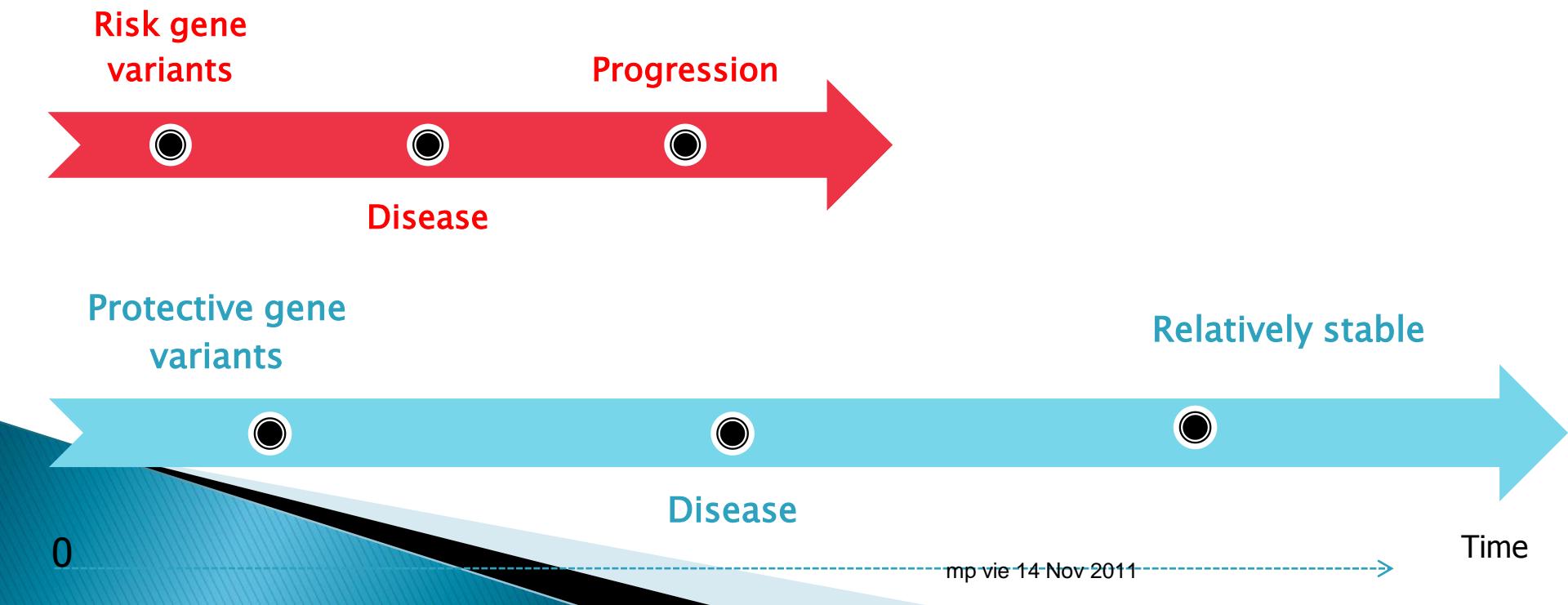
[Penz P, Bucova M, Lietava J, Blazicek P, Paulovicova E, Mrazek F, Bernadic M, Buckingham TA, Petrek M.](#) Association of the BDNF Val66Met polymorphism with blood pressure in ischemic heart disease asymptomatic subjects. *Bratislavské Lekárske Listy*. 2011 Jun;112(6):343-347. doi: 10.5507/bl.2011.112.6.11203

[Stahelova A, Petrkova J, Motakova N, Taborsky M, Mrazek F, Petrek M.](#) The BDNF Val66Met polymorphism is associated with blood pressure in ischemic heart disease asymptomatic subjects. *Cytokine*. 2011 Jan;53(1):13-4. Epub 2010 Sep 16. (IF 3.13)

[Popa OM, Bojinca M, Bojinca V, Ciofu C, Dutescu MI, Bardan A, Sfrent-Cornateanu R, Petrek M, Petrek M.](#) Association of the BDNF Val66Met polymorphism with blood pressure in ischemic heart disease asymptomatic subjects. *Int J Immunogenet*. 2010 Dec;37(6):513-6. (IF 3.13)

# Genetic markers and patient stratification

- ▶ Identification of risk gene variants => prognosis, therapeutic options, ...



# Current state of knowledge of immunopathological mechanisms of complex disease:



**Clarification of disease  
pathogenesis**

**Possibilities for patient  
stratification**

**Follow-up of disease clinical  
course**



mp vie 14 Nov 2011