Imunogenom

- ✓ Imunitní funkce jako komplexní znak(y)
- ✓ Imunitní funkce jako základ obrany proti infekčním nemocem
- ✓ Imunogenom jako funkční celek v evolučním kontextu

Imunogenom a selekce

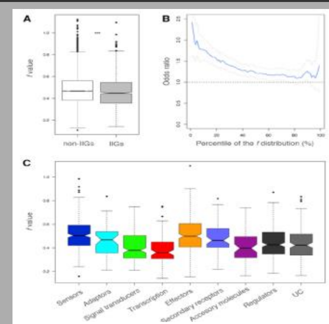
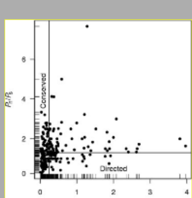


Figure 1. Varying Degrees of Selective Constraints Targeting Innate Immunity Genes

Deschamps, Quintana-Murci 2016

Imunogenom a selekce



Horizontal axis: ratio of the synonymous and nonsynonymous mutation rates (Ka/Ks)
Vertical axis: ratio of number of synonymous and nonsynonymous SNPs in the genes (Pn/Ps)

Table 1. Innate Immunity Genes Presenting the Strongest Signatures of Purifying Selection at the Genome-wide Level

Functional Category	Genes
Sensors	*DHX9*
Adaptors	*CNKSR2, CTNNB1, SRC, SYK*
Signal transducers	*CAMK2B, MTOR, TRAF3*
Transcription	*GATA3, HNRNPL, SMARCA2, SMARCA4, STAT1*
Effectors	*AGO1, AGO2, AGO3*
Secondary receptors	*EGFR*
Accessory molecules	*HSP90AB1, UBC*
Regulators	*CYLD, HDAC1, KHSRP, MID2, USP7*
UC	*ACTB, ACTG1, CYFIP2, DOCK1, FSCN1, ITPR1, NCKAP1, TUBB4B*

Table 2. Innate Immunity Genes Showing the Strongest Signatures of Positive Selection

Population	Innate Immunity Genes
YRI	*VSP45, CD1D, FCER1A, LTBP1, CCDC88A, LY75, IFIH1, LTF, CCR2, CD80, MAPK10, CD36, ZFPM2, TRIM55, CHUK, DAK, POLR3B, HIF1A, CEACAM1, TNRC6B, MYH9*
CEU	*CCDC88A, TLR10, TLR1, TLR6, MAP3K1, IL4, IRGM, TRIM27, EYA4, ARPC1A, ZC3HAV1, SRPK2, SMARCA2, SIRT1, DUOX1, ADAM10*
CHB	*ARHGEF2, ADAM15, LYST, PELI1, ACTR2, MERTK, ERBB4, SP100, RAF1, LRRFIP2, CLEC3B, RHOA, GAB1, FER, ITPR3, EGFR, BLK, NRG1, SIRT1, OTUB1, ARHGEF7, PIAS4*

Deschamps, Quintana-Murci 2016
Ortutay, Vihinen Human Mutation 2012

Imunogenom, selekce, adaptace

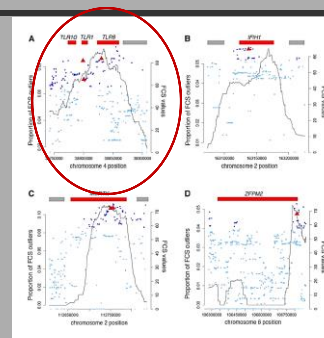


Figure 3. Innate Immunity Genes Presenting High-Confidence Signals of Geographic Adaptation

Vývoj člověka, imunogenom, selekce

http://ancients-bg.com/wp-content/uploads/2016/04/0021.jpg

Vývoj člověka, imunogenom, selekce

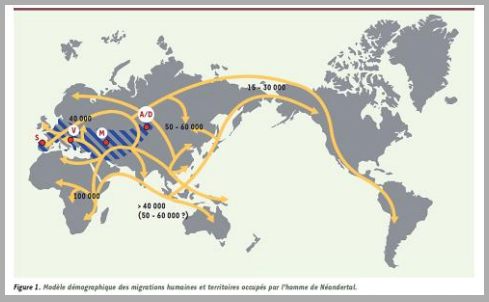


Figure 1. Modèle démographique des migrations humaines et territoires occupés par l'homme de Néandertal.

Deschamps, Quintana-Murci 2016

Vývoj člověka, imunogenom, selekce

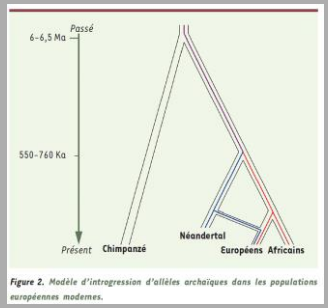


Figure 2. Modèle d'introgression d'allèles archaïques dans les populations européennes modernes.

Deschamps, Quintana-Murci 2016

Vývoj člověka, imunogenom, adaptace

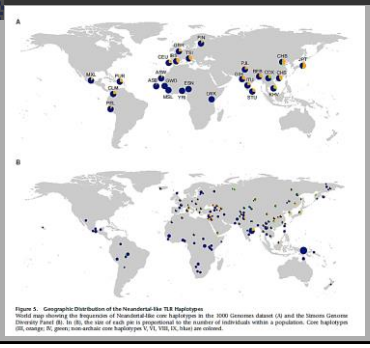


Figure 5. Geographic Distribution of the Neandertal-like TLR Haplotypes
World map showing the frequencies of Neandertal-like core haplotypes in the 1000 Genomes dataset (A) and the Simons Genome Diversity Panel (B). In (B), the size of each pie is proportional to the number of individuals within a population. Core haplotypes (III, orange; IV, green; non-archaic core haplotypes V, VI, VIII, IX, blue) are colored.

Introgression of Neandertal- and Denisovan-like Haplotypes Contributes to Adaptive Variation in Human Toll-like Receptors

Michael Dannemann,[1] Alla M. Andrés,[1] and Janet Kelso[1,*]

The American Journal of Human Genetics 98, 22–33, January 7, 2016

Imunogenom, evoluce, selekce

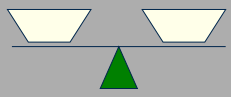
- ✓ Sympatrie hoinoidních populací
- ✓ „Differential pathogen resistance“
- ✓ Nižší diversita neandertálců
- ✓ MHC, OAS, TLR 1/6/10
- ✓ *H. pylori,* alergie“ hygienická hypotéza

Skylla and Charybda odolnosti/vnímavosti k nemocem

Věčné dilema:
Silná nebo slabá imunitní odpověď?

Protektivní imunita
Resistence k infekci

Autoimunita, alergie
Zánět



Imunogenom a selekce

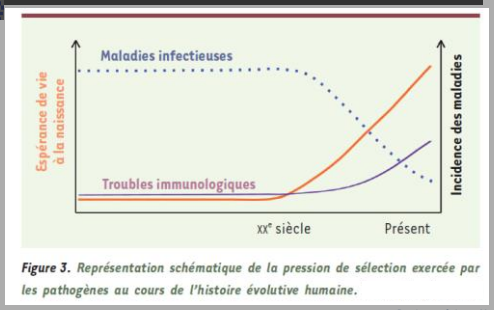
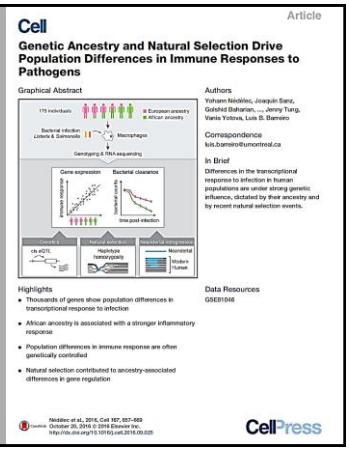


Figure 3. Représentation schématique de la pression de sélection exercée par les pathogènes au cours de l'histoire évolutive humaine.

Deschamps, Quintana-Murci 2016

Vývoj člověka, imunogenom, selekce

http://ancients-bg.com/wp-content/uploads/2016/04/0021.jpg



Article

Cell

Genetic Ancestry and Natural Selection Drive Population Differences in Immune Responses to Pathogens

Graphical Abstract

Authors

Correspondence

In Brief

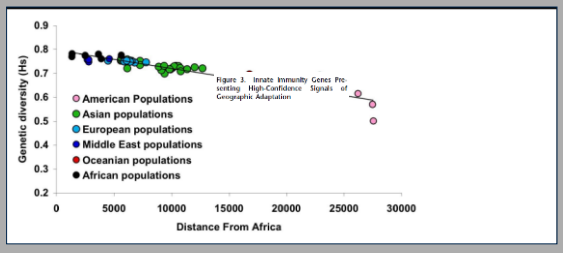
Highlights

- Thousands of genes show population differences in transcriptional response to infection
- African ancestry is associated with a stronger inflammatory response
- Population differences in immune response are often genetically controlled
- Natural selection contributed to ancestry-associated differences in gene regulation

Data Resources

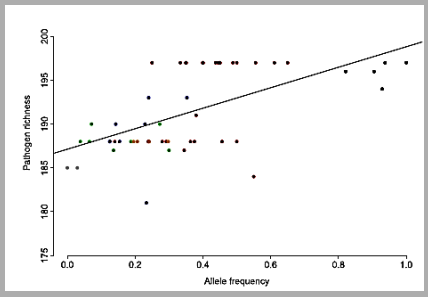
CellPress

Genetická diversita a „pathogen richness“ *MHC*



Prugnolle et al. Curr Biol 2007

Genetická diversita a „pathogen richness“ *IL18RAP*



Sironi, Clerici 2010

Imunogenom, evoluce, selekce

- ✓ Patogeny a evoluce
- ✓ IR genes jako geny přežití
- ✓ Otisky (signatures) evolučních interakcí mezi hostitelem a patogenem v genomu patogenů i imunogenomu hostitele
- ✓ Imunogenom a adaptace na prostředí/patogeny
- ✓ Příklad: Introgrese archaických genů/alel ve vývoji člověka