

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

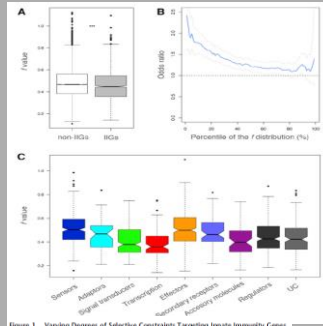
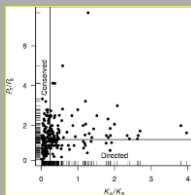


Figure 1. Varying Degrees of Selective Constraints Targeting Innate Immunity Genes

Deschamps, Quintana-Murci 2016

Imunogenom a selekce



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

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

Functional Category	Genes
Sensors	ZNF59
Adaptors	CXCR2, CTNNA1, SRC, SYK
Signal transducers	CARD6, SYK, TRAF3
Transceptors	GAT3L, PRRN1, MMR2, MMR2L4, MMR7
Effectors	ACT1, BCL2L1, BCL2L2
Secondary receptors	ROBO
Accessory molecules	ADPM1, EPC
Regulators	CH2L1, RFX5, RFX5L, RFX5L2, RFX5L3, RFX5L4, RFX5L5, RFX5L6, RFX5L7, RFX5L8, RFX5L9, RFX5L10, RFX5L11, RFX5L12, RFX5L13, RFX5L14, RFX5L15, RFX5L16, RFX5L17, RFX5L18, RFX5L19, RFX5L20, RFX5L21, RFX5L22, RFX5L23, RFX5L24, RFX5L25, RFX5L26, RFX5L27, RFX5L28, RFX5L29, RFX5L30, RFX5L31, RFX5L32, RFX5L33, RFX5L34, RFX5L35, RFX5L36, RFX5L37, RFX5L38, RFX5L39, RFX5L40, RFX5L41, RFX5L42, RFX5L43, RFX5L44, RFX5L45, RFX5L46, RFX5L47, RFX5L48, RFX5L49, RFX5L50, RFX5L51, RFX5L52, RFX5L53, RFX5L54, RFX5L55, RFX5L56, RFX5L57, RFX5L58, RFX5L59, RFX5L60, RFX5L61, RFX5L62, RFX5L63, RFX5L64, RFX5L65, RFX5L66, RFX5L67, RFX5L68, RFX5L69, RFX5L70, RFX5L71, RFX5L72, RFX5L73, RFX5L74, RFX5L75, RFX5L76, RFX5L77, RFX5L78, RFX5L79, RFX5L80, RFX5L81, RFX5L82, RFX5L83, RFX5L84, RFX5L85, RFX5L86, RFX5L87, RFX5L88, RFX5L89, RFX5L90, RFX5L91, RFX5L92, RFX5L93, RFX5L94, RFX5L95, RFX5L96, RFX5L97, RFX5L98, RFX5L99, RFX5L100
UC	ACT1, ACT1L1, CYP11B, DKK1, FSTL1, FSTL2, MMR2, TRAF3

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

Population	Innate Immunity Genes*
YRI	ADAM10, ADAM11, ADAM12, ADAM13, ADAM14, ADAM15, ADAM16, ADAM17, ADAM18, ADAM19, ADAM20, ADAM21, ADAM22, ADAM23, ADAM24, ADAM25, ADAM26, ADAM27, ADAM28, ADAM29, ADAM30, ADAM31, ADAM32, ADAM33, ADAM34, ADAM35, ADAM36, ADAM37, ADAM38, ADAM39, ADAM40, ADAM41, ADAM42, ADAM43, ADAM44, ADAM45, ADAM46, ADAM47, ADAM48, ADAM49, ADAM50, ADAM51, ADAM52, ADAM53, ADAM54, ADAM55, ADAM56, ADAM57, ADAM58, ADAM59, ADAM60, ADAM61, ADAM62, ADAM63, ADAM64, ADAM65, ADAM66, ADAM67, ADAM68, ADAM69, ADAM70, ADAM71, ADAM72, ADAM73, ADAM74, ADAM75, ADAM76, ADAM77, ADAM78, ADAM79, ADAM80, ADAM81, ADAM82, ADAM83, ADAM84, ADAM85, ADAM86, ADAM87, ADAM88, ADAM89, ADAM90, ADAM91, ADAM92, ADAM93, ADAM94, ADAM95, ADAM96, ADAM97, ADAM98, ADAM99, ADAM100
CEU	ADAM10, ADAM11, ADAM12, ADAM13, ADAM14, ADAM15, ADAM16, ADAM17, ADAM18, ADAM19, ADAM20, ADAM21, ADAM22, ADAM23, ADAM24, ADAM25, ADAM26, ADAM27, ADAM28, ADAM29, ADAM30, ADAM31, ADAM32, ADAM33, ADAM34, ADAM35, ADAM36, ADAM37, ADAM38, ADAM39, ADAM40, ADAM41, ADAM42, ADAM43, ADAM44, ADAM45, ADAM46, ADAM47, ADAM48, ADAM49, ADAM50, ADAM51, ADAM52, ADAM53, ADAM54, ADAM55, ADAM56, ADAM57, ADAM58, ADAM59, ADAM60, ADAM61, ADAM62, ADAM63, ADAM64, ADAM65, ADAM66, ADAM67, ADAM68, ADAM69, ADAM70, ADAM71, ADAM72, ADAM73, ADAM74, ADAM75, ADAM76, ADAM77, ADAM78, ADAM79, ADAM80, ADAM81, ADAM82, ADAM83, ADAM84, ADAM85, ADAM86, ADAM87, ADAM88, ADAM89, ADAM90, ADAM91, ADAM92, ADAM93, ADAM94, ADAM95, ADAM96, ADAM97, ADAM98, ADAM99, ADAM100
CHB	ADAM10, ADAM11, ADAM12, ADAM13, ADAM14, ADAM15, ADAM16, ADAM17, ADAM18, ADAM19, ADAM20, ADAM21, ADAM22, ADAM23, ADAM24, ADAM25, ADAM26, ADAM27, ADAM28, ADAM29, ADAM30, ADAM31, ADAM32, ADAM33, ADAM34, ADAM35, ADAM36, ADAM37, ADAM38, ADAM39, ADAM40, ADAM41, ADAM42, ADAM43, ADAM44, ADAM45, ADAM46, ADAM47, ADAM48, ADAM49, ADAM50, ADAM51, ADAM52, ADAM53, ADAM54, ADAM55, ADAM56, ADAM57, ADAM58, ADAM59, ADAM60, ADAM61, ADAM62, ADAM63, ADAM64, ADAM65, ADAM66, ADAM67, ADAM68, ADAM69, ADAM70, ADAM71, ADAM72, ADAM73, ADAM74, ADAM75, ADAM76, ADAM77, ADAM78, ADAM79, ADAM80, ADAM81, ADAM82, ADAM83, ADAM84, ADAM85, ADAM86, ADAM87, ADAM88, ADAM89, ADAM90, ADAM91, ADAM92, ADAM93, ADAM94, ADAM95, ADAM96, ADAM97, ADAM98, ADAM99, ADAM100

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

Imunogenom, selekce, adaptace

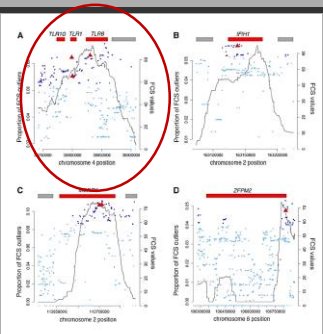


Figure 2. Innate Immunity Genes Presenting High-Confidence Signals of Convergent Adaptation

Vývoj člověka, imunogenom, selekce



<http://landmarks.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

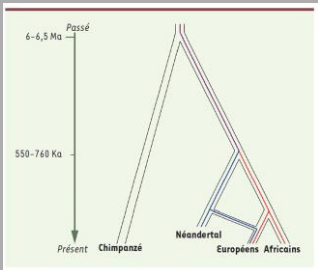


Figure 2. Modèle d'introsion d'allèles archaïques dans les populations européennes modernes.

Deschamps, Quintana-Murci 2016

Vývoj člověka, imunogenom, adaptace

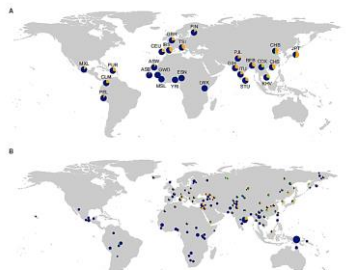


Figure 3. Geographic Distribution of the Neanderthal-like TLR8 Haplotypes

World map showing the geographic distribution of Neanderthal-like core haplotypes in the 1000 Genomes dataset (A) and the Simons Genome Diversity Project (B). In (B), the size of each dot is proportional to the number of individuals within a population. Core haplotypes (20) are highlighted in blue. Haplotype IDs are indicated by the color of the dot.

Introsion of Neanderthal- and Denisovan-like Haplotypes: Contributions to Adaptive Variation in Human Toll-like Receptors

Deschamps, Quintana-Murci, et al. 2016

The American Journal of Human Genetics, 98, 20-33, January 7, 2016

Imunogenom, evoluce, selekce

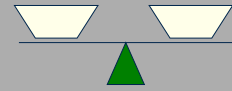
- ✓ Sympatrie hoinoidních populací
- ✓ „Differential pathogen resistance“
- ✓ Nižší diversita neandertálců
- ✓ MHC, OAS, TLR 1/6/10
- ✓ *H. pylori*, alergie“ hygienická hypotéza

Skylla and Charybda odolnosti/vnímatvosti k nemocem



Věčné dilema:
Silná nebo slabá imunitní odpověď?

Protektivní imunita Autoimunita, alergie
Resistance k infekci Zánět



Imunogenom a selekce

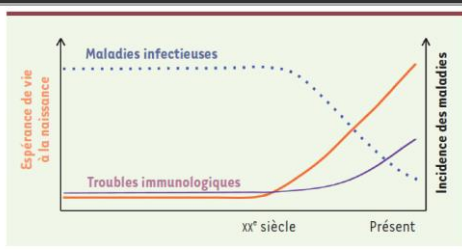


Figure 3. Représentation schématique de la pression de sélection exercée par les pathogènes au cours de l'histoire évolutive humaine.

Deschamps, Quintana-Murci 2016

Vývoj člověka, imunogenom, selekce



<http://arxiv.org/abs/1604.00211>



Cell Article

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

Graphical Abstract

Authors
Yuhang Ni, Ziqiang Song, Gabriel Ballester, ... Jinyang Tang, Maria Vitoria, Luis B. Barreiro

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In Brief
Differences in the transcriptional response to infection in human populations are under strong genetic influence, dictated by their ancestry and by recent natural selection events.

Highlights

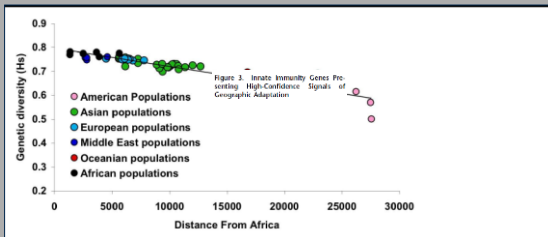
- Thousands of genes show population differences in transcriptional response to infection
- African ancestry is associated with a stronger inflammatory response
- Population differences in immune response are often genetically controlled
- Natural selection contributed to ancestry-associated differences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

Data Resources
GSE65166

Heidecker et al., 2018, Cell 187, 657–669
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https://doi.org/10.1016/j.cell.2018.08.020

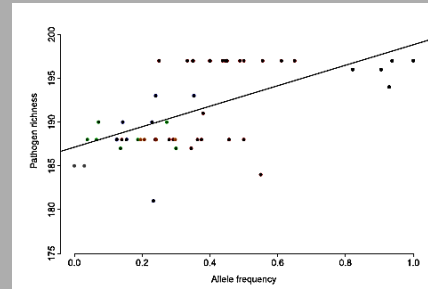
CellPress

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