Host defence against Borrelia
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The 14th LDA Conference
September 12th 2015
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Borreliosis (Lyme disease)

Erythema Migrans
Lyme Disease

Borrelia sensu lato
-Bovis (EU)
-Scapularis (USA)

Lyme disease: after a tick bite

Nature Communications

Ötzi’s DNA reveals health risks and relations.
Ötzi’s genome hints at heart disease, bacterial infection and common ancestry with modern-day Sardinians.

"Ötzi’s genome also hints at other health problems: Zink’s team found almost two-thirds of the genome of "Borrelia burgdorferi", a bacterium that causes Lyme disease."
Infection of Humans with Borrelia

Borrelia infections in The Netherlands

1 Early disease→ EM (75% of patients)
2 Early disseminated phase→ multiple EM, neurologic, and/or cardiac findings, malaise
3 Late (persistent) Lyme disease→ joint swelling and pain, neurologic manifestations, paralysis, chronic arthritis
B. burgdorferi: Arthritis
B. afzelii: Skin disorders; ACA
B. garinii: Neurological disorders; paralysis

How ticks get infected with *Borrelia* spirochetes

*Radboundumc*

*Borrelia* belongs to the family of Spirochetes

Causative agents: *Borrelia burgdorferi* sensu lato (*B. burgdorferi, B. afzelii, B. garinii*)

*Radboundumc*

Dissemination

1. Tick-gut: Osp
2. Tick-human: Salp
3. Human-matrix: Adhesins
4. Human-endothelium: MMPs
5. Human-cell binding: p66 integrin

*Radboundumc*
Escape mechanisms

- Change of coat
- Change of shape?
- Recognition of Borrelia
- Salivary glands
- NFκB
- IL-6
- IFN-γ
- IL-8
- IL-1β
- IL-17
- Innate immune response
- Adaptive immune response
- Pro-/anti-inflammatory cytokines

Innate immunity
Early defense mechanism; fast but unspecific

- Cells of immune system
- Pro-/anti-inflammatory cytokines

Adaptive immunity
Later defense mechanism; slower but specific

- Antibodies
- Memory

Focus of my research

- How does a macrophage know what to eat?
- RECOGNITION
- Surface of Borrelia exists out of building blocks...
- Many types of building blocks...
How is Borrelia recognized?

**Borrelia** bacteria

The host response

Recognition

Cytokine response

PRR-focused research

**PRR** Pattern Recognition Receptor

Secreted PRRs

TLRs

NLRs

PRR-focused research

SNP

silencing

normal

blocking

**PRR** Pattern Recognition Receptor

Secreted PRRs

TLRs

NLRs

**PRR** Pattern Recognition Receptor

Secreted PRRs

TLRs

NLRs
Research using blocking antibodies
Example: PBMC

Recognition by PRRs

Conclusion
*Borrelia* is recognized by TLR1 but not TLR6

Do SNPs in TLRx influence *Borrelia*-derived cytokines?

Link SNPs to clinical outcome

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Clinical signs:
- joint: 20 (2%) 7 (28%)
- back/pain: 20 (6%) 23 (24%)
- heart: 6 (6%) 0 (0%)
- ACA: 6 (6%) 0 (0%)

no Lyme: 62 (62%) 18 (16%)
Lyme in past: 27 (27%) 5 (24%)
possible Lyme: 9 (9%) 1 (4%)
not known: 3 (3%) 1 (4%)
What we demonstrated so far

- Study effect of microbiome and habits on immune responses
  1. N = 500
  2. Lyme patients

Future plans

What can we do with this knowledge?

- In the future: inhibit or prevent infection with Borrelia
- Screen patients on variants to predict clinical outcome
- Personalize treatment strategies

Acknowledgements

*Department of Internal Medicine*
Marije Doppenberg-Oosting
Sanne Brouwer
Kathrin Schnur
Hidde Vrijmoeth
Marnix Kerschmidt
Martijn Jager
Kathleen Karurganis
Jos van der Meer

*Microbiology Department*

*Department of Genetics*

*Department of Laboratory Medicine*

*Harvard/Broad Institute*

http://www.humanfunctionalgenomics.org