



Public Health
England

Lyme disease conference

Overview of Lyme disease pathology and immunology

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Overview

Basics of an infection

The race between man and spirochaete

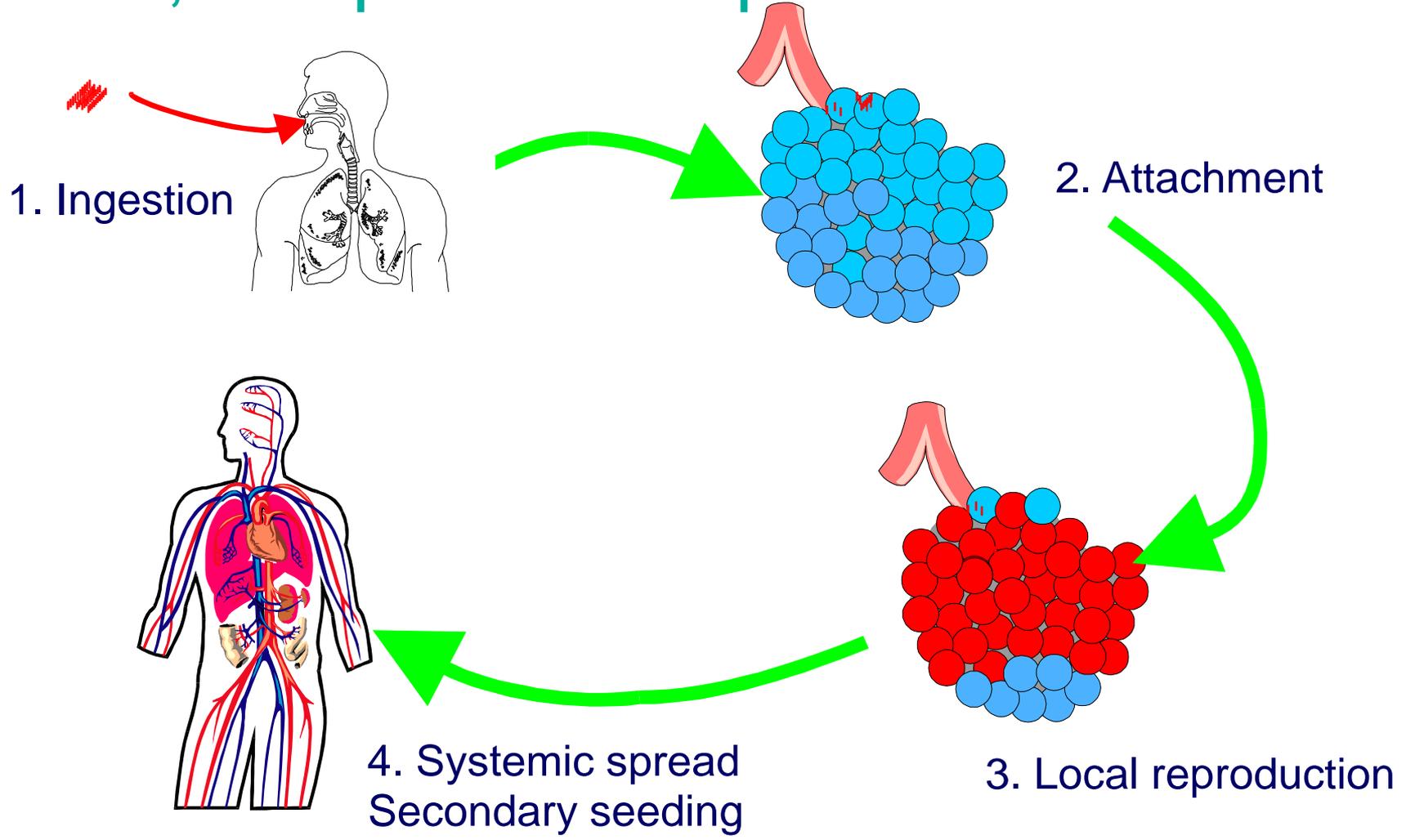
Anatomy of a pathogen: designed to fight

Stepping through the infection process

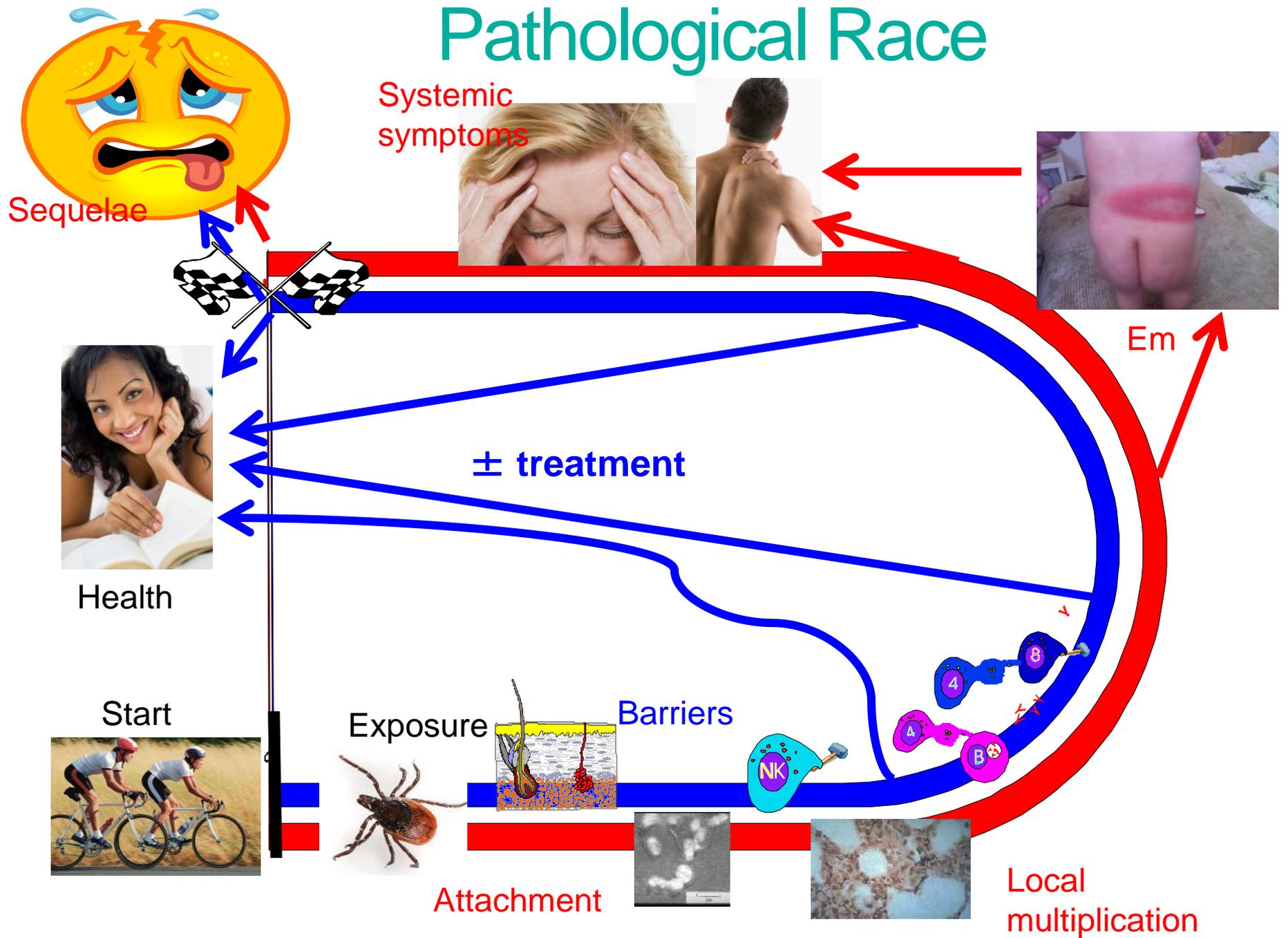
The immune reaction and how to evade it

Individuals and patterns

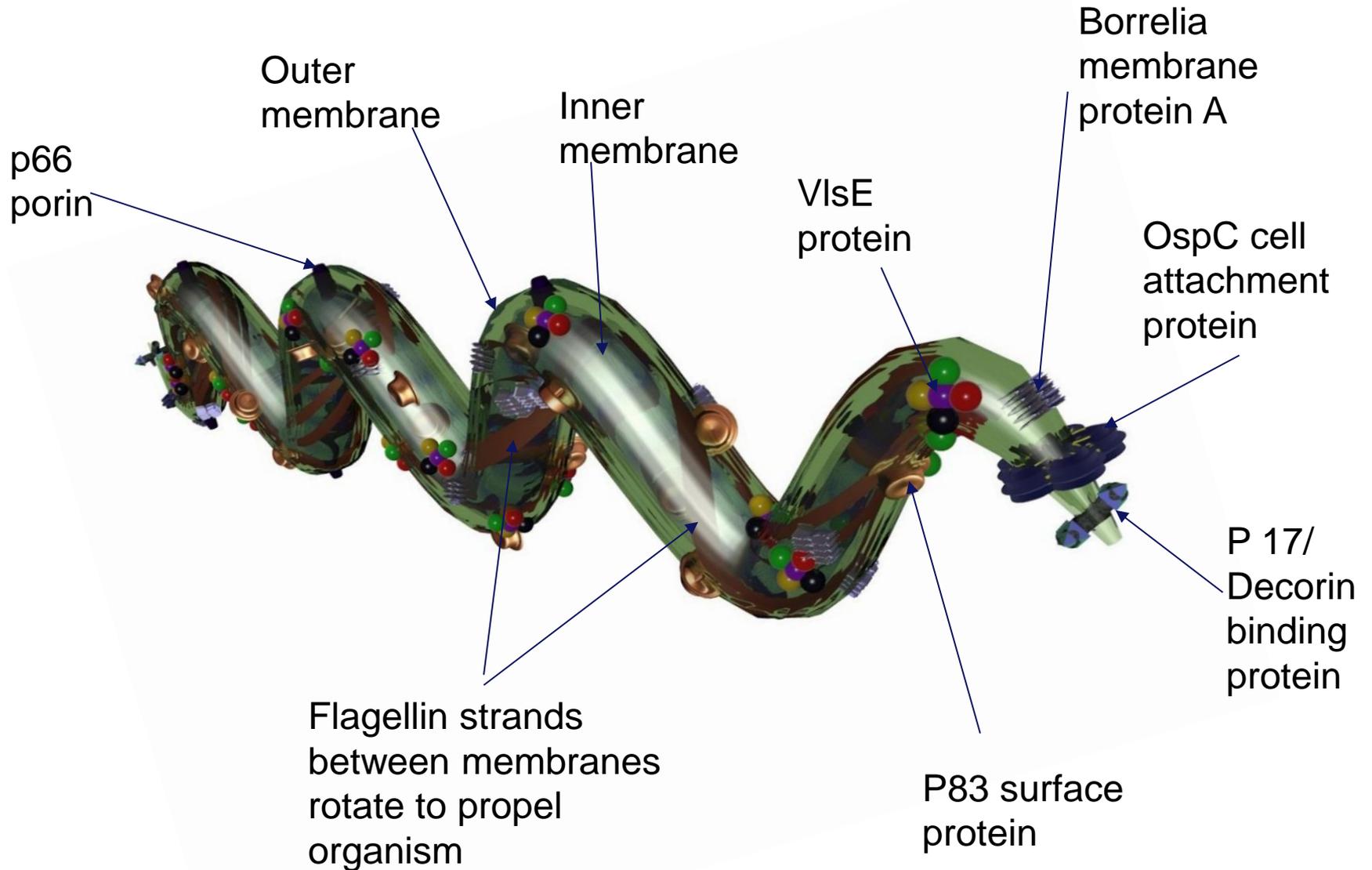
Invasion, multiplication & spread



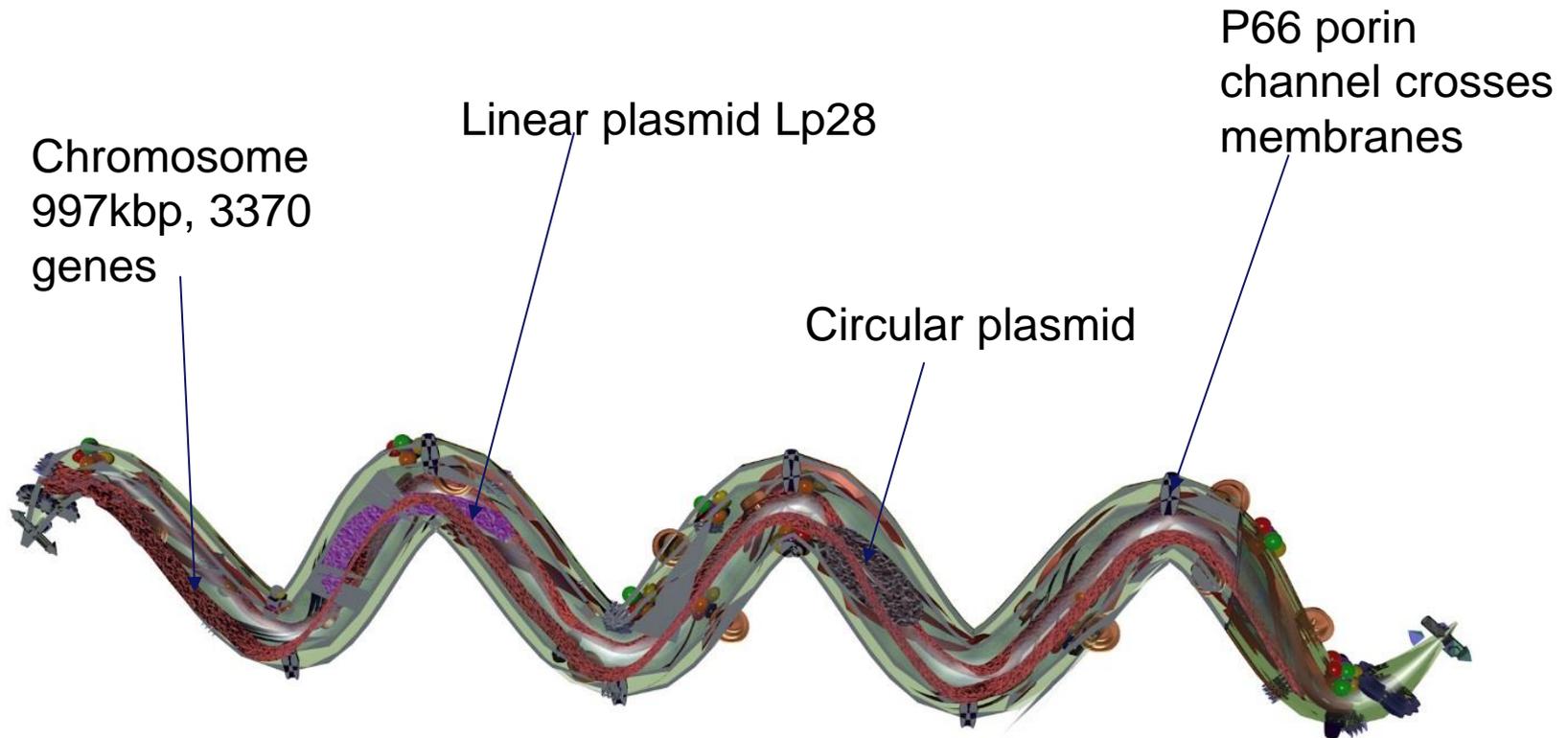
Pathological Race



Anatomy of a professional



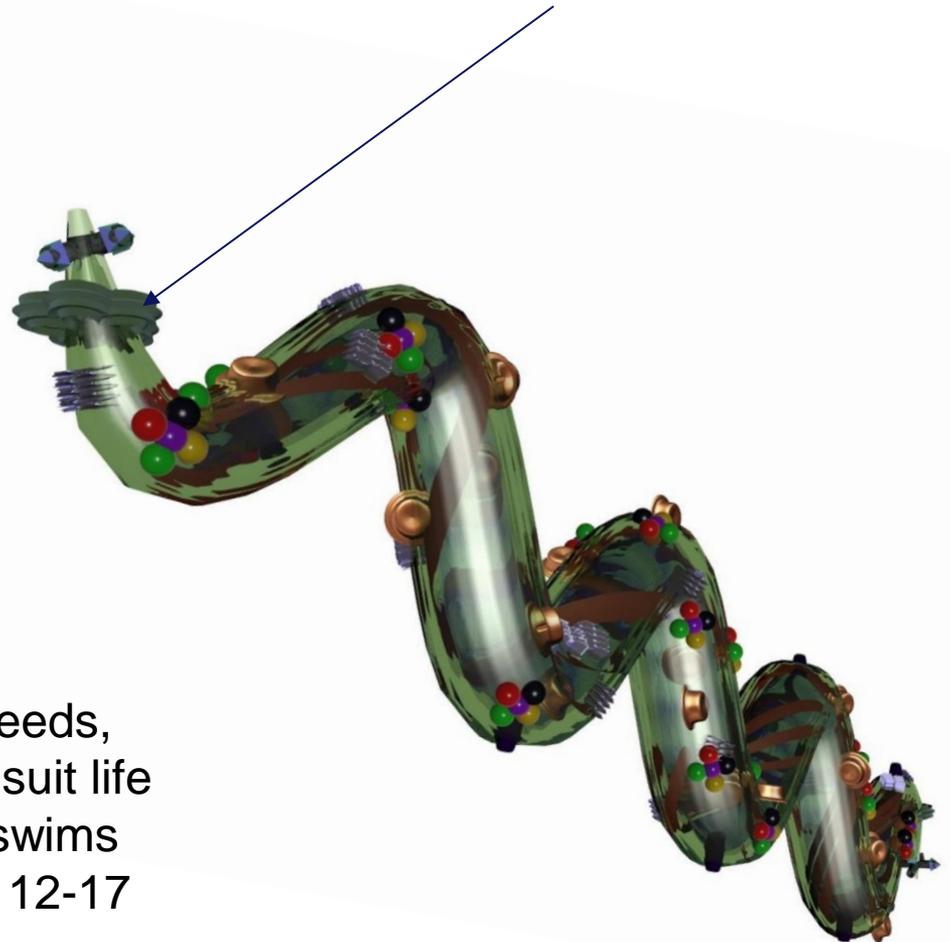
Inside the spirochaete



Borrelia have at least 27 plasmids
which can be exchanged in whole
or part between organisms

In the tick

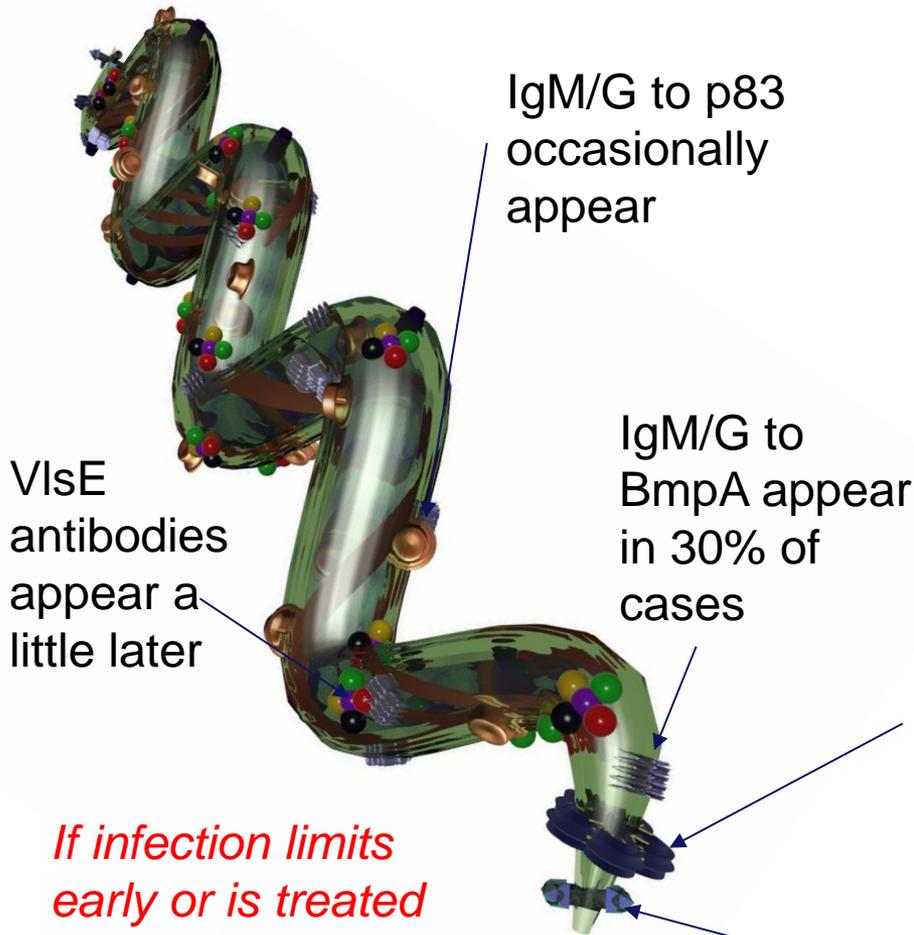
Organism expresses OspA to bind to tick tissue



As blood rushes in when tick feeds, OspA is replaced by Osp C to suit life in mammals and spirochaete swims upwards reaching new host in 12-17 hours

Early infection

Rash may be absent in up to 30% of cases



VlsE antibodies appear a little later

IgM/G to p83 occasionally appear

IgM/G to BmpA appear in 30% of cases

As organism starts to proliferate IgM and then IgG to OspC appear. They are short-lived

Organism can be found in skin biopsy

If infection limits early or is treated antibodies may not have time to develop

Many people develop p17 IgM/G

Disseminated infection

Antibody pattern

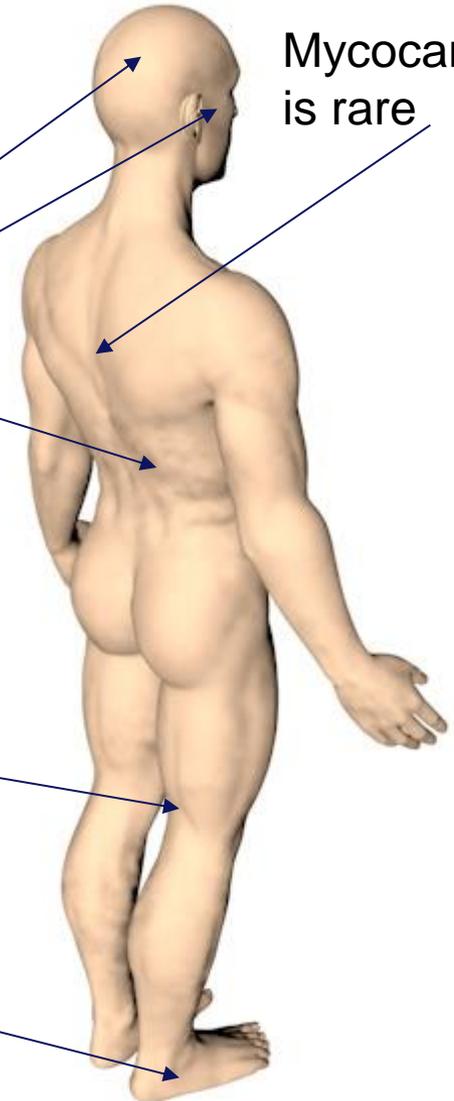
All antibodies may appear
OspC antibodies decline early
IgM slowly disappears leaving variable patterns of IgG responses
Pattern may correlate to species in some cases
VlsE dominates

Neuroborreliosis
Pcr occasionally positive
IgM in CSF

Arthritis
PCR Negative

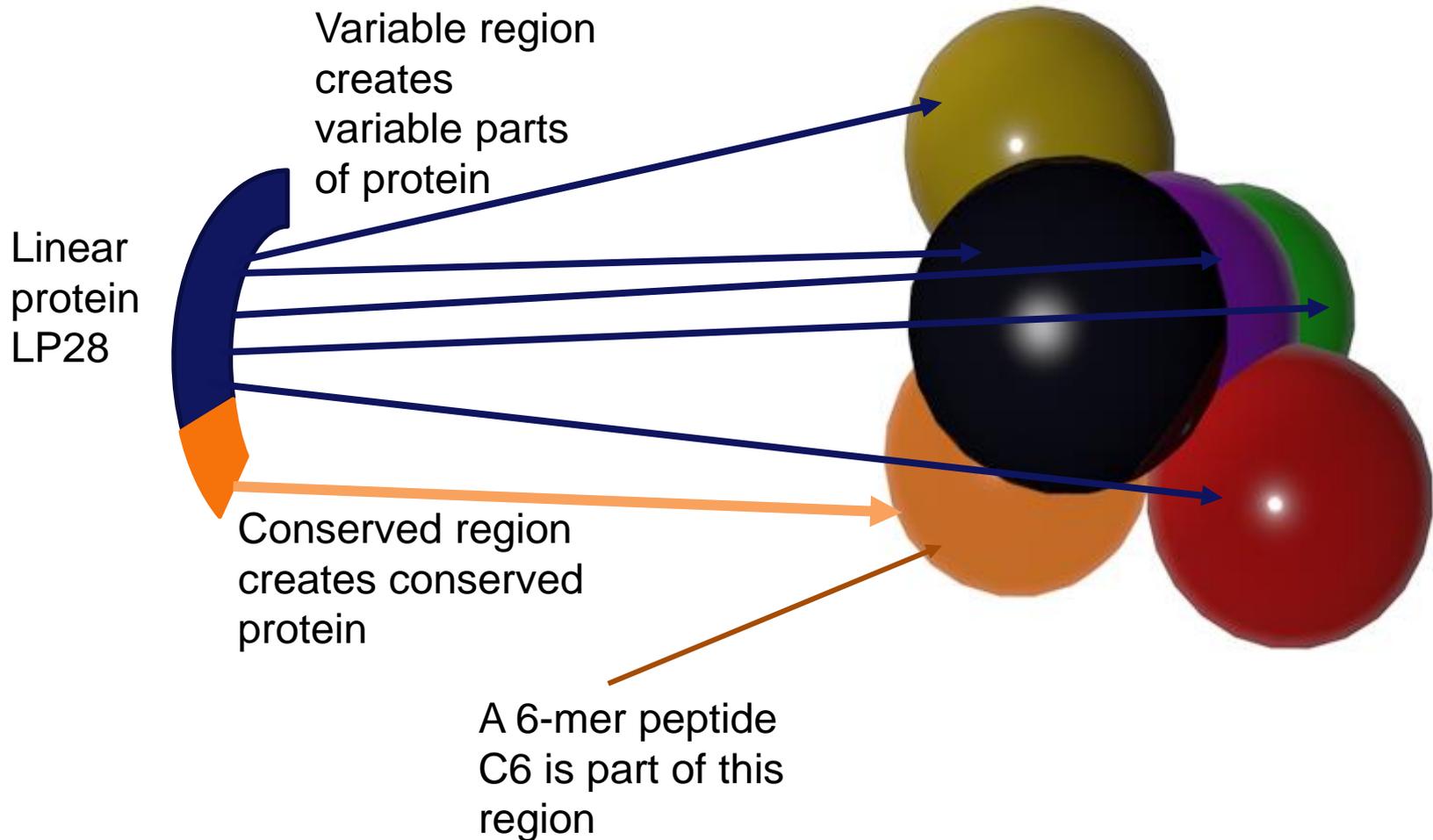
Acrodermatitis
chronicum atrophans
Pcr may be positive

Mycocarditis is rare





Making the VlsE protein



Evading the immune system



Conserved regions stay constant and C6 peptide stimulates antibodies across all variants

As VlsE changes many people are anti-VlsE negative when tested on a single protein

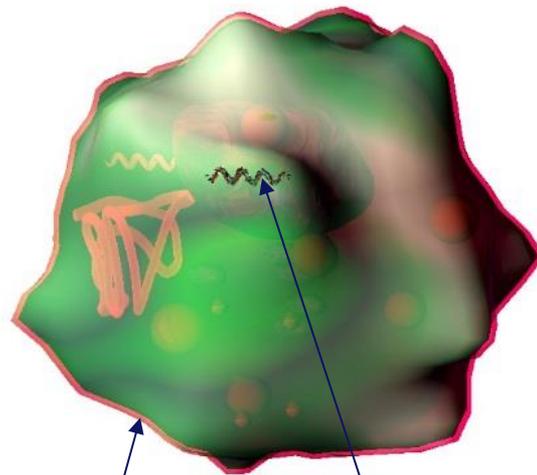
VlsE constantly changes so organism keeps ahead of immune system. At least 15 variants exist



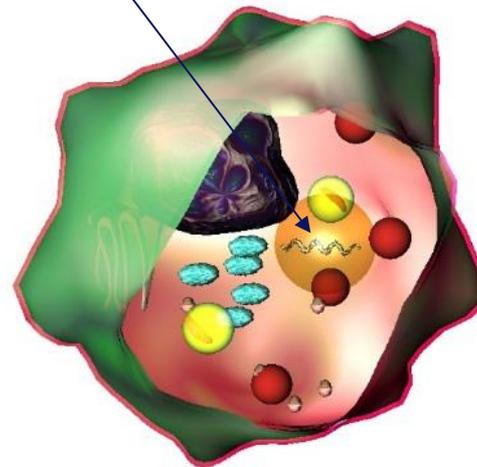
Pattern of antibodies to VlsE epitopes is linked to persistence of symptoms

Antigen presentation

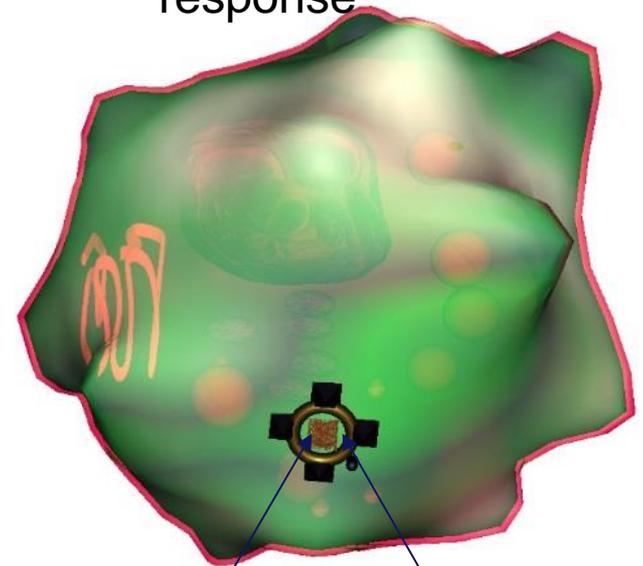
Borrelia in phagosome



Macrophage recognises Borrelia and locks on



Macrophage engulfs Borrelia and processes it into protein fragments



Antigen fragment

MHC and T-cell trigger complex

Antigen is presented on macrophage surface in MHC complex and triggers CD4 T cells to help generate immune response



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Persistent symptoms

Tissue damage

Cf. healing scars, poliomyelitis

On-going immune reaction against self antigens

Cf. Goodpasture's syndrome, Guillain-Barre syndrome, Rheumatoid arthritis

Untreated disease

Re-infection

Research is needed to define each of these



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Summary

Infection with *Borrelia* may:

- Be asymptomatic
- Cause Erythema migrans
- Cause infection with no rash
- Cause disseminated disease
- Abort at any stage

The immune response

- May be abrogated by treatment
- May not appear if disease self-limits early
- Does not protect against re-infection
- Is present in established infection but may be variable



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