De klinische waarde van de C1q bepaling; aandacht voor zowel lage als hoge levels.

Leendert Trouw
Dept Immunohematology and Bloodtransfusion
Overview of the presentation

Introduction on complement and C1q

Low levels of C1q (C1q deficiency)

High levels of C1q (Tuberculosis)

Implications and future directions
The complement system

Classical Pathway
- Immune complexes
- Apoptotic cells

Lectin Pathway
- Carbohydrates
- IgA

Alternative Pathway
- Bacterial surfaces
- LPS
- IgA

C1q → C4b2a → C3 → C3b → C5b-9 (MAC)

MBL → C4b2a → C3bBb

C3H2O → C3bBb

Chemotaxis
- C3a
- C5a

Opsonisation
- C3b

Lysis
- C5b-9 (MAC)
Roles of the complement system

Complement system

Innate immunity
- Opsonization
- Lysis of pathogens
- Chemotaxis
- Inflammation
- Cell activation

Disposal system
- Clearance of immune complexes and apoptotic cells

Adaptive immunity
- Augmentation of antibody response
- Promotion of T-cell response
- Elimination of self-reactive B cells
- Enhancement of immunologic memory
Assembly and functions of C1q

Produced by: Macrophages, Dendritic cells
Serum conc.: 200 μg/ml
Mol Weight: 460 kD

Beurskens Mol Immunol 2015
Gaboriaud Trends Imm 2004
C1q binding to IgG.

A. Fluid phase IgG binding
   - Low avidity binding
     - IgG monomers

B. Solid phase IgG binding
   - High avidity binding
     - IgG hexamer formation

Figure 7:31 The Immune System, 2/e (© Garland Science 2005)

Figure 7:34 part 1 of 2 The Immune System, 2/e (© Garland Science 2005)
Maturation of Dendritic cells abrogates C1q production.

Castellano et al. Blood 2004
## Complement deficiencies and clinical presentation

<table>
<thead>
<tr>
<th>Complement protein</th>
<th>Effects of deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1, C2, C4</td>
<td>Immune-complex disease</td>
</tr>
<tr>
<td>C3</td>
<td>Susceptibility to capsulated bacteria</td>
</tr>
<tr>
<td>C5–C9</td>
<td>Only effect is susceptibility to Neisseria</td>
</tr>
<tr>
<td>Factor D, properdin (factor P)</td>
<td>Susceptibility to capsulated bacteria and Neisseria but no immune-complex disease</td>
</tr>
<tr>
<td>Factor I</td>
<td>Similar effects to deficiency of C3</td>
</tr>
<tr>
<td>DAF, CD59</td>
<td>Autoimmune-like conditions including paroxysmal nocturnal hemoglobinuria</td>
</tr>
</tbody>
</table>

*Figure 9-9 The Immune System, 2/e © Garland Science 2005*
The complement system is involved in the prevention of SLE
The lupus paradox
Michael C. Carroll

Department of Pathology, Harvard Medical School, Boston, Massachusetts 02115, USA. e-mail: mcarroll@warren.med.harvard.edu
C1q deficient mice develop lupus like disease

Homozygous C1q deficiency causes glomerulonephritis associated with multiple apoptotic bodies

Marina Botto¹, Chiara Dell’Agnola¹, Anne E. Bygrave¹, E. Mary Thompson², H. Terence Cook³, Franz Petry⁴, Michael Loos⁴, Pier Paolo Pandolfi⁵ & Mark J. Walport¹
Waste disposal hypothesis
Male, 24 years old

Age 1  Systemic lupus erythematosus
Butterfly rash, sunlight hypersensitivity, ANA, ENA
Male, 24 years old

Age 1  Systemic lupus erythematosus  
Butterfly rash, sunlight hypersensitivity, ANA, ENA

Age 3  Poly-arthritis, oral ulcers, fever/malaise.

Age 7  Frequent upper airway infections, skin infections

Age 19  Staph aureus septicemia - bloedvergiftiging

Age 20  Varicella zoster - gordelroos
C1q deficient patient with SLE

Male, 24 years old

Age 1  Systemic lupus erythematosus
Butterfly rash, sunlight hypersensitivity, ANA, ENA

Age 3  Poly-arthritis, oral ulcers, fever/malaise.

Age 7  Frequent upper airway infections, skin infections

Age 19  Staph aureus septicemia

Age 20  Varicella zoster

Age 24  Nephritis

Class V LN, ‘nearly’ full-house IF

Van Schaarenburg et al. Front Imm 2016
Male, 24 years old

Age 1  Systemic lupus erythematosus
       Butterfly rash, sunlight hypersensitivity, ANA, ENA
Age 3  Poly-arthritis, oral ulcers, fever/malaise.
Age 7  Frequent upper airway infections, skin infections
Age 19 Staph aureus septicemia
Age 20 Varicella zoster
Age 24 Nephritis
Age 24 Neuro-psychiatrical SLE

**NP-SLE** with an inflammatory and ischemic phenotype

Patient presented with low minimal state examination for age and education level. Decreased vision and decreased function of left arm.
Repeatedly low/undetectable CH50 (classical pathway activity)!!
C1q deficient patient with SLE

C1q ELISA

C1q Western blot

Van Schaarenburg et al. Front Imm 2016
C1q deficient patient with SLE

Mutation: Gly>Arg on pos 34 C1qC
Female C1q deficient patient with SLE

Compound heterozygous mutations of C1QC: c.100G>A p.(Gly34Arg); c.205C>T p.(Arg69X).
Infections
Age 0  -  recurring infections
Age 6  -  sepsis caused by *Strep pneumoniae*
Age 12 - herpes zoster infection
Age 18 - hospitalized for infections; *Escheria coli* and candidiasis.

SLE (like disease)
Age 4  -  SLE, many symptoms but no anti-dsDNA.
  SLE treated with immunosuppressives with serious side effects.
  SLE with C1q deficiency; treatment with Fresh Frozen Plasma, also side effects.

Cerebral involvement
Age 14  -  she was hospitalized with cerebral problems, EEG confirmed lesions.
Age 18  -  repeated episodes of anxiety and difficulty in speech.
C1q def. and Neuro-Psychiatrical problems
NP-SLE in C1q def >20% and in wt SLE <5%
**Complement and onset of SLE**

Human genetic deficiencies

- C1q - 80% SLE
- C4 - 70% SLE
- C2 - 10% SLE
- C3 - 5% SLE

The complement system is involved in the prevention of SLE.
C1q deficient patient with no SLE

Male
7 years old

Recurrent infections of the airways
Osteomyelitis of the tibia
Pneumococcal meningitis
No signs of autoimmunity

Splice site mutation within $C1qB$

Van Schaarenburg et al. Immunobiol 2014
C1q deficiency

Systemic lupus erythematosus

From Wikipedia, the free encyclopedia

"Lupus" redirects here. For other uses, see Lupus (disambiguation).

Systemic lupus erythematosus (stəmətik ləˈpəs ɪˈtʃi məˈriːəsəs), often abbreviated as SLE or lupus, is a systemic autoimmune disease (or autoimmune connective tissue disease) that can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage. It is both a type II and a type III hypersensitivity reaction in which bound antibody-antigen pairs (immune complexes) precipitate and cause a further immune response.

SLE most often harms the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system. The course of the disease is unpredictable, with periods of illness (called flares) alternating with remissions. The disease occurs nine times more often in women than in men, especially in women in child-bearing years ages 15 to 35, and is also more common in those of non-European descent.[3][4]

There is no cure for SLE. It is treated with immunosuppression, mainly with cyclophosphamide, corticosteroids and other immunosuppressants. SLE can be fatal. The leading cause of death is from cardiovascular disease due to accelerated atherosclerosis. Survival for people with SLE in the United States, Canada, and Europe has risen to approximately 95% at five years, 90% at 10 years, and 78% at 20 years,[5] and now approaches that of matched controls without lupus.

Childhood systemic lupus erythematosus generally presents between the ages of 3 and 15, with girls outnumbering boys 4:1, and typical skin manifestations being butterfly eruption on the face and photosensitivity.[1]

Lupus is Latin for wolf. In the 18th century, when lupus was just starting to be recognized as a disease, it was thought that it was caused by the bite of a wolf.[6] This may have been because of the distinctive rash characteristic of lupus. (Once full-blown, the round, disk-shaped rashes heal from the inside out, leaving a bite-like imprint.)

A number sign (#) is used with this entry because C1q deficiency can be caused by...
Problem:

Most papers only report on the moment of identification of C1q deficiency and the mutation involved, but no follow up.
C1q deficiency

Questionnaire on life expectancy and complications

Gender
Age of diagnosis
Parents related?
SLE (Diagnosis)
Still alive? (No, cause of death)
Received Plasma
Stem cell transplantation consideration
Quality of life
Age of diagnosis vs current age
### Country of origin and Number of patients

<table>
<thead>
<tr>
<th>Country of origin</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1</td>
</tr>
<tr>
<td>Greenland</td>
<td>3</td>
</tr>
<tr>
<td>Iraq</td>
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<tr>
<td>Kosovo</td>
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</tr>
<tr>
<td>Netherlands</td>
<td>7</td>
</tr>
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<td>Pakistan</td>
<td>7</td>
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<td>Sweden</td>
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</tr>
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<td>Sudan</td>
<td>2</td>
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<td>Tunisia</td>
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<td>Turkey</td>
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<td>United Kingdom</td>
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<td>USA</td>
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### C1q deficient individuals

<table>
<thead>
<tr>
<th>C1q deficient individuals</th>
<th>Number of cases</th>
<th>Percentage of cases</th>
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</thead>
<tbody>
<tr>
<td>Sex M/F</td>
<td>22/23</td>
<td>49/51</td>
</tr>
<tr>
<td>Deceased Y/N</td>
<td>9/36</td>
<td>20/80</td>
</tr>
<tr>
<td>Deceased Males</td>
<td>3</td>
<td>14</td>
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<tr>
<td>Deceased Females</td>
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<td>26</td>
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### Clinical presentation

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<td>SLE Y/N</td>
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<td>80/20</td>
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<tr>
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<td>20</td>
<td>44</td>
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<tr>
<td>Only Infections</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Both SLE + Infections</td>
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<td>36</td>
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<tr>
<td>No symptoms</td>
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<td>7</td>
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### Therapy

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<tr>
<td>FFP given</td>
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<td>31</td>
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<tr>
<td>HSCT performed</td>
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<td>7</td>
</tr>
<tr>
<td>HSCT considered</td>
<td>10</td>
<td>22</td>
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</tbody>
</table>

Van Schaarenburg et al. J Autoimmun. 2015
C1q deficient patients

Age of diagnosis vs. current age

Van Schaarenburg et al. J Autoimmun. 2015
Outcome of disease

Infections

Quality of life

The median quality of life is 7

Van Schaarenburg et al. J Autoimmun. 2015
## Therapy options

<table>
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<tr>
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<tr>
<td>HSCT considered</td>
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<td>22</td>
</tr>
</tbody>
</table>

Van Schaarenburg et al. J Autoimmun. 2015
Bone marrow transplantation in mice restores C1q levels and reduces autoimmunity

Reconstitution of the Complement Function in C1q-Deficient (C1qa<sup>−/−</sup>) Mice with Wild-Type Bone Marrow Cells<sup>1</sup>

Franz Petry,<sup>2,a</sup> Marina Botto,<sup>7</sup> Rafaela Holtappels,<sup>2</sup> Mark J. Walport,<sup>7</sup> and Michael Loos<sup>a</sup>

Restoration of C1q levels by bone marrow transplantation attenuates autoimmune disease associated with C1q deficiency in mice

Josefina Cortes-Hernandez<sup>1</sup>, Liliane Fossati-Jimack<sup>1</sup>, Franz Petry<sup>2</sup>, Michael Loos<sup>2</sup>, Shozo Izui<sup>3</sup>, Mark J. Walport<sup>1</sup>, H. Terence Cook<sup>4</sup> and Marina Botto<sup>1</sup>

Petry et al. J. Immunol 2001

HSCT in humans can restore C1q production

Successful cure of C1q deficiency in human subjects treated with hematopoietic stem cell transplantation

Peter D. Arkwright, MD, PhD, Philip Riley, MD, Stephen M. Hughes, MD, PhD, Hana Alachkar, MD, Robert F. Wynn, MD

**TABLE I. Changes in complement and autoantibody titters after matched sibling bone marrow transplantation for C1q deficiency**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal range</th>
<th>Before BMT</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>12</th>
<th>16</th>
<th>24</th>
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<tbody>
<tr>
<td>Leukocyte engraftment</td>
<td></td>
<td>1.50-6.00</td>
<td>1.50</td>
<td>0.05</td>
<td>3.85</td>
<td>5.15</td>
<td>3.09</td>
<td>1.61</td>
<td>3.20</td>
</tr>
<tr>
<td>Neutrophils (× 10^9/L)</td>
<td></td>
<td>1.50</td>
<td>0.05</td>
<td>3.85</td>
<td>5.15</td>
<td>3.09</td>
<td>1.61</td>
<td>3.20</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes (× 10^9/L)</td>
<td></td>
<td>1.50-4.50</td>
<td>1.62</td>
<td>0.07</td>
<td>0.25</td>
<td>0.40</td>
<td>0.12</td>
<td>0.29</td>
<td>0.46</td>
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<tr>
<td>Monocytes (× 10^9/L)</td>
<td></td>
<td>0.10-1.50</td>
<td>0.20</td>
<td>0.54</td>
<td>0.65</td>
<td>0.36</td>
<td>0.21</td>
<td>0.23</td>
<td>0.22</td>
</tr>
<tr>
<td>CD3 (× 10^9/L)</td>
<td></td>
<td>622-2402</td>
<td>761</td>
<td>32</td>
<td>36</td>
<td>233</td>
<td>96</td>
<td></td>
<td></td>
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<td>Complement</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CH50 (U/mL)</td>
<td>392-1019</td>
<td>&lt;275</td>
<td>&lt;275</td>
<td>588</td>
<td>838</td>
<td>967</td>
<td>978</td>
<td>659</td>
<td></td>
</tr>
<tr>
<td>C1q (mg/L)</td>
<td>70-140</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>&lt;75</td>
<td>70</td>
<td>69</td>
<td>76</td>
<td></td>
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<tr>
<td>Autoantibodies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS-A60 (Ro) AI</td>
<td>9.0-9.9</td>
<td>&gt;8.0</td>
<td>&gt;8.0</td>
<td>&gt;8.0</td>
<td>&gt;8.0</td>
<td>&gt;8.0</td>
<td>5.2</td>
<td>4.0</td>
<td>3.3</td>
</tr>
<tr>
<td>SS-B (La) AI</td>
<td>9.0-9.9</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
</tr>
<tr>
<td>dsDNA (U/mL)</td>
<td>9.0-9.9</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Anti-cardiolipin IgG (GPLU)</td>
<td>9.5-7.7</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>12.0</td>
<td>6.9</td>
</tr>
</tbody>
</table>

Arkwright et al. J. Allergy Clin Immunol 2014
Unfortunately, the boy developed severe acute GVHD and died 4 months after transplantation due to intracerebral haemorrhage and multiorgan failure.

Olsson et al. Transplantation 2016
Conclusions C1q deficiency

Absence of early classical components is associated with SLE

Remarkable differences between deficient individuals

Not only SLE but also infections very prominent risk in CP deficiency

Neurological problems are prominent

HSCT now tested as a therapeutical option in C1q deficiency
Most SLE patients are NOT genetically deficient

Complement activation contributes to inflammation and tissue damage in ‘conventional’ SLE patients
C1q low in SLE but what about C1q high?
C1q low in SLE but what about C1q high?

40,000 C1q measurements in routine diagnostics

Time (1999 - 2018)
C1q low in SLE but what about C1q high?
C1q low in SLE but what about C1q high?
Tuberculosis
Mycobacterium tuberculosis (Mtb) infection:

1/4 - 1/3 of the world population is infected

> 10,4 million people develop TB disease

~ 1,7 million die every year of TB (incl. 370,000 HIV coinfected)
**Background**

*Mycobacterium tuberculosis*

**Phases:**  
- Active disease  
- Latent infected TB

Biomarkers do not discriminate!!

Collaboration with Simone Joosten, LUMC
C1q expression in PBMCs in several large studies

Lubbers et al Front Immunol. 2018
C1q expression in PBMCs in several large studies

Lubbers et al. Front Immunol. 2018
C1q protein levels are increased in active TB

Lubbers et al. Front Immunol. 2018
Increased C1q levels normalize following treatment

Lubbers et al Front Immunol. 2018
C1q levels normalize following successful treatment

E

F

C1q µg/ml

CTRL LTBI TB Past TB

<0.0001 <0.0001 <0.0001

<0.0001

<0.0650

TB 1 2 6 TB contacts

months of treatment

Lubbers et al Front Immunol. 2018
Increased C1q levels are rather specific for active TB

Differential diagnoses
Discrimination of active TB vs rest using C1q serum levels

B

C

<table>
<thead>
<tr>
<th>TB vs</th>
<th>AUC</th>
<th>Std Error</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTRL</td>
<td>0.841</td>
<td>0.027</td>
<td>[0.789 ; 0.893]</td>
</tr>
<tr>
<td>LTBI</td>
<td>0.765</td>
<td>0.033</td>
<td>[0.699 ; 0.830]</td>
</tr>
<tr>
<td>PastTB</td>
<td>0.789</td>
<td>0.034</td>
<td>[0.722 ; 0.856]</td>
</tr>
<tr>
<td>Leprosy</td>
<td>0.749</td>
<td>0.036</td>
<td>[0.680 ; 0.819]</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>0.693</td>
<td>0.044</td>
<td>[0.607 ; 0.779]</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.925</td>
<td>0.020</td>
<td>[0.889 ; 0.965]</td>
</tr>
<tr>
<td>All</td>
<td>0.799</td>
<td>0.024</td>
<td>[0.752 ; 0.845]</td>
</tr>
</tbody>
</table>
C1q also present in the lungs of active TB

Lubbers et al Front Immunol. 2018
Non-human primates – TB – C1q

Collaboration with Karin Dijkman at the BPRC in Rijswijk
Non-human primate TB model in Macaques.
BCG vaccination trial with post-hoc analysis of sera and BAL.

A

B

Weeks post challenge

Relative C1q

Absorbance 415nm

BAL pre

BAL AUT
C1q mRNA’s are upregulated in PBMCs, indicating indirect stimulation

C1q protein levels are increased in patients with active TB compared to controls

Non human primates show similar increase in C1q after experimental TB challenge

Lubbers et al. *Frontiers in Immunology* 2018
C1q mRNA’s are upregulated in PBMCs, indicating indirect stimulation

C1q protein levels are increased in patients with active TB compared to controls

Non human primates show similar increase in C1q after experimental TB challenge

But why would a pathogen want more C1q?
C1q mRNA's are upregulated in PBMCs, indicating indirect stimulation. C1q protein levels are elevated significantly in patients with active TB compared to relevant controls. Non-human primates show a similar increase in C1q after experimental challenge.

Why would a pathogen want more C1q?

Ling et al. Science 2018

**C1q restrains autoimmunity and viral infection by regulating CD8^+ T cell metabolism**

Guang Sheng Ling, Greg Crawford, Norzawani Buang, Istvan Bartok, Kunyuan Tian, Nicole M. Thielens, Isabelle Bally, James A. Harker, Philip G. Ashton-Rickardt, Sophie Rutschmann, Jessica Strid, Marina Botto*  

Deficiency of C1q, the initiator of the complement classical pathway, is associated with the development of systemic lupus erythematosus (SLE). Explaining this association in terms of abnormalities in the classical pathway alone remains problematic because C3 deficiency does not predispose to SLE. Here, using a mouse model of SLE, we demonstrate that C1q, but not C3, restrains the response to self-antigens by modulating the mitochondrial metabolism of CD8^+ T cells, which can themselves propagate autoimmunity. C1q deficiency also triggers an exuberant effector CD8^+ T cell response to chronic viral infection leading to lethal immunopathology. These data establish a link between C1q and CD8^+ T cell metabolism and may explain how C1q protects against lupus, with implications for the role of viral infections in the perpetuation of autoimmunity.
Hypothesis

TB is using C1q as an immune evasion strategy

But increased C1q would mean more classical pathway
Unless there is also enhanced complement inhibition
Endogenous complement inhibitors

Classical pathway
- C1q & C1r/C1s
- C1-INH
- C4BP
- Factor I
- CR1 (CD35)
- MCP (CD46)
- DAF (CD55)

Lectin pathway
- MBL & MASP
- C1-INH
- MASP19
- MASP44

Alternative pathway
- C3(H2O)

Terminal pathway
- C5a
- C3bBbC3b
- C5b
- C5b-9
- CD59
- Vitronectin
- Clusterin

FHR-1

C4BP
- Factor H
- FHL-1
- DAF (CD55)
Expression of complement inhibitors in active TB
C1-INH protein levels

A - Italy
B - Korea
C - The Gambia
D - South Africa

Lubbers et al submitted 2020
C1-INH in active TB versus differential diagnoses

A

B

C

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>Std Error</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>CTRL</td>
<td>0.789</td>
<td>0.032</td>
<td>[0.726; 0.852]</td>
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<tr>
<td>LTBI</td>
<td>0.669</td>
<td>0.038</td>
<td>[0.594; 0.744]</td>
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<td>Leprosy</td>
<td>0.791</td>
<td>0.034</td>
<td>[0.725; 0.857]</td>
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<td>Sarcoidosis</td>
<td>0.713</td>
<td>0.044</td>
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<td>Pneumonia</td>
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<td>0.032</td>
<td>[0.772; 0.900]</td>
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<td>ALL</td>
<td>0.747</td>
<td>0.029</td>
<td>[0.690; 0.804]</td>
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</table>
C1-INH levels normalize after successful treatment

A. Italy Treatment

B. Gambia Treatment

Graphs showing C1-INH levels over different time periods and conditions.
C1q and C1-INH

Lubbers et al submitted 2020
C1q and C1-INH as biomarkers for active TB

- Control (n=92):
  - Not increased
  - C1q
  - C1-INH
  - C1q+C1-INH

- Gambia Contacts (n=50):
  - Not increased
  - C1q
  - C1-INH
  - C1q+C1-INH

- TB Gambia (n=50):
  - Not increased
  - C1q
  - C1-INH
  - C1q+C1-INH

**Score** | **AUC** | **95% CI** | **Sensitivity** | **Specificity**
--- | --- | --- | --- | ---
C1q | 0.68 | [0.57 ; 0.79] | 48% | 88%
C1-INH | 0.75 | [0.65 ; 0.85] | 56% | 94%
C1q+C1-INH | 0.66 | [0.55 ; 0.77] | 36% | 96%
C1-INH only |  |  |  |  |
C1q only |  |  |  |  |
C1q+C1-INH | 0.77 | [0.67 ; 0.87] | 68% | 86%
Conclusions

C1q expression and protein levels are increased in active TB vs latent disease

C1-INH, the inhibitor of C1q, is also increased in active TB

Together C1q levels and C1-INH levels are a reasonable biomarker for active TB

Upregulation of both proteins is suggesting immune escape mechanisms

Main message:
C1q suppresses T cell activity

Main message:
C1q suppresses Th-17 activity and stimulates T-reg function


JCI Insight. 2019 May 21;5.
Future directions

How is the local TB infection driving systemic C1q / C1-INH levels?

Do other intracellular pathogens use the same mechanism?

What is the relative contribution of C1q on the immune response to TB?

How does C1q impact on the (adaptive) immune system?
Both ends of the spectrum are informative!!

Bacterial immune escape

SLE

TB

Neuro-psychiatrical problems
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COMPLEMENT

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