Webinar: Update on SARS-CoV-2

May 27th, 2020

The disease looked at by the immunologist

Arnaud Marchant
Institute for Medical Immunology
Université libre de Bruxelles
Immunology of SARS-CoV-2 infection: current knowledge

- Pathogenesis of COVID-19: role of inflammatory response
- Therapeutic interventions targeting the immune system
- Immunity induced by SARS-CoV-2 infection
- Targets for vaccine development
COVID-19 as an inflammatory disease

No symptom  Mild symptoms (cough, anosmia,..)  Severe symptoms (severe hypoxia,..)  Critical symptoms (ARDS,..)

Blood markers of disease severity: cytokines, chemokines C-Reactive Protein Fibrin degradation products

Mononuclear cell infiltrate of the lung

Ackermann, NEJM, 2020
Control of SARS-CoV-2 infection and immunopathology

- Alveolar macrophages recognize and phagocytose apoptotic cells.
- Neutralizing antibody binds and inactivates virus.
- CD4+ T cell mediates efficient immune response.
- Healthy immune response:
  - Infected cells rapidly cleared
  - Virus inactivated by neutralizing antibodies
  - Minimal inflammation and lung damage
- Vzirui Tay, Nat Rev Immunol, 2020
Control of SARS-CoV-2 infection and immunopathology

Healthy immune response
- Infected cells rapidly cleared
- Virus inactivated by neutralizing antibodies
- Minimal inflammation and lung damage

Dysfunctional immune response
- Excessive infiltration of monocytes, macrophages and T cells
- Systemic cytokine storm
- Pulmonary oedema and pneumonia
- Widespread inflammation and multi-organ damage

Alveolar macrophages recognize and phagocytose apoptotic cell

CD4+ T cell mediates efficient immune response

CD8+ T cell recognizes and eliminates infected cells

Neutralizing antibody binds and inactivates virus

No virus release

FCN1+ macrophage

T cell

Monocyte

Cytokine storm (IL-6, IP-10, IFNγ, IL-2, IL-10, G-CSF, MIP1α, TNF)

Non-neutralizing antibody may cause ADE of infection

Leakage caused by vascular permeability

Vzirui Tay, Nat Rev Immunol, 2020
Role of type I interferon response

Coronaviruses interfere with type 1 interferon responses

Potential impact of kinetics and magnitude of interferon response

Prompt and efficient response: viral control

Delayed response: viral replication

Delayed and exacerbated response: immunopathology

Vabret, Immunity, 2020
Macrophage hyperactivation: origin and role

- Organs are infiltrated with activated macrophages
- Macrophages are potentially activated by multiple signals
- They contribute to the cytokine storm

Merad, Nat Rev Immunol, 2020
Coagulopathy: role of endothelial cells and macrophages

- Severe disease is associated with intravascular coagulation and tissue necrosis
- Potential interplay between endothelial cells and macrophages

Ackermann, NEJM, 2020

Merad, Nat Rev Immunol, 2020
Severe COVID-19 is associated with:

- Lymphopenia: recruitment to organs and depletion (AICD?)
- Potentially exhausted T cells
- IL-6-producing T cells
- Reduced regulatory T cell functions
Immune-based therapeutic interventions

- Immune modulation by chloroquine
- Anti-cytokine antibodies
- Antibody-based therapies
Immunity induced by SARS-CoV-2 infection

- Antibodies induced 1 to 2 weeks after onset of symptoms
- Severe disease associated with high titers of antibodies (pathogenic role?)
- B lymphocyte memory may be short-lived. Could be compensated by T cell memory
- Quality and duration of immunity against re-infection and carriage is unknown
Targets for vaccines against SARS-CoV-2

Neutralizing antibodies
Targets for vaccines against SARS-CoV-2

Neutralizing antibodies

Cytotoxic T lymphocytes
Targets for vaccines against SARS-CoV-2

Neutralizing antibodies

Cytotoxic T lymphocytes

Live attenuated
Inactivated
Recombinant subunits + adjuvants
Recombinant viral vectors
Nucleic acids
Targets for vaccines against SARS-CoV-2

- Neutralizing antibodies
- Cytotoxic T lymphocytes

Pathogen-agnostic immunity

Live attenuated
Inactivated
Recombinant subunits + adjuvants
Recombinant viral vectors
Nucleic acids

- Live vaccine, e.g., BCG
- Monocyte
- TLRs
- CD14
- Th1 polarizing cytokines
- Reactive oxygen species
Immunology of SARS-CoV-2 infection: take home messages

- Strong evidence for a role of immunopathology in severe COVID-19
- Dual role for macrophages, T lymphocytes and antibodies
- Determinants of severe disease are unknown (relation with risk factors?)
- Potential for therapeutic interventions targeting the immune system
- Humoral immunity induced by SARS-CoV-2 infection may be short lived, at least in some patients
- Targets for vaccine development: - neutralizing antibodies
  - role of cytotoxic T cells?
  - no disease enhancement
  - impact on carriage?