Introduction to the Webinar "Detecting Predictive Biomarkers for Severe COVID-19"

Predictive Factors for COVID-19 Severity

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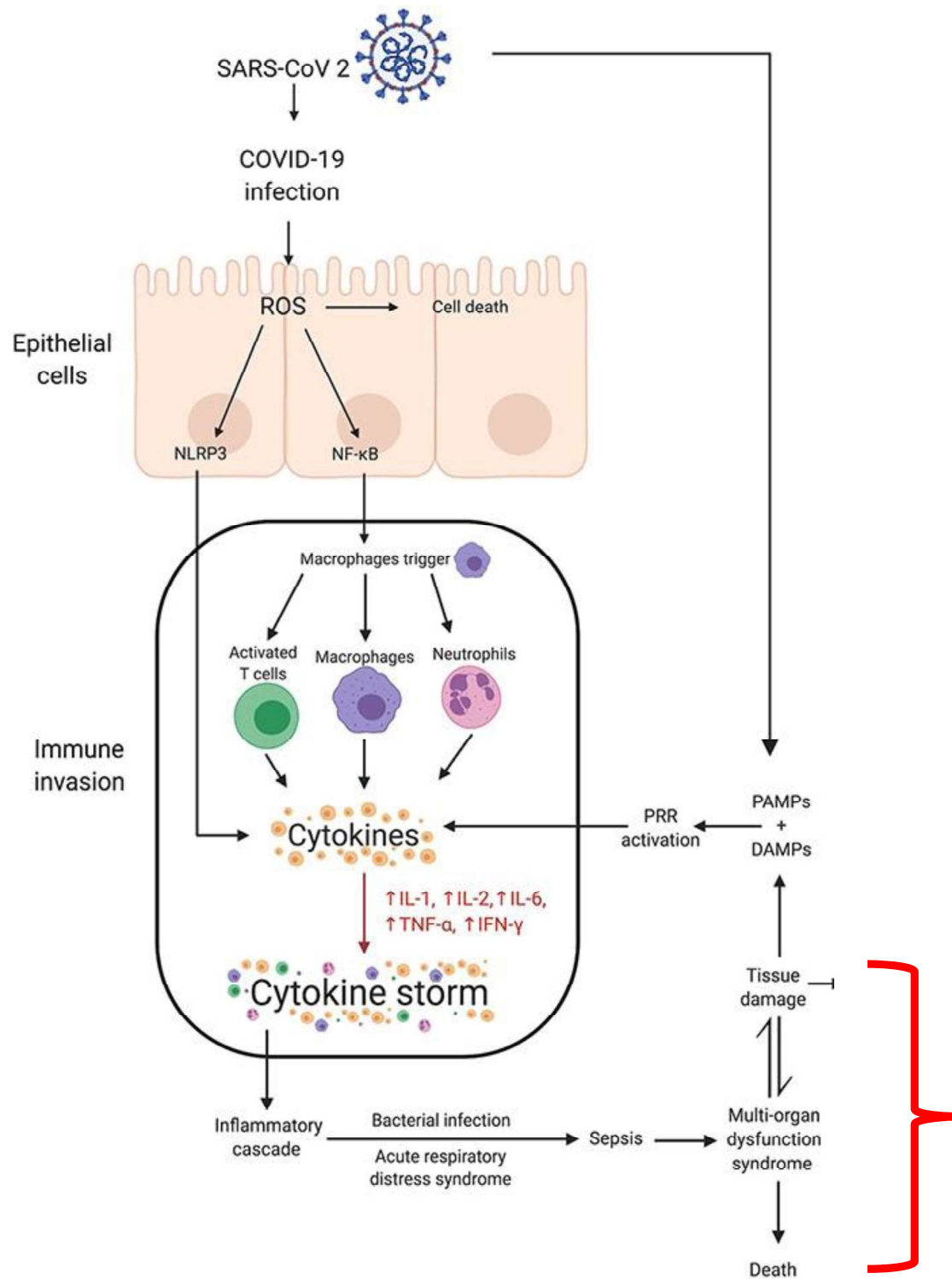**visiting fellow**
at JICA Ogata Research Institute
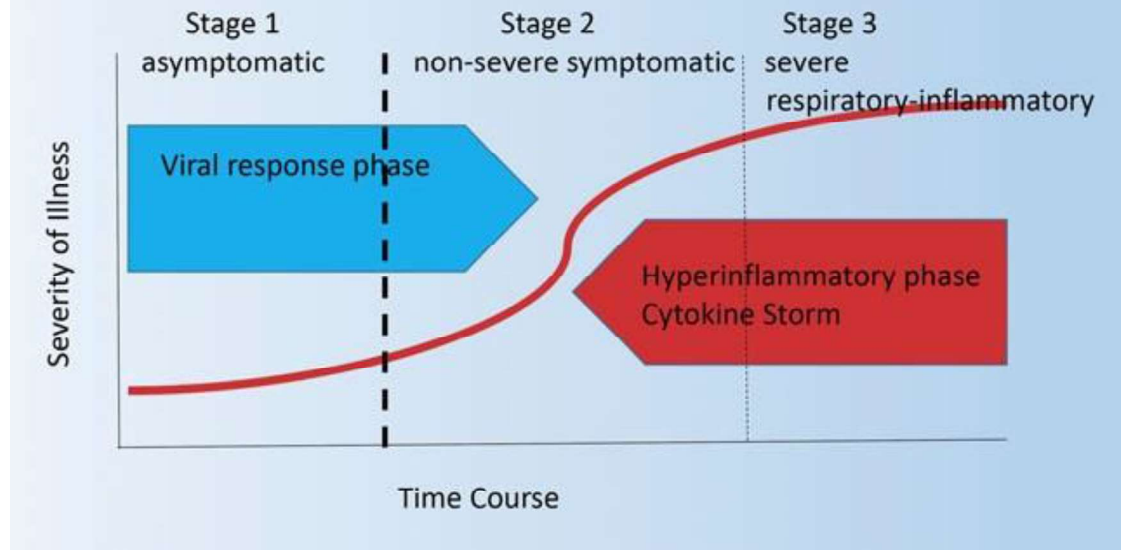
Generally, it is said that:
➢ Around 20~30 % of infected cases need to be hospitalized.
➢ About 20% of hospitalized cases require intensive cares.

Among asymptomatic cases/ cases with mild symptoms, there are:
➢ Sudden death cases
➢ Rapidly deteriorating case

So, it is very critical to detect these cases with sever conditions in the very early stages.

SARS-CoV 2

COVID-19 infection

Epithelial cells

ROS → Cell death

NLRP3   NF-κB

Immune invasion

Macrophages trigger

Activated T cells   Macrophages   Neutrophils

Cytokines

↑IL-1, ↑IL-2, ↑IL-6, ↑TNF-α, ↑IFN-γ

Cytokine storm

PRR activation

PAMPs + DAMPs

Tissue damage

Inflammatory cascade   Bacterial infection   Sepsis   Multi-organ dysfunction syndrome
Acute respiratory distress syndrome

Death

Bhaskar et al.: https://www.frontiersin.org/articles/10.3389/fimmu.2020.01648/full

Possible risk factors/markers related to severity/mortality due to COVID-19

➤ Demographic factors/ clinical conditions

- Sex: Male
- Aging: More than 70 years old
- Co-morbidity with Heart disease, DM, Dyslipidemia, COPD etc.

➤ General laboratory markers (examples)
- Factors related to inflammation
  - Leucocytes/Lymphocytes
  - CRP (C Reactive protein)
  - Procalcitonin   etc.

- Factors related to coagulopathy
  - Platelet
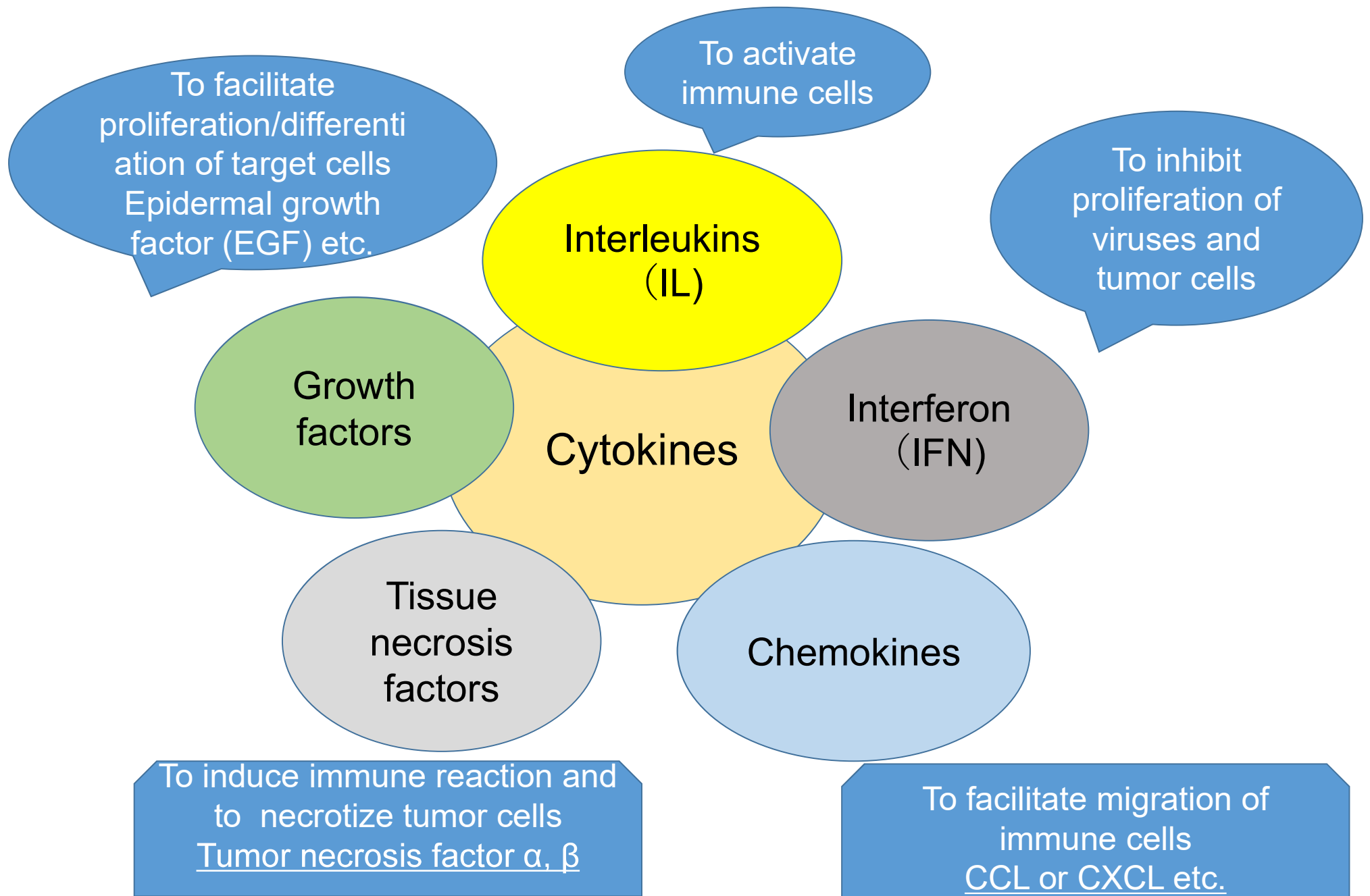 - D-dimer   etc.

- Factors related to tissue damage
  - Lactate dehydrogenase (LDH)
  - Troponin
  - eGFR (estimated glomerular filtration rate)   etc.

☐ Kermali M *et al*. The role of biomarkers in diagnosis of COVID-19 - A systematic review. *Life Sci* 2020;254:117788.
☐ Hodges G et al: https://bmjopen.bmj.com/content/10/12/e041295

Classification of cytokines (example)

To activate immune cells

To facilitate proliferation/differentiation of target cells
Epidermal growth factor (EGF) etc.

To inhibit proliferation of viruses and tumor cells

Interleukins （IL）

Cytokines

Growth factors

Interferon （IFN）

Tissue necrosis factors

Chemokines

To induce immune reaction and to necrotize tumor cells
Tumor necrosis factor α, β

To facilitate migration of immune cells
CCL or CXCL etc.

Possible predictive biomarkers related to inflammatory system

➤ **Interleukin** (IL); -1β, -2, **-6**, -7, -10

➤ Interferon (IFN); IFN γ -induced protein 10 (IP10)

➤ Chemokine;
Monocyte chemoattractant protein-1 (MCP1) (CCL2)
Macrophage inflammatory protein 1-alpha (MIP1A), (α: CCL3, β: CCL4)

➤ Growth factor;
Granulocyte colony stimulatingfactor (GCSF)

➤ Tumor necrosis factor –alpha (TNF-α)

➤ Others;
Intercellular adhesion molecule 1 (ICAM 1)
Activaed leukocyte cell adhesion molecule (ALCAM) **etc.**

☐ Keddie S et al.:https://www.sciencedirect.com/science/article/abs/pii/S1521661620307749?via%3Dihub
☐ Rebillard ME et al; https://www.jci.org/articles/view/145853
☐ Fajgenbaum DC et al.: https://www.nejm.org/doi/full/10.1056/NEJMra2026131

Additional information

ACE2:
     https://www.atsjournals.org/doi/pdf/10.1164/rccm.202101-0142LE

Viral load (CT value of PCR):
     https://www.medrxiv.org/content/10.1101/2021.01.04.21249236v1