UNIVERSITÀ DEGLI STUDI DI MILANO

Sistema Socio Sanitario
Regione Lombardia
ASST Santi Paolo e Carlo

# Immunopathogenesis of long-COVID: future directions

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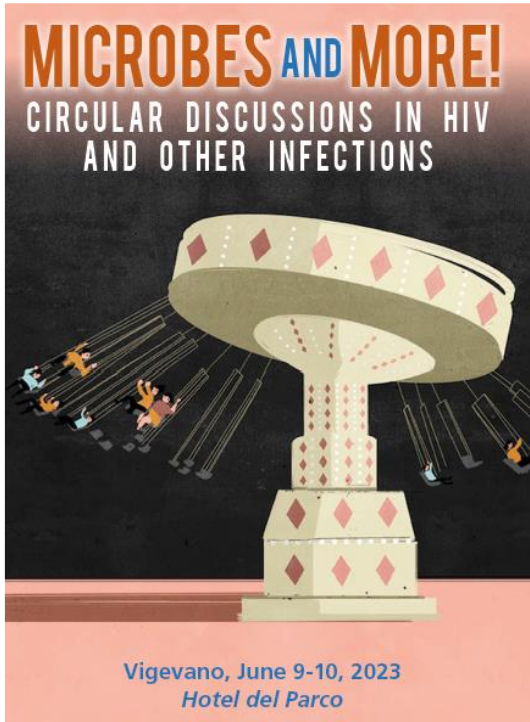

# Presentation outline

1. MIDAS project

2. Transcriptomic project

# MIDAS project

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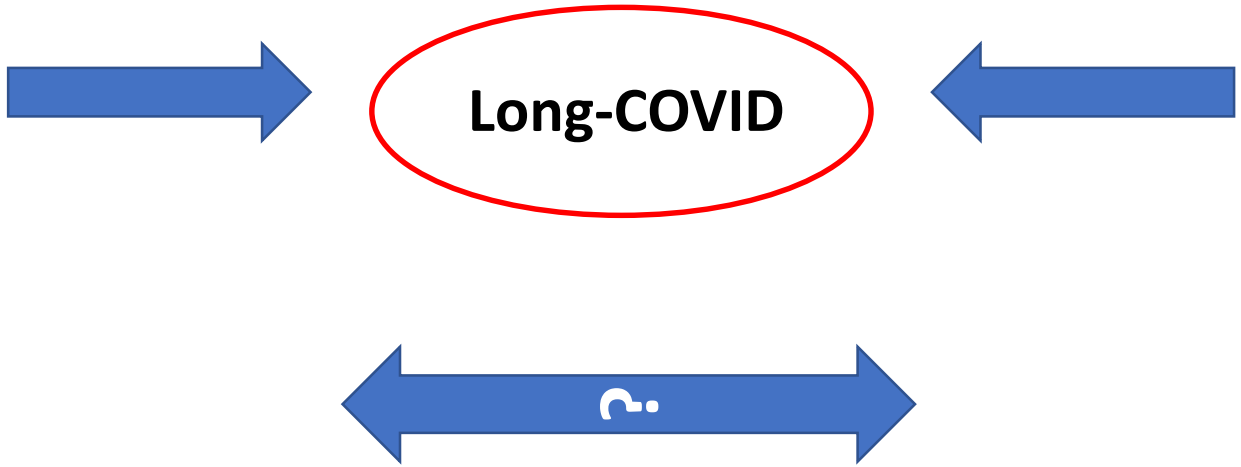
# MIDAS project: background

**Dysregulated host immune responses**

- reduced SARS-CoV-2-specific T cells, increased inflammation, exhausted CD8 T-cells, atypical and naïve B-cells at 1-7 months from symptoms onset;
- increased SARS-CoV-2-specific T cells but reduced functionality (pulmonary symptoms);
- Poorer SARS-CoV-2-specific humoral response.

References: Peluso M et al, Cell Rep, 2021-J Infect Dis 2021; Torres-Ruiz et al, Clin Transl Med 2021; Littlefield K et al, PLoS Pathog, 2022; Garcia-Abellan J et al, Front Immunol, 2022.




**Gut dysbiosis**

- Gut microbiota dysbiosis at 1 year after infection;
- Gut and airway microbiota dysbiosis is associated with long-COVIDneurological symptoms.

References: D. Zhang et al 2023 JKMS; G. Ancona et al, Front Immunol 2023; Q. Su et al MBJ 2023.

# MIDAS project: aim of the project

## Immunity

**γδ T cell responses**
Immunophenotype: CD3, Vδ1, Vδ2, α4β7, CD103, CCR9, HLA-DR
ICS (PMA+IONO stimulation): CD3, Vδ1, Vδ2, PD-1, IFN-γ, TNF- α, IL-17

## Gut dysbiosis

**Microbiome**
Sequencing: whole blood

**Gut barrier damage**
ELISA: iFABP, Zonulin, cadherin
**MT**
ELISA: flagellin, LBP, EndoCAB, β-glucan

**Long-COVID**

**Sample size:**
1. 20 LC-
2. 20 LC+

**Time points:**
T0: acute phase of disease
T1: 2-4 months from acute disease

# Transcriptomic project

R. Rovito[1], E. Margiotta[2], M. Machyna[2], M. Sala[1], F. Bai[1], C. Tincati[1], G.H.R. Quintanares[2], R. König[2], G. Marchetti[1]

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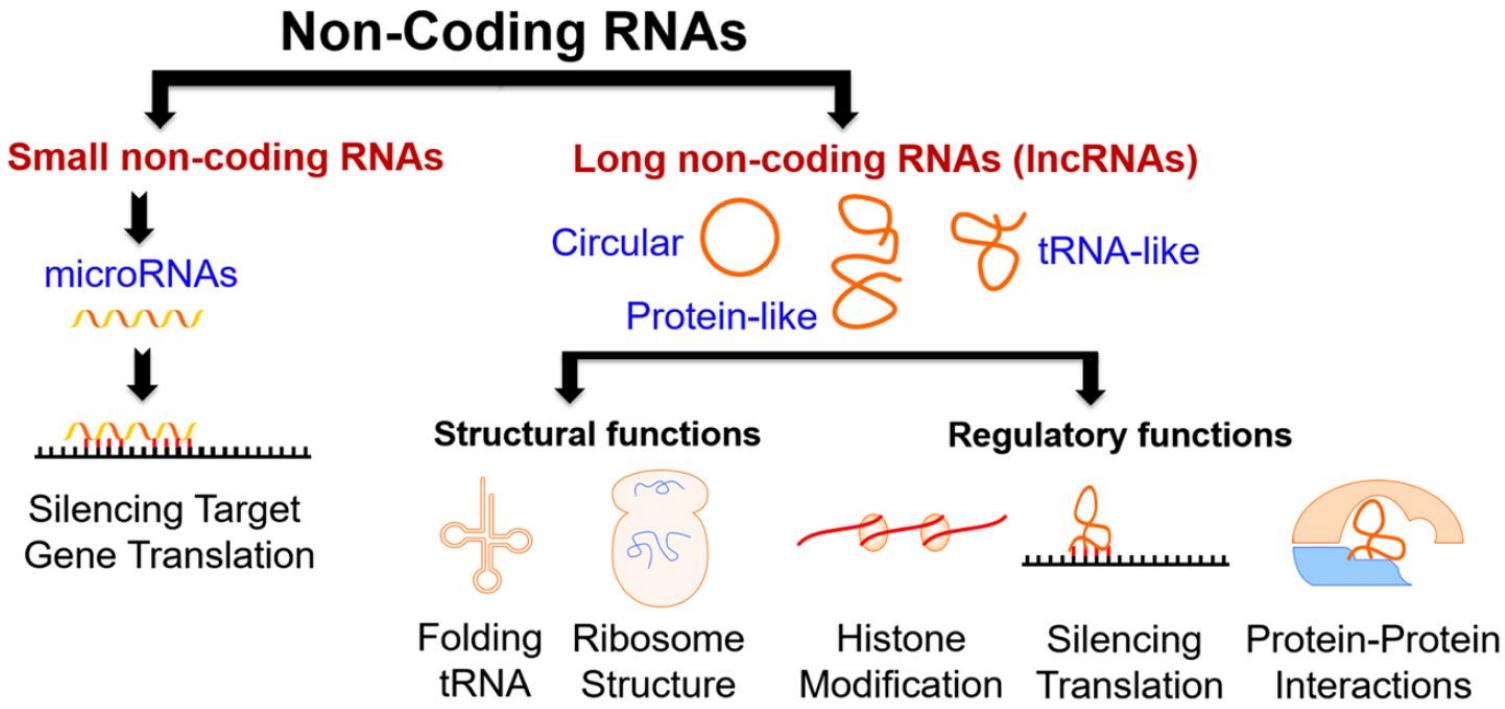
# Transcriptomic project: background

1. Non-coding RNA (miRNAs and lncRNAs) modulates gene expression at transcriptional and post-transcriptional level
2. Released in extracellular fluids, including plasma and saliva
3. Alteration associated with disease, including acute COVID-19




R. Paulmurugan et al, 2019, J Mol med

# Transcriptomic project: aim of the project

Identification of a ncRNA immunesignature associated with long-COVID

# Transcriptomic project: methods

Noncoding RNAs (miRNAs + lncRNAs) characterization: next generation sequencing (NGS) on plasma and PBMCs samples

**Sample size:**

1. 18 LC-
2. 29 LC+

**Time points:**

T0: acute phase of disease

T1: 2-4 months from acute disease

Validation on plasma samples