

## Plan for a



### **Miklos Lipcsey**

Professor, överläkare

Uppsala universitet/Akademiska sjukhuset

### **Michael Hultström**

Docent, spec. läkare

# Background



Hugo Zeberg

MD/PhD, asst. prof.



Miklós Lipcsey

MD/PhD, prof.



Robert Frithiof

MD/PhD, assoc. prof



Michael Hultström

MD/PhD, assoc. prof.



Jonathan Grip

MD/PhD



Oskar Eriksson

MD/PhD



Nicolas Tardif


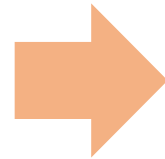
PhD, asst. prof



# Genetic determinants of severe COVID-19

**Pronmed**  
**Uppsala University**  
**376 Critically ill patients**

**Karolinska Institutet**  
**200 Critically ill patients**

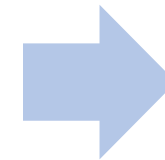


SweCovid

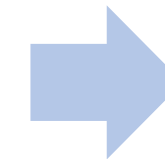
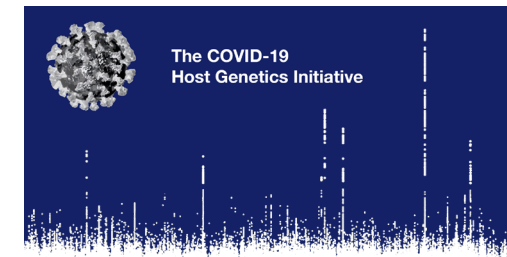
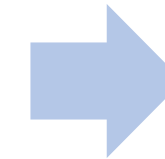
**500 Genotyped patients**

**400 Whole Exome Sequences**

**137 Phenotypes**



**OAS1 consortium**



**MBL collaboration**

# Some results from SweCOVID

**nature medicine** **ARTICLES**  
<https://doi.org/10.1038/s41591-021-01281-1>  
 Check for updates

## A Neanderthal OAS1 isoform protects individuals of European ancestry against COVID-19 susceptibility and severity

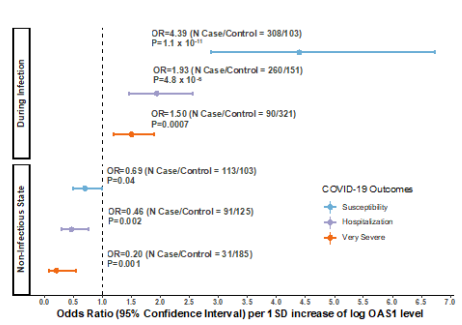
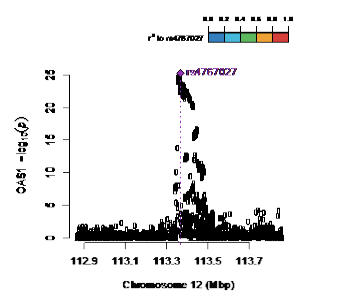
Sirui Zhou<sup>1,2,23</sup>, Guillaume Butler-Laporte<sup>1,2,23</sup>, Tomoko Nakanishi<sup>1,3,4,5,23</sup>, David R. Morrison<sup>1</sup>, Jonathan Afilalo<sup>1,2,6</sup>, Marc Afilalo<sup>1,7</sup>, Laetitia Laurent<sup>1</sup>, Maik Pietzner<sup>8</sup>, Nicola Kerrison<sup>8</sup>, Kaiqiong Zhao<sup>1,2</sup>, Elsa Brunet-Ratnasingham<sup>9,10</sup>, Danielle Henry<sup>1</sup>, Nofar Kimchi<sup>1</sup>, Zaman Afrasiabi<sup>1</sup>, Nardin Rezk<sup>1</sup>, Meriem Bouab<sup>1</sup>, Louis Petitjean<sup>1</sup>, Charlotte Guzman<sup>1</sup>, Xiaoqing Xue<sup>1</sup>, Chris Tselios<sup>1</sup>, Branka Vulesevic<sup>1</sup>, Olumide Adeleye<sup>1</sup>, Tala Abdullah<sup>1</sup>, Noor Almamlouk<sup>1</sup>, Yiheng Chen<sup>1,3</sup>, Michaël Chassé<sup>9</sup>, Madeleine Durand<sup>9</sup>, Clare Paterson<sup>11</sup>, Johan Normark<sup>12</sup>, Robert Frithiof<sup>13</sup>, Miklós Lipcsey<sup>13,14</sup>, Michael Hultström<sup>13,15</sup>, Celia M. T. Greenwood<sup>1,2,16</sup>, Hugo Zeberg<sup>17</sup>, Claudia Langenberg<sup>8,18</sup>, Elin Thyseil<sup>19</sup>, Michael Pollak<sup>1,20</sup>, Vincent Mooser<sup>3</sup>, Vincenzo Forgetta<sup>1</sup>, Daniel E. Kaufmann<sup>9,21</sup> and J. Brent Richards<sup>9,21</sup>

**EXPOSURE**  
 Association of circulating protein levels with genome-wide genotypes from six studies

Study	Sample size
Pietzner et al.	10,708
Yao et al.	6,861
Folkersen et al.	3,394
Sun et al.	3,301
Emilsson et al.	3,200
Shure et al.	997

**OUTCOME**  
 Association of the three COVID-19 outcomes with genome-wide genotypes from meta-analysis of 26 studies of European ancestry in the COVID-19 HGI

	Cases	Controls
Very severe	4,336	623,902
Hospitalized	6,406	902,088
Susceptible	14,134	1,284,876



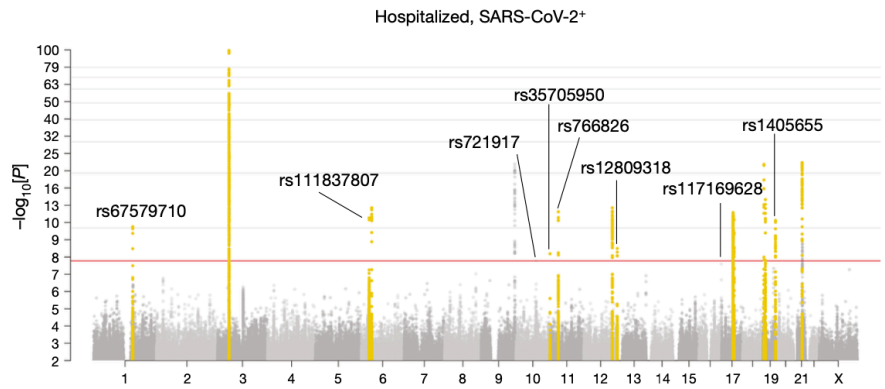
**nature**  
**Mapping the human genetic architecture of COVID-19**

COVID-19 Host Genetics Initiative\*<sup>✉</sup>

**nature**  
**A first update on mapping the human genetic architecture of COVID-19**

COVID-19 Host Genetics Initiative\*<sup>✉</sup>

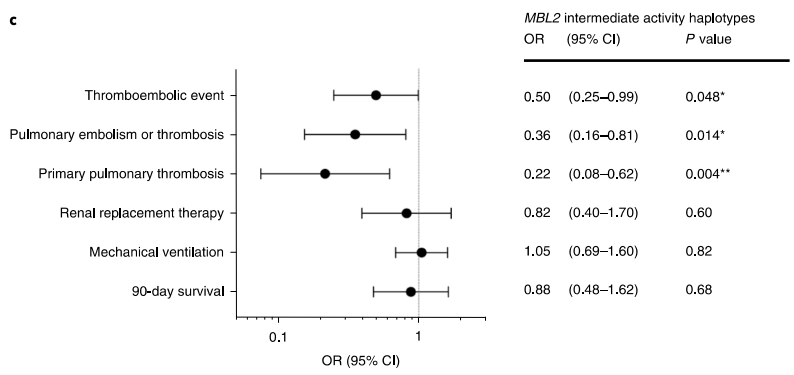
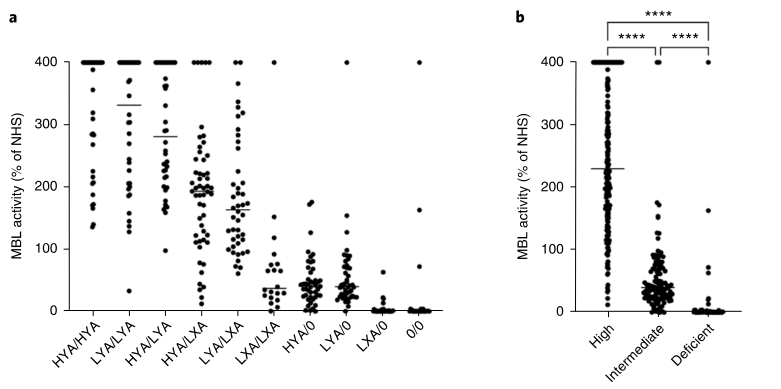
- 125,584 SARS-COV-2 patients
- 2,500,000 population controls
- 60 participating studies
- 25 countries represented
- 26 loci identified
- 3,100 authors



**nature immunology** **MATTERS ARISING**  
<https://doi.org/10.1038/s41590-022-01227-w>  
 Check for updates

## Genetic determinants of mannose-binding lectin activity predispose to thromboembolic complications in critical COVID-19

Michael Hultström<sup>1,2,3,4,13</sup>, Robert Frithiof<sup>1,13</sup>, Jonathan Grip<sup>5,6,13</sup>, Linnea Lindelöf<sup>7,13</sup>, Olav Rooijackers<sup>5,6</sup>, Sara Pigazzini<sup>8</sup>, Mari Niemi<sup>8</sup>, Mattia Cordioli<sup>8</sup>, Lindo Nkambule<sup>8</sup>, Tomislav Maricic<sup>9</sup>, Kristina Nilsson Ekdahl<sup>7,10</sup>, Bo Nilsson<sup>7</sup>, Miklós Lipcsey<sup>1,11</sup>, Hugo Zeberg<sup>9,12,13</sup> and Oskar Eriksson<sup>7,13</sup>



# Some results from SweCOVID

**nature medicine** **ARTICLES**  
<https://doi.org/10.1038/s41591-021-01281-1>  
 Check for updates

**nature**  
**Mapping the human genetic architecture of COVID-19**  
 COVID-19 Host Genetics Initiative\*✉

**nature immunology** **MATTERS ARISING**  
<https://doi.org/10.1038/s41590-022-01227-w>  
 Check for updates

## A Neanderthal OAS1 isoform protects individuals of European ancestry against COVID-19 susceptibility and severity

Sirui Zhou<sup>1,2,23</sup>, Guillaume Butler-Laporte<sup>1,2,23</sup>, Tomoko Nakanishi<sup>1,3,4,5,23</sup>, David R. Morrison<sup>1</sup>, Jonathan Afilalo<sup>1,2,6</sup>, Marc Afilalo<sup>1,7</sup>, Laetitia Laurent<sup>1</sup>, Maik Pietzner<sup>8</sup>, Nicola Kerrison<sup>8</sup>, Kaiqiong Zhao<sup>1,2</sup>, Elsa Brunet-Ratnasingham<sup>9,10</sup>, Danielle Henry<sup>1</sup>, Nofar Kimchi<sup>1</sup>, Zaman Afrasiabi Nardin Rezk<sup>1</sup>, Meriem Bouab<sup>1</sup>, Louis Petitjean<sup>1</sup>, Charlotte Guzman<sup>1</sup>, Xiaoqing Xue<sup>1</sup>, Chris Tselios<sup>1</sup>, Branka Vulesevic<sup>1</sup>, Olumide Adeleye<sup>1</sup>, Tala Abdullah<sup>1</sup>, Noor Almamlouk<sup>1</sup>, Yiheng Chen<sup>1,3</sup>, Michaël Chassé<sup>9</sup>, Madeleine Durand<sup>9</sup>, Clare Paterson<sup>11</sup>, Johan Normark<sup>1,2</sup>, Robert Frithiof<sup>1,3</sup>, Miklós Lipcsey<sup>13,14</sup>, Michael Hultström<sup>13,15</sup>, Celia M. T. Greenwood<sup>1,2,16</sup>, Hugo Zeberg<sup>17</sup>, Claudia Langenberg<sup>8,18</sup>, Elin Thyseil<sup>19</sup>, Michael Pollak<sup>1,20</sup>, Vincent Mooser<sup>3</sup>, Vincenzo Forgetta<sup>1</sup>, Daniel E. Kaufmann<sup>9,21</sup> and J. Brent Richards<sup>1,2,3,22</sup> ✉

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Early Treatment with Pegylated Interferon Lambda for Covid-19

G. Reis, E.A.S. Moreira Silva, D.C. Medeiros Silva, L. Thabane, V.H.S. Campos, T.S. Ferreira, C.V.Q. Santos, A.M.R. Nogueira, A.P.F.G. Almeida, L.C.M. Savassi, A.D. Figueiredo-Neto, A.C.F. Dias, A.M. Freire Júnior, C. Bitarães, A. C. Milagres, E.D. Callegari, M.I.C. Simplicio, L.B. Ribeiro, R. Oliveira, O. Harari, L.A. Wilson, J.I. Forrest, H. Ruton, S. Sprague, P. McKay, C.M. Guo, E.H. Limbrick-Oldfield, S. Kanters, G.H. Guyatt, C.R. Rayner, C. Kandel, M.J. Biondi, R. Kozak, B. Hansen, M.A. Zahoor, P. Arora, C. Hislop, I. Choong, J.J. Feld, E.J. Mills, and J.S. Glenn, for the TOGETHER Investigators\*

## Genetic determinants of mannose-binding lectin activity predispose to thromboembolic implications in critical COVID-19

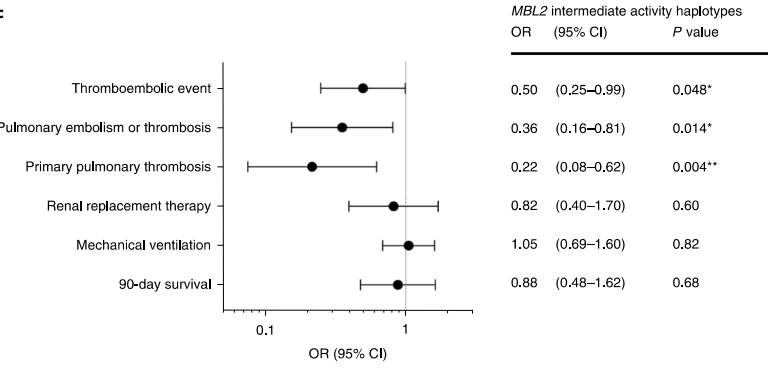
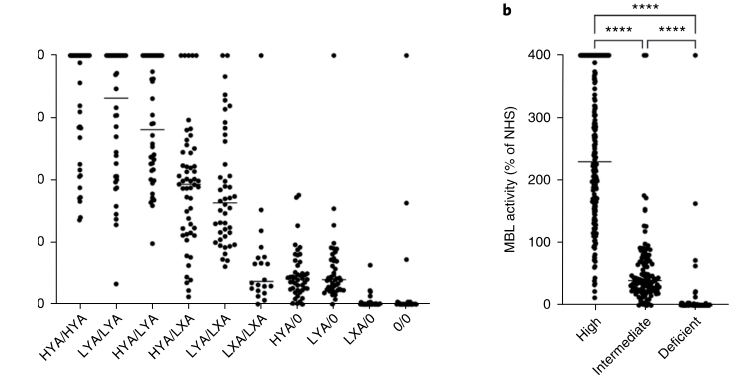
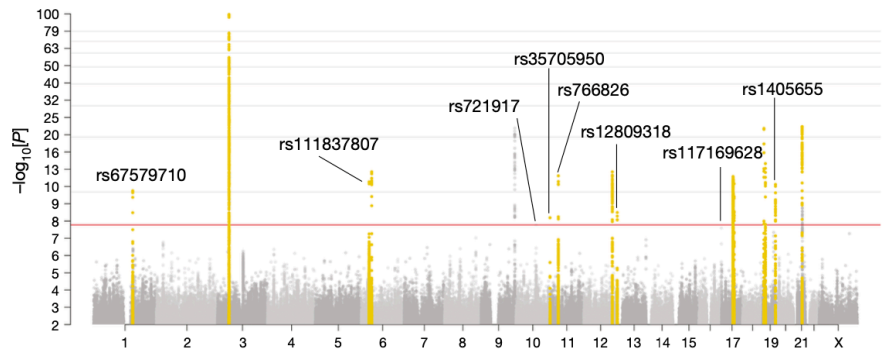
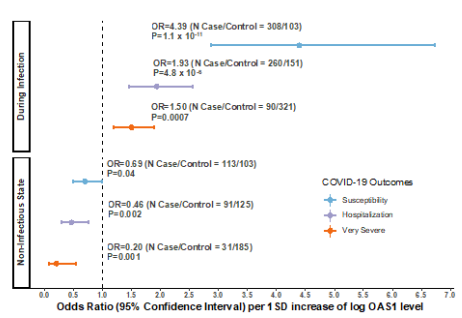
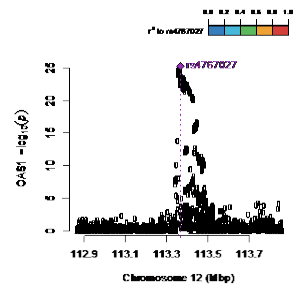
Michael Hultström<sup>1,2,3,4,13</sup>, Robert Frithiof<sup>1,13</sup>, Jonathan Grip<sup>5,6,13</sup>, Linnea Lindelöf<sup>7,13</sup>, v Rooijackers<sup>5,6</sup>, Sara Pigazzini<sup>8</sup>, Mari Niemi<sup>8</sup>, Mattia Cordioli<sup>8</sup>, Lindo Nkambule<sup>8</sup>, islav Maricic<sup>9</sup>, Kristina Nilsson Ekdahl<sup>10</sup>, Bo Nilsson<sup>7</sup>, Miklós Lipcsey<sup>1,11</sup>, Hugo Zeberg<sup>9,12,13</sup> ✉ Oskar Eriksson<sup>7,13</sup> ✉

**EXPOSURE**  
 Association of circulating protein levels with genome-wide genotypes from six studies

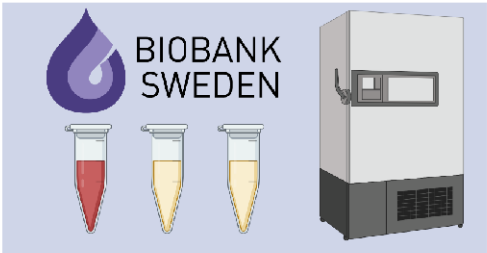
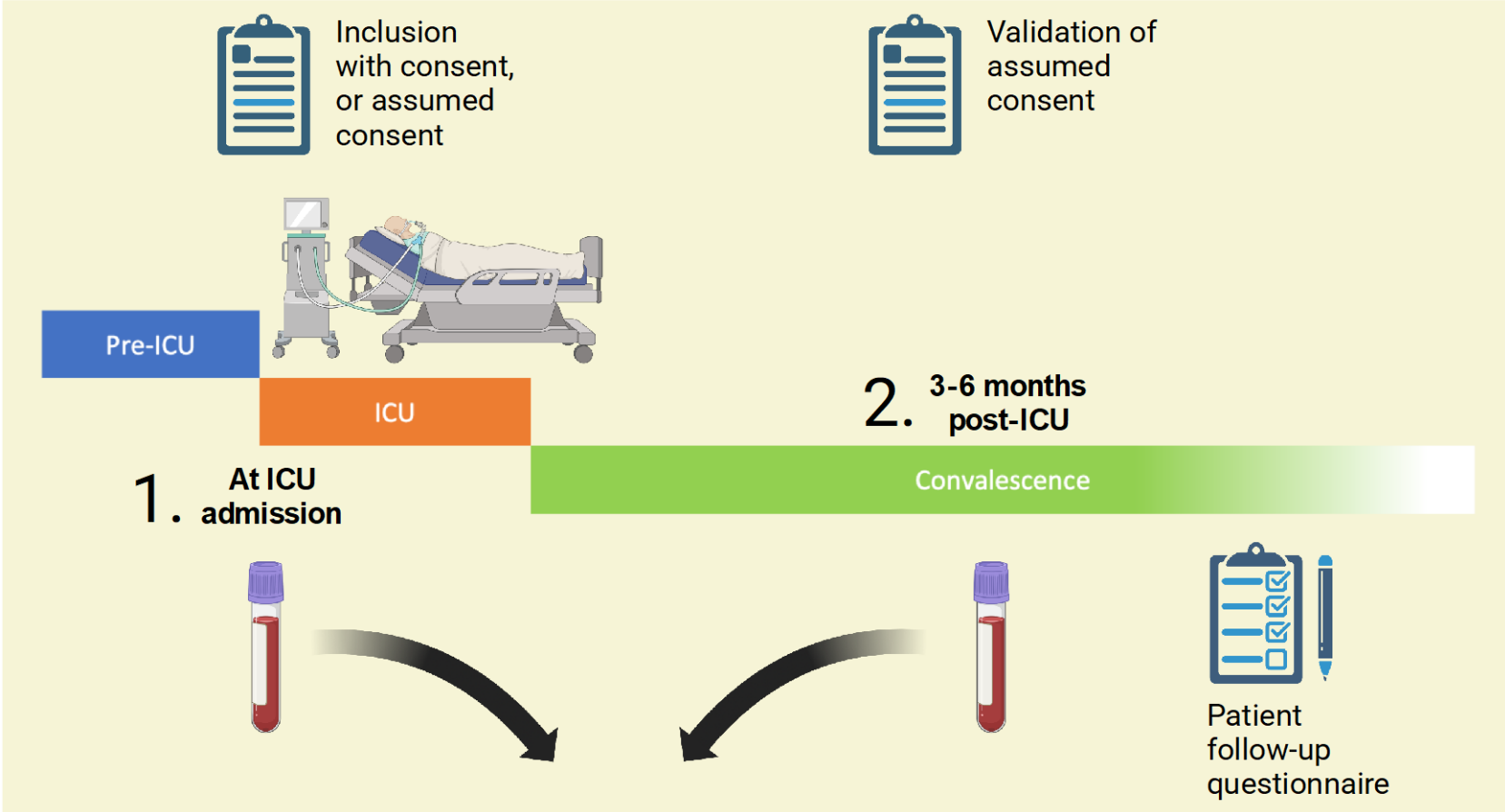
Study	Sample size
Pietzner et al.	10,708
Yao et al.	6,861
Folkersen et al.	3,394
Sun et al.	3,301
Emilsson et al.	3,200
Shure et al.	997

**OUTCOME**  
 Association of the three COVID-19 outcomes with genome-wide genotypes from meta-analysis of 26 studies of European ancestry in the COVID-19 HGI

	Cases	Controls
Very severe	4,336	623,902
Hospitalized	6,406	902,088
Susceptible	14,134	1,284,876

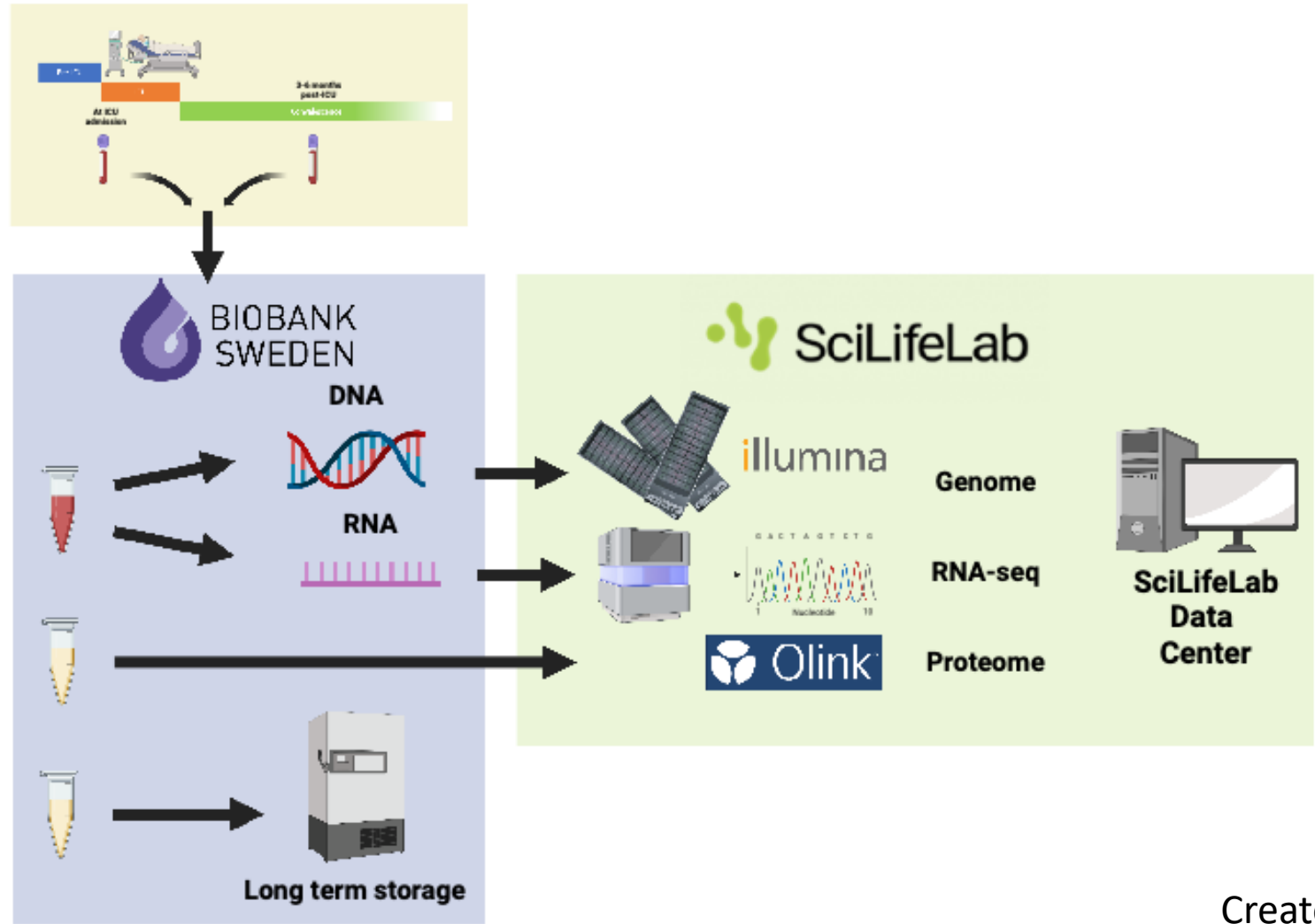


# Patient events in SWIC-B



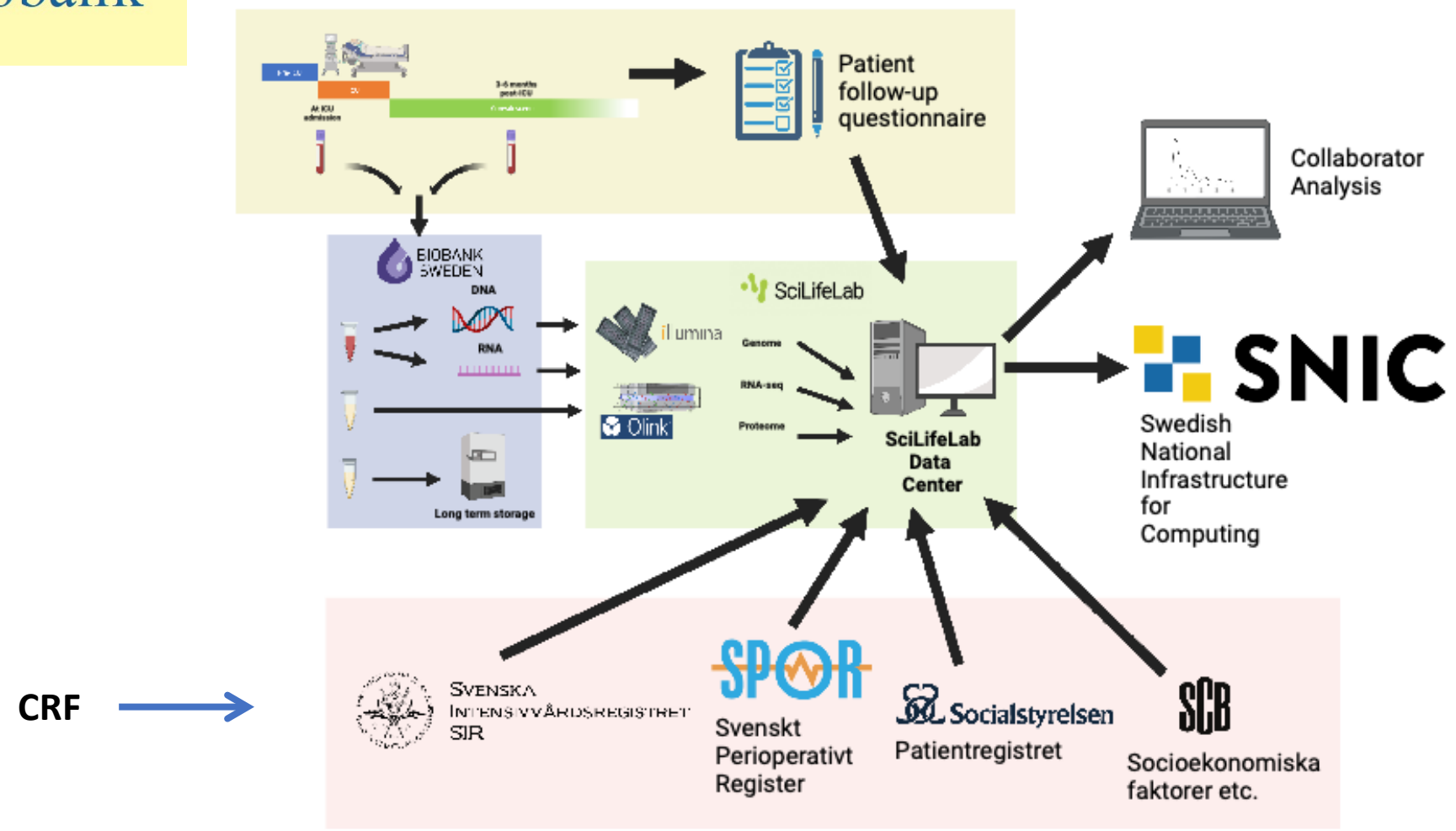


# Sample flow in SWIC-B





# Data flow in SWIC-B

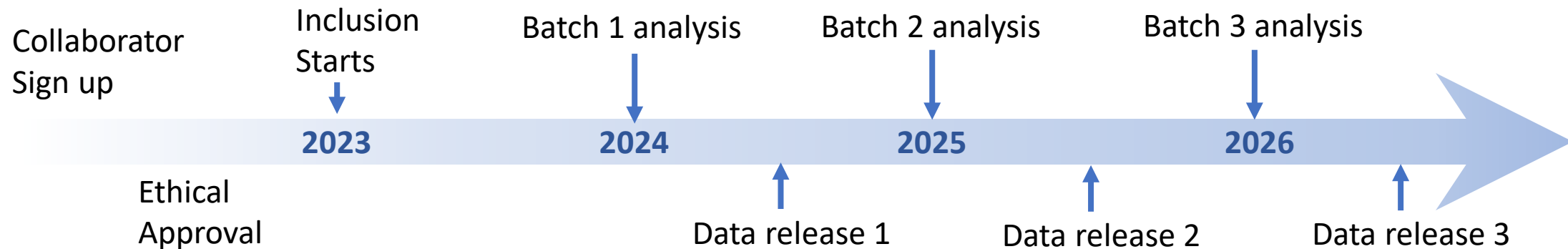






# Time line

- Contact list for collaborating ICUs – **now**
- Ethics – **autumn 2022**
- Sample collection – **start in 2023**
- Data release to collaborators – **Data freeze 1 summer 2024**






# Collaborating ICU tasks

- Provide ICU contact person for Ethical and Biobank permissions
- Include patients
- Submit clinical report form (CRF)
- Collect admission samples with routine admission samples
- Contact patients for follow-up questionnaire and samples
- Fund inclusion and sample collection
  - Co-financing of a PhD-student or research nurse

# Clinical Report Form


## Akuta inläggningen


**Inskrivningsrapport till Svensk Intensivvårdsbiobank**  
 Admission Case Report form to the Swedish Intensive Care Biobank

**Inklusionsdatum (ÅÅÅÅ-MM-DD):**  
**Personnummer (ÅÅÅÅ-MM-DD-NNNN):**  
**Namn:**  
**Ålder:**  
**Inläggningsorsak:**

**Underliggande sjukdomar (som ej säkert finns i slutenvårdsregistret)**  
**Hypertension:** Ja/Nej  
**Diabetes:** Ja/Nej      Tablettbehandling: Ja/Nej  
    Insulinbehandling: Ja/Nej  
**Hjärtkärlsjukdom:** Ja/Nej      Hjärtsvikt: Ja/Nej  
    Tidigare hjärtinfarkt: Ja/Nej  
    Tidigare TIA/Stroke: Ja/Nej  
**Lungsjukdom:** Ja/Nej      KOL: Ja/Nej  
    Astma: Ja/Nej  
**Njursjukdom:** Ja/Nej  
**Leversjukdom:** Ja/Nej  
**Psykiatrisk sjukdom:** Ja/Nej      Depression/Ångest: Ja/Nej  
    Psykossjukdom: Ja/Nej  
**Neurologisk sjukdom:** Ja/Nej      Epilepsi: Ja/Nej  
    Kognitiv svikt: Ja/Nej  
**Inflammatorisk sjukdom:** Ja/Nej      Reumatoid artrit: Ja/Nej  
**Malignitet:** Tidigare / Pågående / Nej  
**Rökning:** Tidigare / Pågående / Nej

## Uppföljningen


**Uppföljningsrapport till Svensk Intensivvårdsbiobank**  
 Follow-up Case Report form to the Swedish Intensive Care Biobank

**Uppföljningsdatum (ÅÅÅÅ-MM-DD):**  
**Utskrivningsdatum från intensivvården (ÅÅÅÅ-MM-DD):**  
**Personnummer (ÅÅÅÅ-MM-DD-NNNN):**  
**Namn:**  
**Ålder:**  
**Avliden:** Ja/Nej      **Avliden datum (ÅÅÅÅ-MM-DD):**  
**Informationsgivare:** Patient / Anhörig / Vårdpersonal

**Livssituation**  
**Aktuell bostad/vistelse:** Hemmet: Ja/Nej  
    Korttidsboende: Ja/Nej  
    Långtidsboende: Ja/Nej  
    Sjukhus: Ja/Nej  
    Intensivvård: Ja/Nej  
**Sysselsättning innan IVA:** Förvärsarbete/arbetsökande/studerande: Ja/Nej  
    Sjukskriven: Ja/Nej  
    Förtidspensionär/Socialbidrag: Ja/Nej  
    Pensionär: Ja/Nej  
**Aktuell sysselsättning:** Förvärsarbete/arbetsökande/studerande: Ja/Nej  
    Sjukskriven: Ja/Nej  
    Förtidspensionär/Socialbidrag: Ja/Nej  
    Pensionär: Ja/Nej

**Kvarvarande symptom på uppföljningsdagen**

	0	1	2	3	4	Förrädd
<b>Svärighet att gå</b>	Inga	Lätta	Måttliga	Svåra	Kan ej	Ja/Nej
<b>Svärighet att tvätta/klä</b>	Inga	Lätta	Måttliga	Svåra	Kan ej	Ja/Nej
<b>Svärighet med valiga akt.</b>	Inga	Lätta	Måttliga	Svåra	Kan ej	Ja/Nej
<b>Smärta</b>	Ingen	Lätt	Måttlig	Svår	Extrem	Ja/Nej
<b>Oro/Nedstämdhet</b>	Ingen	Lätt	Måttlig	Svår	Extrem	Ja/Nej

	0	1	2	Förrädd
<b>Andfåddhet</b>	Normal vid ansträngning	Vid lätt ansträngning	I vila	Ja/Nej
<b>Trötthet</b>	Ingen begränsning	Blir lätt uttröttad	Alltid trött	Ja/Nej
<b>Svaghet (lyfta 10kg)</b>	Inga problem	Vissa problem	Kan ej	Ja/Nej
<b>Kognitiva problem</b>	Inga problem	Viss hjärndimma	Svåra	Ja/Nej



# Ethical application

- Huvudman: Uppsala Universitet
- Medverkande: Alla regioner
- Biobanksansvarig: Varje region för sina patienter
- Patient ID: Varje region/IVA och Biobank Sverige



# Collaborating ICU benefits

- Early data access
- Computing access to data through SNIC/UPPMAX
- Co-authors on collaboration publications
- Suggest collaborative analyses



Thank you for your time

e-mail me: [miklos.lipcsey@surgsci.uu.se](mailto:miklos.lipcsey@surgsci.uu.se)