

## Supplemental Online Content

Lugar M, Eugster A Achenbach P, et al. SARS-CoV-2 infection and development of islet autoimmunity in early childhood. *JAMA*. doi:10.1001/jama.2023.16348

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This supplemental material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Age and Period of Follow-up Visits in 885 Children of Study

<b>Visit No.</b>	<b>Visit Age, Months (Median, IQR)</b>	<b>Visit Date (Median, Range, Month/Year)</b>	<b>Total Period (n, Children)</b>	<b>After June 2020 (n, Children)</b>
2	8.0 (7.3 – 8.5)	4/2020 (4/2018 to 6/2021)	885	333
3	10.0 (9.2 – 10.4)	6/2020 (6/2018 to 8/2021)	885	391
4	13.9 (13.2 – 14.4)	9/2020 (10/2018 to 11/2021)	885	536
5	18.0 (17.9 – 18.2)	1/2021 (1/2019 to 5/2022)	881	637
6	24.0 (23.8 – 24.2)	6/2021 (7/2019 to 6/2022)	765	624

**eTable 2.** Characteristics of Children Included in Follow-up SARS-CoV-2 Antibody Measurements

	<b>Total Study Period</b>	<b>After June 2020</b>
	<b>n = 885</b>	<b>n = 747</b>
Sex, Girls/Boys	441/444	364/383
T1D First Degree Relative	477	384
Country		
- Germany	407	306
- Poland	216	187
- Sweden	160	153
- Belgium	71	71
- United Kingdom	31	30
HLA DR3/DR4-DQ8	478	416

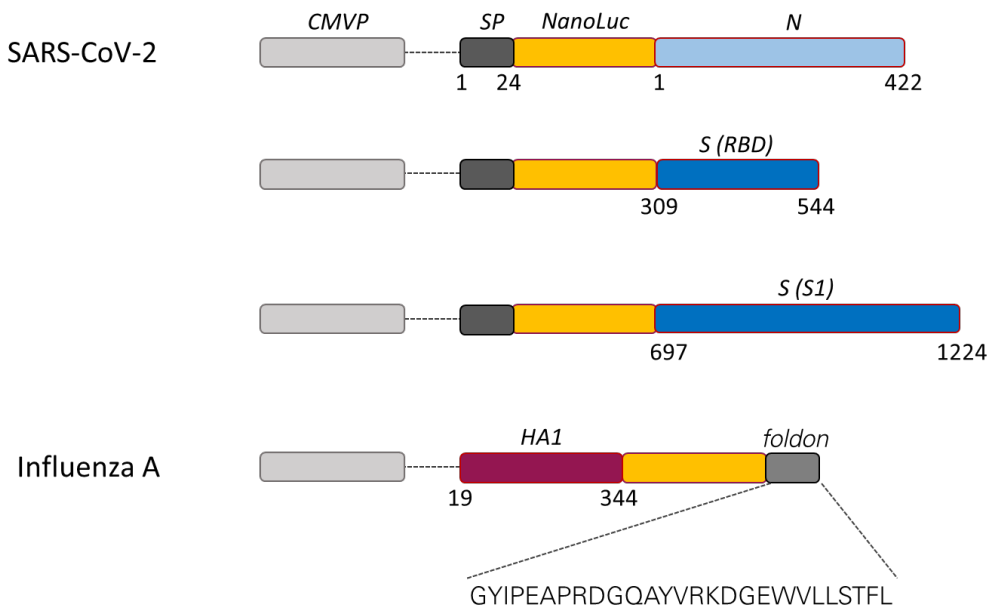
eTable3. Temporal Development of Islet Autoantibodies in Relation to SARS-CoV-2 Antibodies at Age 12 to 16 months.

SARS-CoV-2 Antibody Development at Age 12 to 16 mo (visit 4)	Islet Autoantibody Positive at 12-16 mo (visit 4)	Islet Autoantibody Positive at 18 mo (visit 5)
	Cases No./Total (%)	Cases No./Total (%)
Pre-pandemic (Until June 2020)		
- SARS-CoV-2 Ab Negative	8/341 (2.3%)	5/333 (1.5%)
Pandemic (From July 2020)		
- SARS-CoV-2 Ab Negative	7/480 (1.5%)	4/422 (0.9%)
- SARS-CoV-2 Ab Positive	4/19 (21.1%) <sup>a</sup>	2/15 (13.3%) <sup>b</sup>

<sup>a</sup>  $P < .001$  vs SARS-CoV-2 antibody negative in pandemic period;  $P = .001$  vs SARS-CoV-2 antibody negative in whole period.

<sup>b</sup>  $P = .02$  vs SARS-CoV-2 antibody negative in pandemic period;  $P = .02$  vs SARS-CoV-2 antibody negative in whole period.

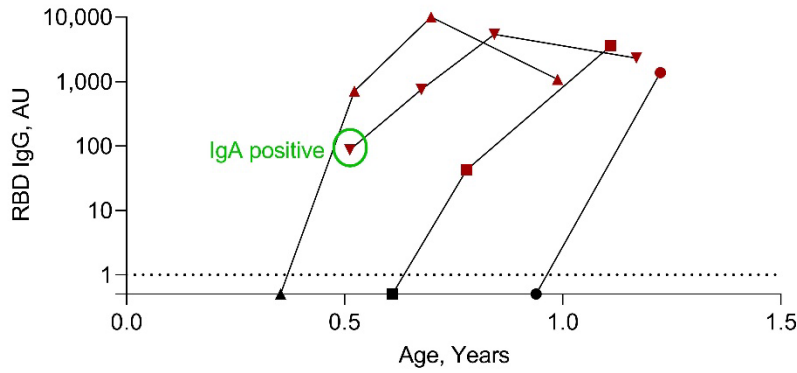
**eFigure 1.** Linear Schematic of Constructs Encoding Antigens Fused to NanoLuc Used in the Luciferase Immunoprecipitation System (LIPS) Assay



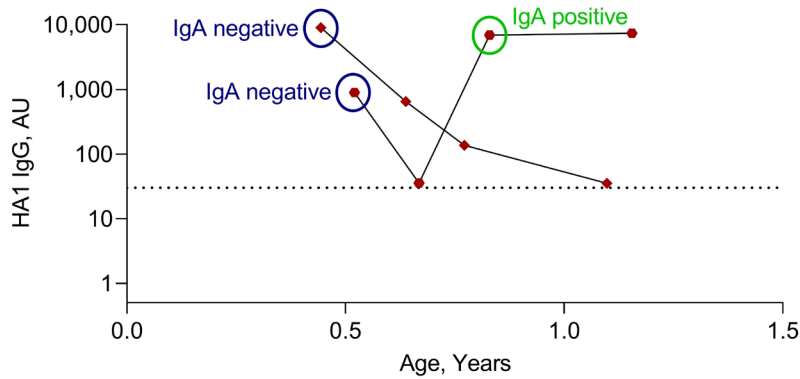
Linear schematic of constructs encoding recombinant SARS-COV-2 and Influenza A antigens fused to NanoLuc. All constructs are driven by the CMV-promotor. *SP*: *IL6* signal peptide; *N*: Nucleocapsid gene; *S*: Spike gene; *RBD*: receptor binding domain; *S1*: S1 part of spike gene; *HA1*: HA1 part of hemagglutinin; *foldon*: bacteriophage T4 fibrin foldon domain (encoded amino acids are shown). Numbers correspond to amino acids encoded.

**eFigure 2.** Examples of SARS-CoV-2 (A) and H1N1 Antibody Titres (B,C) Over Time in Children

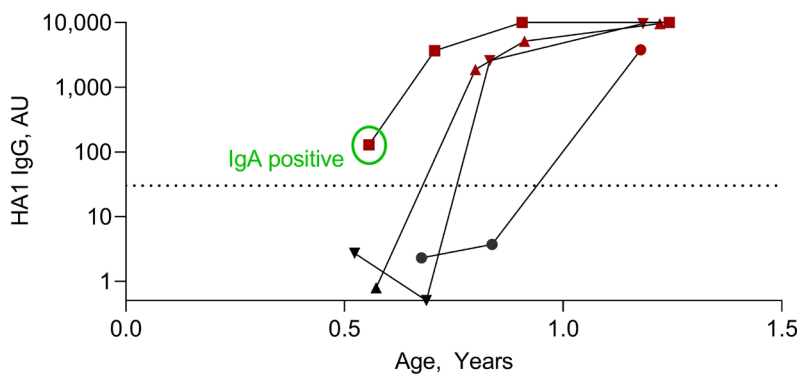
**A**



**B**

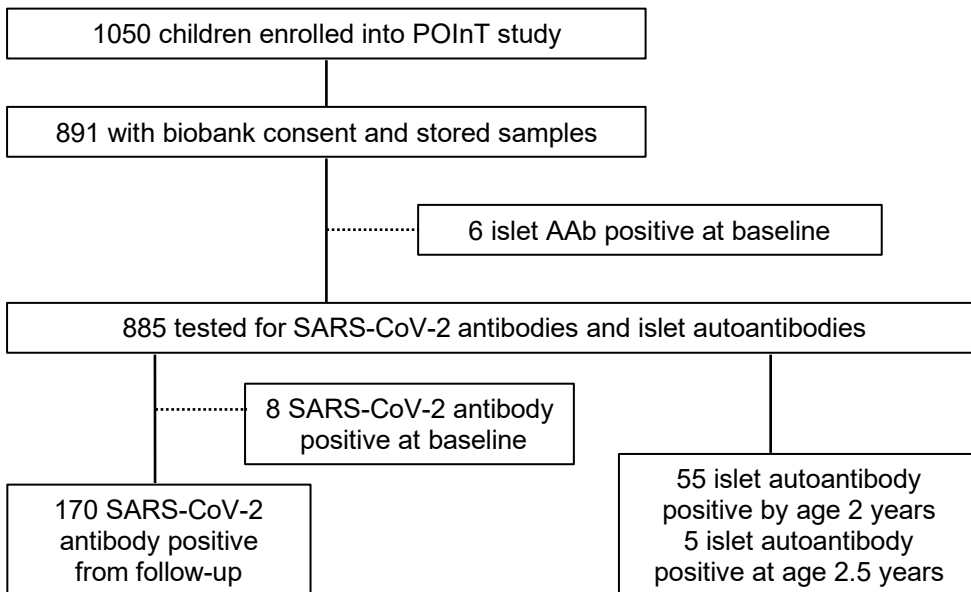


**C**



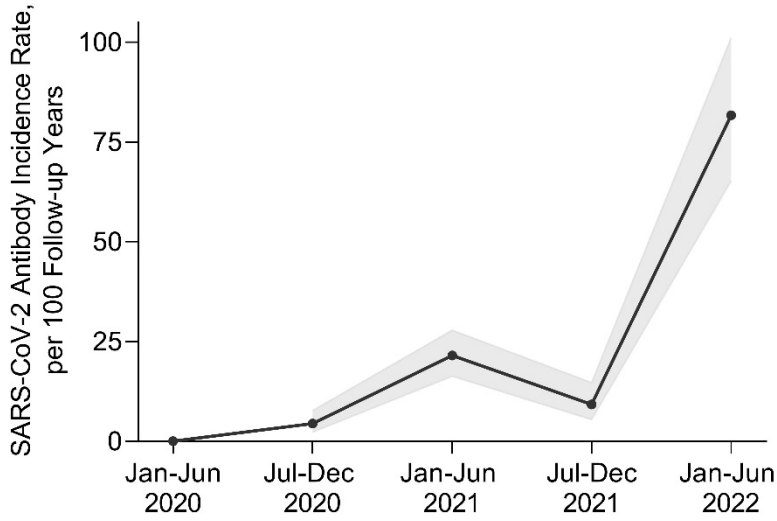
Dots connected with a line represent a set of samples of an individual child. Dashed lines show the threshold for antibody-positivity. Some samples were tested for IgA antibodies to distinguish the child's antibodies from the maternal ones (circled dot, green is IgA positive, blue is IgA negative).

**eFigure 3.** Children in POInT Study Tested in the Ancillary Study



**eFigure 4.** Incidence of SARS-CoV-2 Antibodies during the Pandemic Period (A) at Different Study Sites (B)

**A**



**B**

