Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Two SARS-CoV-2 serology assays detect antibodies in the sera of individuals diagnosed with SARS-CoV-2 Omicron variant

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1. Letter to the editor

The World Health Organization declared the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) Omicron variant, B.1.1.529, a variant of concern (VOC) on Nov. 26, 2021—due to its higher transmissibility than wild type SARS-CoV-2 and other VOCs (Alpha, Beta, Gamma and Delta), and its ability to evade immunity in previously infected or vaccinated people. Omicron has more mutations in its spike protein (S) which harbors the receptor binding domain (RBD) (30 mutations [15 in the RBD], 3 deletions and 1 insertion) than the delta variant B.1.617.2 (9 mutations and 1 deletion) [1,2]. Here, we examined whether two widely used serology assays, based on the wild type S1-RBD, detect antibodies directed against currently dominant Omicron in patient sera.

The Atellica® IM SARS-CoV-2 IgG (sCOVG) and Atellica® IM SARS-CoV-2 Total (COV2T) assays (Siemens Healthcare Diagnostics Inc, Tarrytown, NY, U.S.) are semi-quantitative used for determining anti-S1 RBD IgG or Total (IgG and IgM) antibody levels, respectively. The sCOVG assay is a two-step automated sandwich chemiluminescent immunoassay. Recombinant antigens capture antibodies in the sample. After washing, mouse monoclonal anti-human IgG antibodies labeled with acridinium ester bind captured antibodies, generating a signal. The measuring range is 0.50–150 Index. The COV2T assay is a one-step (i.e., no wash step in between adding capture and detection reagents) automated sandwich chemiluminescent immunoassay that uses antigens to bridge antibodies. Recombinant antigens capture antibodies in the specimen. Recombinant S1 RBD antigen labeled with acridinium ester is added and binds the bound antibodies. The measuring range is 0.60–75.00 Index. An index value of $\geq$ 1.00 indicates a reactive (positive) result for both assays—established with calibrators. Both assays were authorized under the U.S. Food and Drug Administration Emergency Use Authorization (EUA) (Atellica IM sCOVG: March 2021; Atellica IM COV2T: May 2020) [3]. Both assays are calibrated to the WHO 20/136 International Standard Human Reference Material (WHO IS) (sCOVG cutoff index of 1 = WHO 45.1 binding antibody units (BAU)/mL; COV2T cutoff index of 1 = WHO 6.70 BAU/mL [4]. Serum samples were collected from 10 subjects who were infected with Omicron (confirmed by whole SARS-CoV-2 genetic sequencing). The number of days serum was collected post RT-PCR positive test result is listed in Table 1. Samples were purchased from Ellipsis Research Group (Brooklyn, NY, U.S.), which had institutional ethics agreements and donor consent for the collection of specimens. All patients were unvaccinated with no known previous SARS-CoV-2 infection. It was very difficult to obtain blood samples from post RT-PCR positive sequenced samples from unvaccinated individuals with no known prior SARS-CoV-2 infection—hence, the small sample size and very young donors.

Results for the two assays are presented in Table 1. The 10 samples were all reactive (positive) on the sCOVG and COV2T assays. Comparison of results with those for previous variants may indicate some reduction of signal, but the sample number was small. Nevertheless, sCOVG assay antibody levels (in WHO IS units, 83 to > 1750 BAU/mL) were comparable to antibody levels (in BAU/mL) of another anti-S1-RBD IgG assay whose results corresponded to 60 to > 80% vaccine efficacy; note, results were obtained pre-Omicron in 2020–2021 when efficacy was likely against infection by previous variants [5].

Study limitations included the small number of Omicron positive subjects and that we could not rule out concurrent or previous non-symptomatic and/or undiagnosed infections with other variants. Previous infections may have been detected if blood samples were obtained to test for antibodies when samples were collected for sequencing—although unlikely for all subjects. A concurrent infection could have occurred if subjects were infected with another variant shortly after, or on the day blood was collected for sequencing, and it is possible that we detected antibodies to that variant—again, unlikely for all subjects.

In conclusion, the sCOVG and COVT antibody assays appear acceptable for detecting antibodies in the sera of patients diagnosed with Omicron. Studies with more subjects are needed.

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Table 1
Atellica IM sCOVG Assay and Atellica IM Assay results for sera from 10 patients who were infected with the SARS-CoV-2 Omicron variant, B.1.1.529.

								Atellica IM sCOVG Assay		Atellica IM COV2T Assay	
Sample	Sex	Race	Age (y)	Date of serum collection	Date of RT-PCR	Days post RT-PCR Positive	RT-PCR method	(Index)	(BAU/mL)	(Index)	(BAU/mL)
1	M	Other	6	12/28/2021	12/1/2021	27	Roche **cobas**[a]	4.48	171.97	>75.00	>555
2	M	Other	2	12/29/2021	12/3/2021	26	Roche **cobas**	11.75	407.36	>75.00	>555
3	F	White	4	12/28/2021	12/5/2021	23	Vela Virokey[b]	3.05	120.85	7.13	52.12
4	F	Other	4	12/26/2021	12/3/2021	23	Vela Virokey	4.07	157.52	>75.00	>555
5	M	White	76	12/22/2021	12/2/2021	20	Vela Virokey	>150	>1750	>75.00	>555
6	F	White	4	12/26/2021	12/5/2021	21	Vela Virokey	15.58	518.36	52.27	386.59
7	F	White	4	12/27/2021	12/4/2021	23	Vela Virokey	4.98	189.35	>75.00	>555
8	F	Asian	8	1/2/2022	12/1/2021	32	Vela Virokey	4.90	186.57	>75.00	>555
9	F	Other	7	1/3/2022	12/2/2021	32	Vela Virokey	2.02	82.89	>75.00	>555
10	F	White	3 m	1/3/2022	12/16/2021	18	Vela Virokey	37.38	1028.06	>75.00	>555

Serum was collected from unvaccinated donors who had no known previous SARS-CoV-2 infection; M: Male; F: Female; y: years; m: months.
Note, the Atellica IM sCOVG Assay has the same reagent formulations as the ADVIA Centaur® sCOVG assay (Siemens Healthcare Diagnostics Inc, EUA June 17, 2021, updated August 10, 2021) [3].
[a] Roche **cobas**® SARS-CoV-2 (Roche Molecular Systems, Inc. Branchburg, NJ, U.S.)
[b] Vela Virokey SARS-CoV-2 (Vela Diagnostics USA, Inc, Fairfield, NJ, U.S.)

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All authors are full-time employees of Siemens Healthcare Diagnostics Inc, Tarrytown, NY, USA.

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