

Evaluation of COVID-19 IgG/IgM Rapid Test from Orient Gene Biotech

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14 **Abstract**

15 While the COVID-19 pandemic has peaked in many countries already, the current
16 challenge is to assess population immunity on large scale. Many serological tests are available
17 and require urgent independent validation. Here we report performance characteristics of
18 Orient Gene (OG) COVID-19 IgG/IgM Rapid Test Cassette compare it Abbott SARS-CoV-2
19 IgG immunoassay (ASIA). Patients (n=102) with a positive SARS-CoV-2 RT-PCR were
20 tested. They were asymptomatic (n=2), had mild (n=37) or severe symptoms requiring
21 hospitalization in medical (n=35) or intensive care unit (n=28). Specificity was evaluated on
22 42 patients with previous viral and parasitic diseases as well as high level of rheumatic factor.
23 Sensitivity of OG was 95.8% (CI95% 89.6-98.8) for samples collected ≥ 10 days after onset of
24 symptoms which was equivalent to sensitivity of ASIA of 90.5% (IC95% 82.8-95.6). OG
25 uncovered 6 false negative of ASIA, of which two had only IgM with OG. Specificity was
26 100% (CI95% 93.4-100) with both tests on samples including patients infected with endemic
27 coronavirus. Overall, OG performance characteristics indicate that the test is suitable for
28 routine use in clinical laboratories and performance is equivalent to immunoassay. Testing
29 OG on a larger asymptomatic population may be needed to confirm these results.

30 **Introduction**

31 COVID-19 pandemic has had a major impact on clinical microbiology laboratories. The
32 initial challenge was to increase the capacity of acute COVID-19 diagnosis by reverse
33 transcriptase polymerase chain reaction (RT-PCR) (1). The current challenge is to assess
34 immunity to SARS-CoV-2, urged by governments to get people back to work and limit
35 economic damage (2). However, our task remains to balance urgency against proper
36 assessment of hundreds of tests simultaneously becoming available on the market.
37 Seroconversion has been shown to occur as early as 7 days after the onset of symptoms (3).
38 Here, we evaluate the COVID-19 IgG/IgM Rapid Test Cassette (Orient Gene Biotech,
39 Zhejiang, China) (OG) and compare it to the Abbott SARS-CoV-2 IgG (ASIA).

40

41 **Methods**

42 OG is a lateral flow assay (LFA) approved by the European Union (CE mark), the Chinese
43 national medical products administration and the FDA recently issued an emergency use
44 authorization (5/29/2020). This test can be performed with 5 μ L of serum/plasma or 10 μ L of
45 whole blood. The sample is deposited in the specimen well (S) of the test device and two
46 drops of sample buffer to the buffer well (B) immediately. The result is read at 10 minutes.
47 The cassette displays a blue control band that turns red when the test has been performed
48 correctly. IgG and IgM are represented by two separated bands and are read visually. Whole
49 blood samples used in this study were centrifuged at 1200 rpm for 20 minutes and sera were
50 aliquoted and stored at -20°C upon use. Serum samples (n=106) were tested from 102 patients
51 with positive SARS-CoV-2 RT-PCR (Cobas® SARS-CoV-2 Test, Roche, Meylan, France)
52 and at least 4 days (4-40, median=18) since onset of symptoms or positive PCR for
53 asymptomatic patients. Negative samples tested (n=42) were acquired during pre-pandemic
54 period from routine occupational health patients with no known disease (n=14) or

hospitalized patients (n=28) with a previous pulmonary infection with endemic coronavirus (n=16), rhinovirus (n=1), metapneumovirus (n=1), influenzae A (n=1), or syncytial respiratory virus (n=1). Three had recent infection with malaria. Two had with IgM antibodies (Ab) against cytomegalovirus and 2 had IgM Ab against Epstein-Barr Virus. IgG was present against HIV (n=1), hepatitis B virus (n=1) and toxoplasmosis (n=1) and 2 patients had high levels of rheumatic factor. All OG test results were performed and read after 10 min by two clinical microbiologists unblinded regarding the sample group. Indeterminate readings were to be read by a third microbiologist. Concomitantly, all serum samples were tested for IgG using ASIA on Architect Abbott Instrument i2000SR (Abbott, Illinois, USA) using manufacturer's recommended cut-off of 1.4. The study was carried out in accordance with the Declaration of Helsinki. This study was a non-interventional study with no addition sampling to usual procedures. Biological material and clinical data were obtained only for standard viral diagnostic following physicians' prescriptions (no specific sampling, no modification of the sampling protocol). Data analyses were carried out using an anonymized database. According to the French Health Public Law (CSP Art L 1121-1.1), such protocol was exempted from informed consent application. Statistical analyses were performed with Prism GraphPad v6.0.

Results

Patients (n=102) characteristics with a positive SARS-COV-2 RT-PCR are detailed in **Table 1**. Patients were asymptomatic (n=2), had mild symptoms (n=37) and severe symptoms requiring hospitalization in medical (n=35) or intensive care unit (n=28).

OG global sensitivity including all samples regardless of sampling time to onset of symptoms was 93.4% (CI95% 86.9-97.3) (99/106) and 95.8% (CI95% 89.6-98.8) (91/95) for samples collected ≥ 10 days after onset of symptoms or since positive PCR. Results of the test

80 according to day from onset of symptoms are presented in **Figure 1**. Comparatively global
81 sensitivity of ASIA was 88.7% (IC95% 81.1-94.0) (94/106) and 90.5% (IC95% 82.8-95.6)
82 (86/95) for samples collected ≥ 10 days after onset of symptoms or since positive PCR. A total
83 of 6 patients tested positive with OG and negative with ASIA. For two of them, OG shown
84 IgM only. The remaining 4 patients had IgG according to OG. Discrepancies between ASIA
85 and OG in IgG are labeled in Figure 2. All patients had mild symptoms and sera were
86 collected at day 6, 12, 22 and 28 respectively after onset of symptoms. ASIA indexes for
87 these patients were 0.02, 0.16, 0.47 and 1.33 respectively (recommended cut-off: 1.4).

88 Seven patients tested negative with OG; 3 of these were collected < 10 days after onset
89 of symptoms. Out of these 3 patients, one who was sampled at day 9 after onset of symptom,
90 was positive with ASIA with an index of 4.1 while the two others remained negative with
91 respective indexes of 0.05 and 0.46. The remaining 4 patients negative with OG were
92 negative at day 12, 15, 15 and 18 respectively and all displayed acquired immunodeficiencies
93 that could explain an inability to synthesize immunoglobulins. Acquired immunodeficiencies
94 resulted from hematological malignancies (n=2) and metastatic lung carcinoma (n=1) and
95 glioblastoma (n=1) both under chemotherapy and/or radiotherapy associated with severe
96 malnutrition (albumin < 25 g/L). Concomitantly, ASIA was also negative for these 4 patients
97 with indexes < 0.3 in all cases.

98 Four patients displayed only IgM with OG, one of who was negative for IgG at day 19
99 and 30 (see patient orange, Figure 2). For this patient IgG were detected with ASIA with
100 indexes of 3.71 and 4.28 at day 19 and 30 respectively. The 3 other patients were sampled
101 ≤ 15 days after onset of symptoms, 2 of the 3 were also negative in ASIA.

102 Overall agreement between OG and ASIA focusing only on IgG detection was 92.5%
103 (98/106) and results are displayed in **Figure 2**. Both asymptomatic patients tested positive at
104 day 13 and 18 respectively after positive RT-PCR with both techniques. One patient was

105 tested with OG using both serum and whole blood showing bands of similar intensity.
106 Specificity of the test was 100% (CI 95% 93.4-100) with no cross reactivity observed with
107 endemic coronavirus and other infections tested as well as with high level of rheumatic
108 factors known to be a frequent cause of false positive. Specificity of ASIA was tested on the
109 same samples and was also 100% (CI 95% 93.4-100). Among the 106 samples screened, no
110 indeterminate reading required a third reading and all tests were valid according to the control
111 line.

112

113 Discussion

114 In this study, the performance characteristics of OG were evaluated and showed a
115 specificity of 100% and a sensitivity of 95.8% for samples collected ≥ 10 days after onset of
116 symptoms or since positive PCR. This rapid test performance was equivalent to Abbott
117 SARS-CoV-2 IgG assay. This immunoassay sensitivity was 90.5% in our study and 82.4% in
118 a recent publication for samples collected ≥ 10 days after onset of symptoms (4). In that same
119 study, sensitivity was found to be 100% for samples collected ≥ 17 days after onset of
120 symptoms. However, using the 17-days cut-off to evaluate our data, we found a sensitivity of
121 94.9% (IC95% 85.9-98.9). This difference could be explained by a different patient
122 population. Indeed, IgG were not detected with ASIA for samples collected ≥ 10 days from
123 onset of symptoms or since PCR positivity compared to OG in 6 patients, all with mild
124 symptoms, including 5 from occupational health. Bryan *et al.* report their serum specimens
125 came mostly from hospitalized patients and thus probably from patients with a severe or
126 critical disease (4). Furthermore, our population was younger with a mean age of 52 while
127 65.6% were older than 60 in Bryan *et al.* In our study, all patients with IgG detected only with
128 OG were <40 years old. Younger patients may have a different immunoglobulin synthesis
129 kinetics and/or have lower levels of Ab. The ability of this rapid test to detect IgM

concomitantly to IgG is a substantial advantage and global sensitivity was increased compared to ASIA to assess seroreactivity to SARS-CoV-2. OG also performs better than other rapid tests evaluated (5, 6). OG performance characteristics were also assessed very recently in the United Kingdom and showed a sensitivity of 100% for samples collected ≥ 13 days after onset of symptoms. Specificity was 96%, in contrast to the 100% specificity we found (6).

Overall, it is necessary to remind that both tests described here measure seroreactivity, which may or may not reflect immunity. OG characteristics are suitable for routine use in clinical laboratories for patients with onset of symptoms ≥ 10 days ago and performance is equivalent to ASIA. Testing this lateral flow assay on a larger asymptomatic population may be needed to confirm our results. OG could certainly help clinical microbiologists and governments at estimating the number of people who have been infected and provide an acceptable product to be used in outpatient and home settings.

Conflict of interest

The authors declare no conflict of interest.

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155 Zucman S, Cassonnet S, Celli Lebras K, Chabert J, Chaix ML, Chevret S, Clément M,
156 Davoine C, De Castro N, De Kerviler E, De Margerie-Mellon C, Delaugerre C, Depret F,
157 Denis B, Djaghout L Dupin C, Farge-Bancel D, Fauvaux C Feredj E, Feyeux D, Fontaine JP,
158 Fremeaux-Bacchi V, Galicier L, Harel S, Jegu AL Kozakiewicz E Lebel M Baye A, Le Goff
159 J, Le Guen P, Lengline E, Liegeon G, Lorillon G, Madelaine Chambrin I, Martin de Frémont
160 G, Meunier Martine, Molina JM, Morin F, Oksenhendler E, Peffault de la Tour R, Peyrony
161 O, Plaud B, Salmona M, Saussereau J, Soret J.

162 References

- 163 1. **Tang Y-W, Schmitz JE, Persing DH, Stratton CW.** 2020. The Laboratory Diagnosis
164 of COVID-19 Infection: Current Issues and Challenges. *J Clin Microbiol* 1–22.
- 165 2. **Petherick A.** 2020. World Report Developing antibody tests for SARS-CoV-2. *The*
166 *Lancet* **395**:1101–1102.
- 167 3. **Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, Sandt CE, Jia X,**
168 **Nicholson S, Catton M, Cowie B, Tong SYC, Lewin SR, Kedzierska K.** 2020.
169 Breadth of concomitant immune responses prior to patient recovery: a case report of
170 non-severe COVID-19. *Nat Med* 1–10.
- 171 4. **Bryan A, Pepper G, Wener MH, Fink SL, Morishima C, Chaudhary A, Jerome**
172 **KR, Mathias PC, Greninger AL.** 2020. Performance Characteristics of the Abbott
173 Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *J Clin Microbiol*
174 1–19.
- 175 5. **Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, Sun R, Wang Y, Hu B, Chen W, Zhang Y,**
176 **Wang J, Huang B, Lin Y, Yang J, Cai W, Wang X, Cheng J, Chen Z, Sun K, Pan**
177 **W, Zhan Z, Chen L, Ye F.** 2020. Development and Clinical Application of A Rapid
178 IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. *J Med Virol*
179 *jmv.25727–7.*
- 180 6. **Pallett S, Denny S, Patel A, Charani E, Mughal N, Stebbing J, Davies G, Moore L.**
181 2020. Point-of-care serological assays for SARS-CoV-2 in a UK hospital population:
182 potential for enhanced case. *ResearchSquare Preprint*. Doi:10.21203/rs.3.rs-28006/v1

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184 **Table 1. Clinical characteristics of 102 patients with a positive SARS-COV-2 RT-PCR**

185	Characteristics	n (%) Total n=102
	Male	59 (57.8)
	Disease severity	
	Asymptomatic	2 (1.9)
	Mild	37 (36.3)
	Severe (Medical Unit)	35 (34.3)
	Critical (ICU)	28 (27.5)
	Patients with ≥ 2 consecutive sera	4 (3.9)
186	Mean age of the patient population was 52 ($\pm$ 16)	
187	ICU: Intensive care unit	

188 **Figure 1.** Percentage of Orient Gene tests displaying IgM alone, IgG alone or both IgM and IgG
189 according to days from onset of symptoms

190 **Figure 2.** Results global overview of 106 serum samples from patients with a positive SARS-COV-2
191 RT-PCR tested for IgG with Abbott SARS-CoV-2 IgG assay, IgG and IgM with Orient Gene *Rapid*
192 *Test Cassette* (OG). Data are shown according to days from onset of symptom. Positive tests are
193 represented by gray row, negative tests by white rows. *discrepancy between IgG with OG and ASIA,
194 **only positive with IgM on OG. Colored boxes represent samples from the same patients (n=4).



