

Figure S1: GII.4 Sydney_2012 noroviruses present two predominant polymerase types, [P16] and [P31]. (A) Yearly distribution of all GII.4 Sydney_2012 sequences (n= 1237) available in public databases (11), from which the polymerase types were sequenced and characterized. (B) Phylogenetic tree of the major capsid protein (VP1) from GII.4 Sydney_2012 noroviruses. The tips of the time-scaled phylogenetic tree were color-coded based on the polymerase type presented by every viral sequence. The analyses were done using 1449 complete (or near-complete) sequences of Sydney_2012 noroviruses. The phylogenetic trees were calculated as indicated in Figure 1 and the Materials and Methods section.

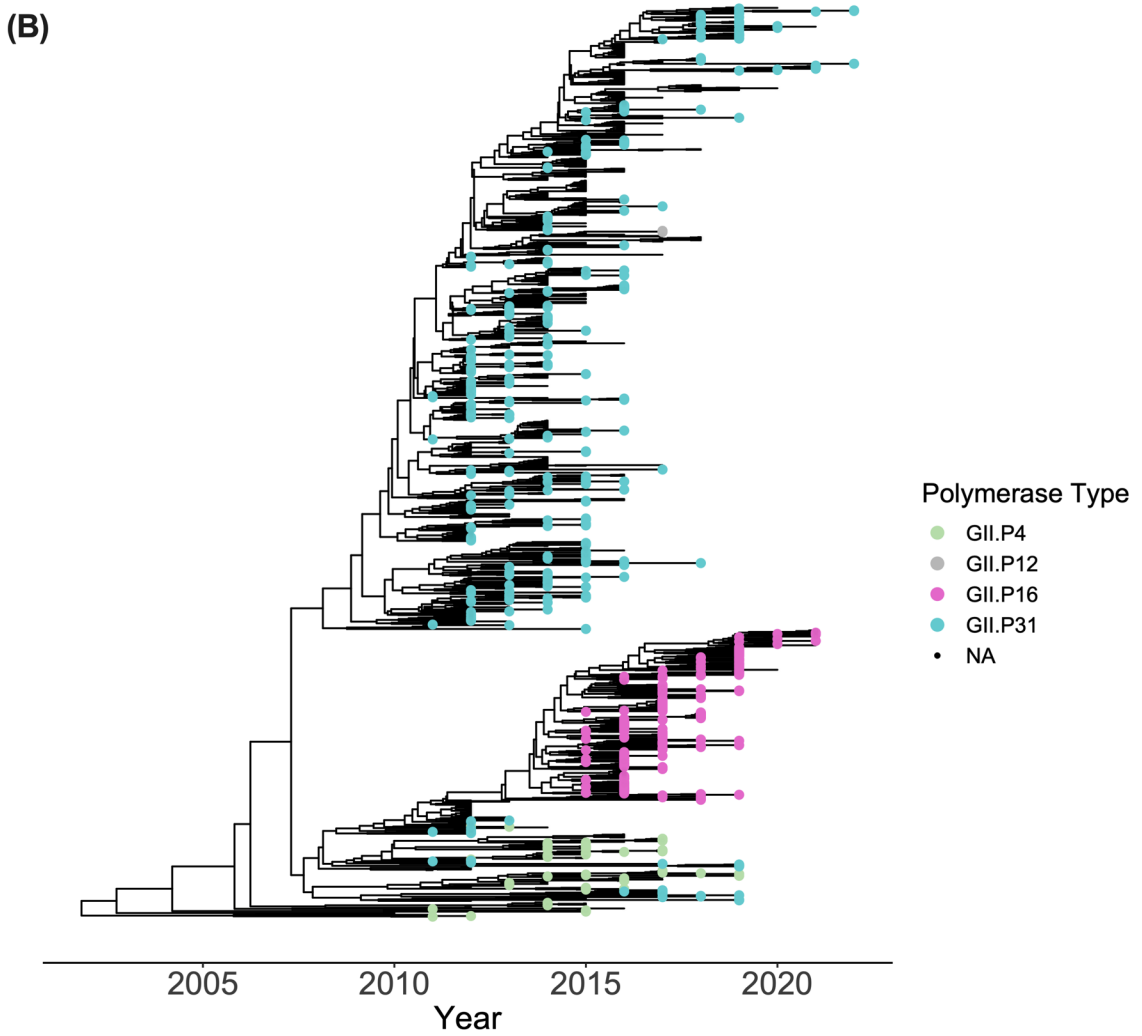
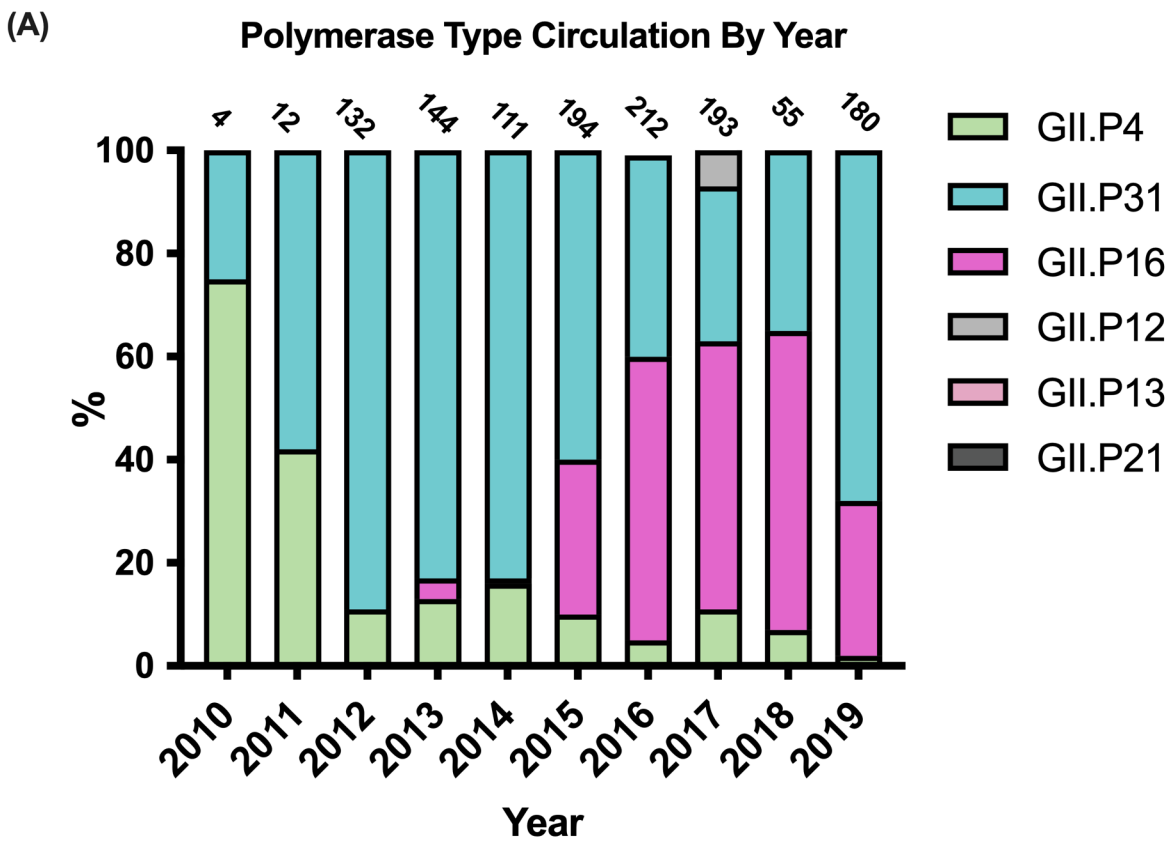


Figure S2: Temporal analyses of divergence of GII.4 Sydney_2012 noroviruses. Root-to-tip divergence of nucleotide sequences on the maximum-likelihood tree was calculated using the same dataset used for time-scaled phylogenetic tree reconstruction from Figure 1.

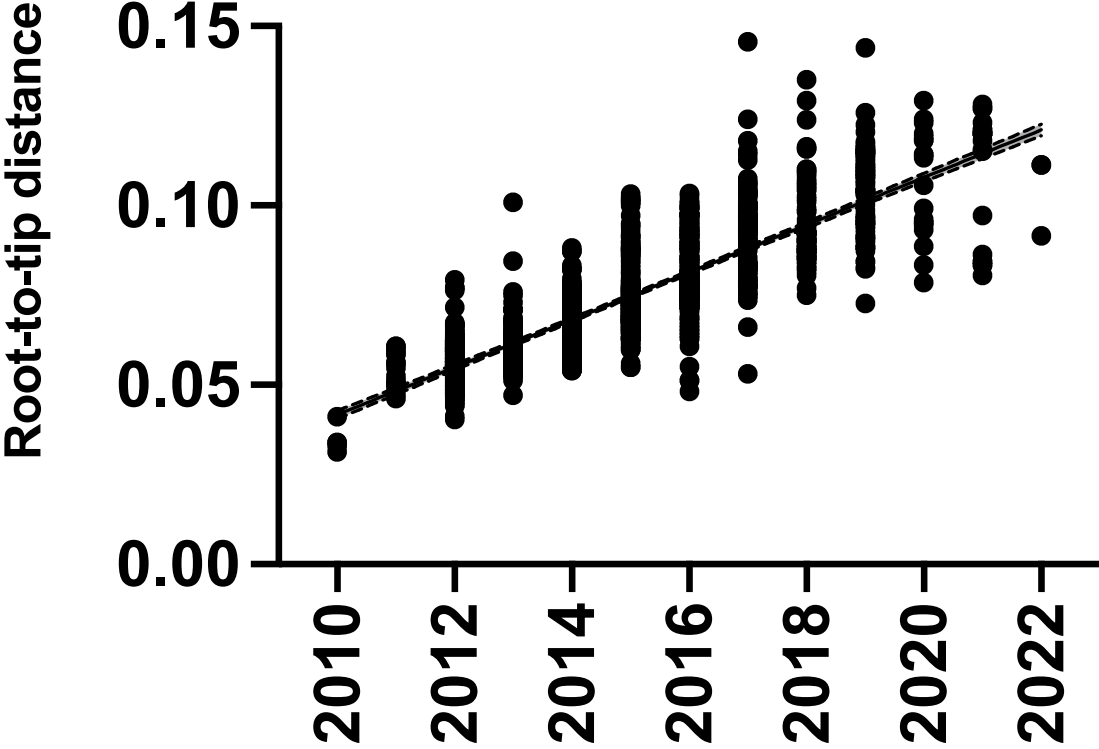


Figure S3: Polyclonal sera responses to wild-type and mutant VLPs from animals immunized with RockvilleD1/US/2012 VLPs and the MD2004-3/US/2004 (a Farmington_Hills_2002 virus) VLPs. Normalized curves are shown for each mouse serum. The EC50 from each curve was used to plot the heatmap from Figure 7B.

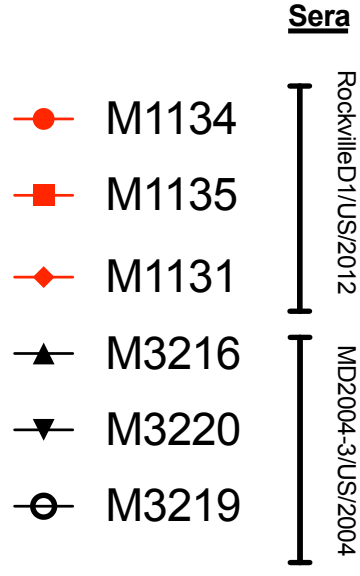
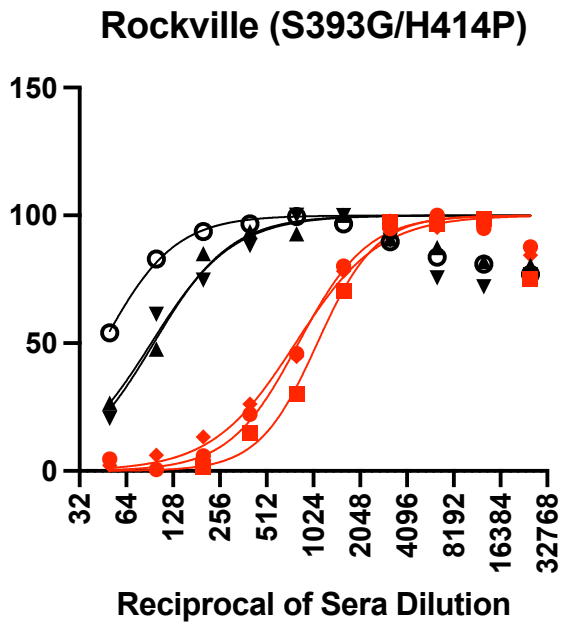
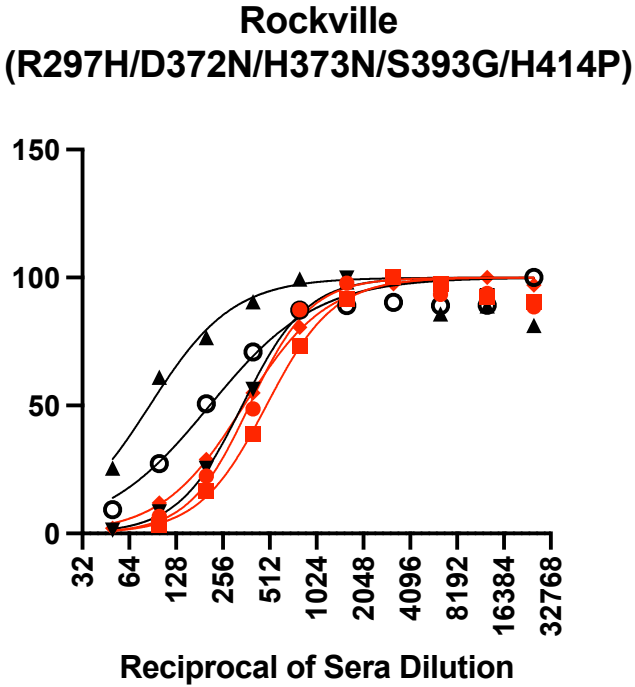
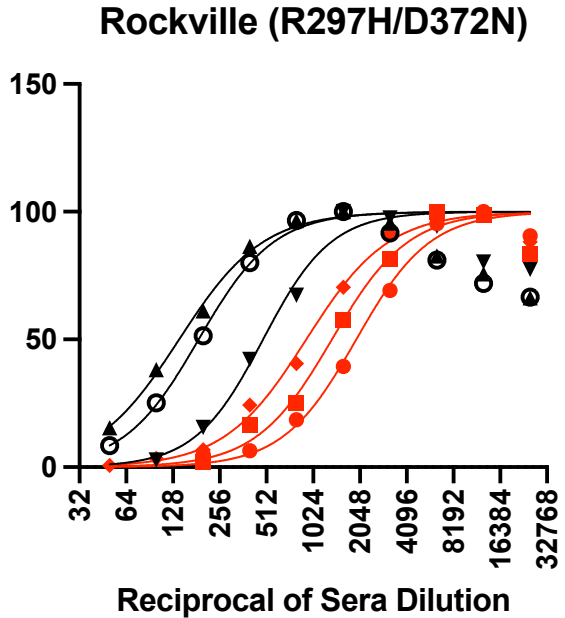
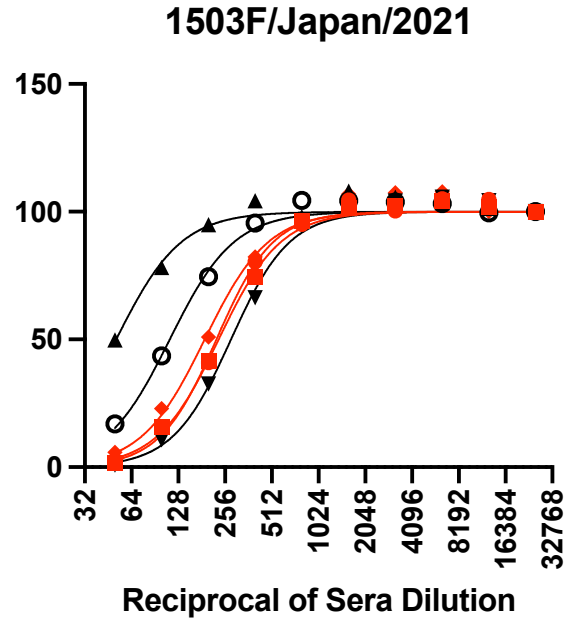
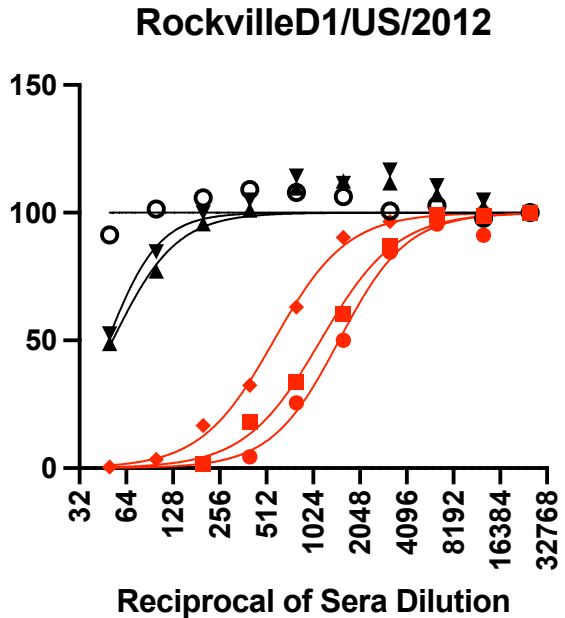
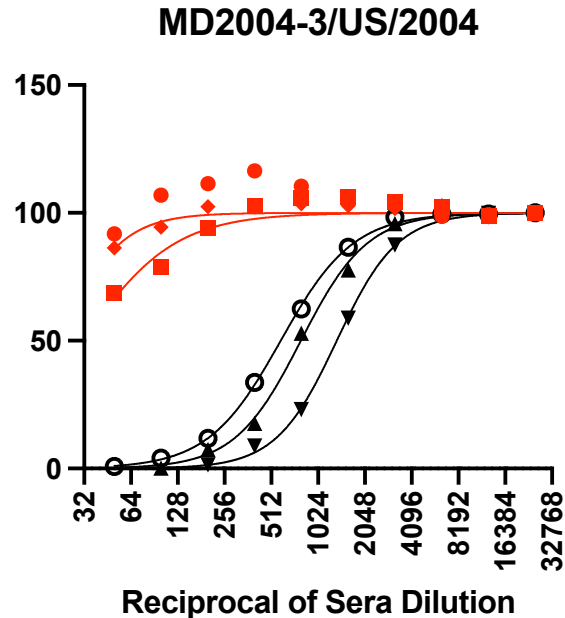


Figure S4: Three-dimensional model of the P domain of GII.4 norovirus VP1 showing the variable antigenic sites. The structural model of the P domain dimer was acquired from the Protein Database (PDB: 2OBS) and the figure was rendered using UCSF Chimera.

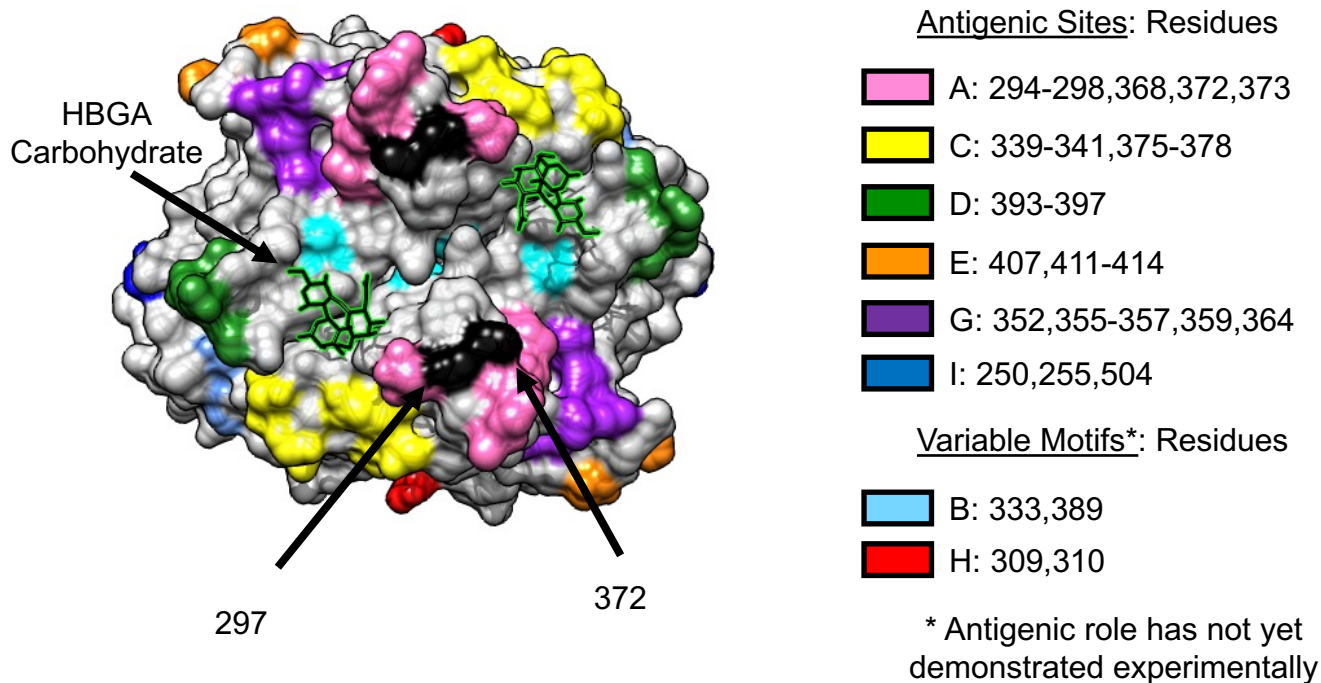


Table S1: Country and year of detection from Sydney 2012 viruses included in this study

Continent	Country	Years														Total
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022		
Americas	Argentina			1		4	1	5	1						12	
	Brazil			3	5	6	4	2							20	
	Canada		1	1	1	1	6	3	1	2	11				27	
	Mexico							3	1						4	
	Paraguay							5							5	
	Peru				3	2									5	
	United_States		1	38	26	19	47	34	57	22	2				246	
Africa	Botswana							1	9	1					11	
	Cambodia						1								1	
	Egypt							4							4	
	Kenya										5				5	
	South_Africa	2	2	5	8										17	
Asia	Bangladesh			4											4	
	Bhutan			7			1								8	
	China			20	14	11	86	131	7	20	22	9	14		334	
	Hong_Kong			3	1	145	23	1	15						188	
	India				3					8	30				41	
	Indonesia							8							8	
	Japan		11	68	31	16	1	4	4		3	8	7	3	156	
	Nepal				2	1									3	
	South_Korea			1	1										2	
	Taiwan			16	6	4	2	18		1					47	
	Thailand						1		4	24	5	3			37	
Viet_Nam				2	1	4								7		
Europe	France			7	1	2									10	
	Germany					15		1							16	
	Hungary						1								1	
	Italy		1	2	1										4	
	Netherlands			2		1									3	
	Russia			1				3	2	1					7	
	Spain							3			3				6	
	United_Kingdom				4	29	36	6							75	
Oceania	Australia			47	8	6	10	15	17						103	
	New_Zealand	3		29											32	
	Total	5	16	255	117	263	224	247	118	79	81	20	21	3	1449	

Table S2. Sequence dataset

No	Accession Number	Strain	Country	Year	Polymerase Type
1	AB972466	Hokkaido4	Japan	2012	GII.P31
2	AB972467	Aomori2	Japan	2012	GII.P31
3	AB972468	Aomori3	Japan	2012	GII.P31
4	AB972469	Aomori5	Japan	2012	GII.P31
5	AB972470	Akita4	Japan	2012	GII.P31
6	AB972472	Iwate4	Japan	2012	GII.P31
7	AB972473	Iwate5	Japan	2012	GII.P31
8	AB972475	Saitama2	Japan	2012	GII.P31
9	AB972477	Niigata4	Japan	2012	GII.P31
10	AB972478	Fukui3	Japan	2012	GII.P31
11	AB972479	Fukui4	Japan	2012	GII.P31
12	AB972480	Fukui6	Japan	2012	GII.P31
13	AB972481	Fukui7	Japan	2012	GII.P31
14	AB972482	Fukui8	Japan	2012	GII.P31
15	AB972483	Ehime5	Japan	2012	GII.P31
16	AB972484	OsakaCity1	Japan	2012	GII.P31
17	AB972485	OsakaCity2	Japan	2012	GII.P31
18	AB972487	Sakai1	Japan	2012	GII.P31
19	AB972488	Sakai2	Japan	2012	GII.P31
20	AB972489	Sakai3	Japan	2012	GII.P31
21	AB972490	Sakai4	Japan	2012	GII.P31
22	AB972491	Sakai5	Japan	2012	GII.P31
23	AB972492	Shimane3	Japan	2012	GII.P31
24	AB972493	Shimane5	Japan	2012	GII.P31
25	AB972494	Hiroshima4	Japan	2012	GII.P31
26	AB972495	Hiroshima5	Japan	2012	GII.P31
27	AB972496	HiroshimaCity3	Japan	2012	GII.P31
28	AB972497	HiroshimaCity4	Japan	2012	GII.P31
29	AB972498	Ehime3	Japan	2012	GII.P31
30	AB972499	GII4-HK01	Japan	2011	GII.P31
31	AB972502	GII4-NG1242	Japan	2011	GII.P31
32	AB972503	GII4-NG1315	Japan	2011	GII.P31
33	AB972504	GII4-NG1343	Japan	2011	GII.P31
34	AB972505	GII4-NG1365	Japan	2011	GII.P31
35	AB972507	Hokkaido3	Japan	2012	NA
36	AB972508	Hokkaido5	Japan	2012	NA
37	AB972510	Aomori4	Japan	2012	NA
38	AB972512	Akita2	Japan	2012	NA
39	AB972516	Aichi2	Japan	2012	NA
40	AB972517	Aichi3	Japan	2012	NA
41	AB972518	Aichi4	Japan	2012	NA
42	AB972519	Aichi5	Japan	2012	NA
43	AB972520	Aichi6	Japan	2012	NA
44	AB972521	Ehime4	Japan	2012	NA
45	AB972522	Niigata2	Japan	2012	NA
46	AB972523	Toyama1	Japan	2012	NA
47	AB972524	Toyama3	Japan	2012	NA
48	AB972526	Fukui5	Japan	2012	NA

49	AB972527	OsakaCity3	Japan	2012	NA
50	AB972528	Hiroshima1	Japan	2012	NA
51	AB972529	Hiroshima2	Japan	2012	NA
52	AB972530	Hiroshima3	Japan	2012	NA
53	AB972531	Shimane1	Japan	2012	NA
54	AB972532	Shimane2	Japan	2012	NA
55	AB972533	Shimane4	Japan	2012	NA
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59	KC175323	Hong_Kong	Hong Kong	2012	GII.P31
60	KC243078	Taichung	Taiwan	2012	NA
61	KC456070	VP1172	China	2012	NA
62	KC456071	VP1214	China	2012	NA
63	KC456072	VP1281	China	2012	NA
64	KC456073	VP1451	China	2012	NA
65	KC473544	Huzhou121	China	2012	NA
66	KC473545	Huzhou122	China	2012	NA
67	KC473546	Huzhou128	China	2012	NA
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232	KM268082	CUHK-NS-237	Hong Kong	2014	NA
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234	KM268084	CUHK-NS-264	Hong Kong	2014	NA
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246	KM268096	CUHK-NS-292	Hong Kong	2014	NA
247	KM268097	CUHK-NS-295	Hong Kong	2014	NA
248	KM268098	CUHK-NS-296	Hong Kong	2014	NA
249	KM268099	CUHK-NS-297	Hong Kong	2014	NA
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256	KM268106	CUHK-NS-307	Hong Kong	2014	NA

257	KM268107	CUHK-NS-309	Hong Kong	2014	NA
258	KM272334	gg-12-08-04	South Korea	2012	GII.P31
259	KM396961	CUHK-NS-339	Hong Kong	2014	NA
260	KM406485	E10082_La_Fleche	France	2013	NA
261	KM514057	CUHK-NS-311	Hong Kong	2014	NA
262	KM514058	CUHK-NS-312	Hong Kong	2014	NA
263	KM514059	CUHK-NS-313	Hong Kong	2014	NA
264	KM514060	CUHK-NS-315	Hong Kong	2014	NA
265	KM514061	CUHK-NS-316	Hong Kong	2014	NA
266	KM514062	CUHK-NS-317	Hong Kong	2014	NA
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279	KM514075	CUHK-NS-332	Hong Kong	2014	NA
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1346	MW711330	NICED-BCH-12017	India	2019	GII.P16
1347	MW711332	NICED-BCH-12074	India	2019	GII.P16
1348	MW711333	NICED-BCH-12083	India	2019	GII.P16

1349	MW711334	NICED-BCH-12085	India	2019	GII.P16
1350	MW711335	NICED-BCH-12109	India	2019	GII.P16
1351	MW711336	NICED-BCH-12112	India	2019	GII.P16
1352	MW711337	NICED-BCH-12118	India	2019	GII.P16
1353	MW711338	NICED-BCH-12150	India	2019	GII.P16
1354	MW711339	NICED-BCH-12157	India	2019	GII.P16
1355	MW711340	NICED-BCH-12172	India	2019	GII.P16
1356	MW711341	NICED-BCH-12187	India	2019	GII.P16
1357	MW725358	NIC-NV-390	India	2018	GII.P16
1358	MW725359	NIC-NV-1415	India	2019	GII.P16
1359	MW725360	IDH-11218	India	2018	GII.P16
1360	MW725361	IDH-11405	India	2018	GII.P16
1361	MW725362	IDH-12747	India	2019	GII.P16
1362	MW726099	BCH-8930	India	2018	GII.P16
1363	MW726100	BCH-9662	India	2018	GII.P16
1364	MW981327	HY-1	China	2019	GII.P31
1365	MZ376651	2012	United Kingdom	2014	NA
1366	MZ478136	G4_11	Mexico	2016	GII.P16
1367	MZ478139	G9_4.5	Mexico	2016	GII.P16
1368	MZ478140	G11_6	Mexico	2016	GII.P16
1369	MZ478141	G19_10	Mexico	2017	GII.P16
1370	MZ546176	Norozj-2	China	2016	GII.P31
1371	MZ546177	Norozj-4	China	2016	GII.P31
1372	MZ546178	Norozj-5	China	2016	GII.P31
1373	MZ546179	Norozj-6	China	2016	GII.P31
1374	MZ546180	Norozj-7	China	2016	GII.P31
1375	MZ546181	Norozj-8	China	2016	GII.P31
1376	MZ546183	Norozj-10	China	2016	GII.P31
1377	MZ958411	Nizhny_Novgorod	Russia	2017	GII.P16
1378	OK148516	GZ19	China	2018	NA
1379	OL336342	12121164	China	2012	NA
1380	OL336343	13023130	China	2013	NA
1381	OL336344	14051034	China	2014	NA
1382	OL336345	15023071	China	2015	NA
1383	OL336346	16121024	China	2016	NA
1384	OL336347	17121019	China	2017	NA
1385	OL336348	18023157	China	2018	NA
1386	OL336349	1914Y151	China	2019	NA
1387	OL336350	20011115	China	2020	NA
1388	OL336351	2105Y0824	China	2021	NA
1389	OL336352	2105Y1677	China	2021	NA
1390	OL336353	2105Y1888	China	2021	NA
1391	OL336354	2105Y1889	China	2021	NA
1392	OL336355	2105y1919	China	2021	NA
1393	OL336356	2105Y1920	China	2021	NA
1394	OL336357	2105Y1922	China	2021	NA
1395	OL336358	20051042	China	2020	NA
1396	OL336359	21011037	China	2021	NA
1397	OL336360	20121007	China	2020	NA
1398	OL336361	20153074	China	2020	NA
1399	OL336362	2005Y130	China	2020	NA
1400	OL336363	21121067	China	2021	NA

1401	OL336364	1908Y813	China	2019	NA
1402	OL336365	21161058	China	2021	NA
1403	OL336366	21161051	China	2021	NA
1404	OL336367	20161008	China	2020	NA
1405	OL336382	19121200	China	2019	GII.P16
1406	OL336383	20062001	China	2020	GII.P16
1407	OL336384	20051046	China	2020	GII.P16
1408	OL336385	21063054	China	2021	GII.P16
1409	OL336386	1915Y216	China	2019	GII.P16
1410	OL336387	20153072	China	2020	GII.P16
1411	OL336388	21161049	China	2021	GII.P16
1412	OL336389	21051018	China	2021	GII.P16
1413	OL546296	14051141	China	2014	NA
1414	OL721917	P6	China	2017	GII.P31
1415	OL898508	Rochester14691	United States	2015	GII.P31
1416	OL898509	Nashville13076	United States	2015	GII.P31
1417	OL898510	Nashville13089	United States	2015	GII.P31
1418	OL898511	Cincinnati10188	United States	2015	GII.P31
1419	OL898512	Kansas11006	United States	2015	GII.P16
1420	OL898514	Kansas0843	United States	2016	GII.P16
1421	OL898515	Kansas1621	United States	2017	GII.P16
1422	OL898516	Kansas0853	United States	2017	GII.P4
1423	OL913976	Houston11006	United States	2015	GII.P31
1424	OL913977	Houston11136	United States	2015	GII.P31
1425	OM368933	FS159	China	2018	GII.P31
1426	OM372476	FS161-2	China	2018	GII.P31
1427	OM372477	FS163	China	2018	GII.P31
1428	OM372478	FS167	China	2018	GII.P31
1429	OM372479	FS168	China	2018	GII.P31
1430	OM372480	FS177	China	2018	GII.P31
1431	OM372481	FS178	China	2018	GII.P31
1432	OM372485	FS560	China	2019	GII.P31
1433	OM372490	FS744	China	2019	GII.P31
1434	OM372672	FS180	China	2018	GII.P31
1435	OM372682	FS192	China	2018	GII.P31
1436	OM373200	FS203	China	2018	GII.P31
1437	OM373207	FS236	China	2018	GII.P31
1438	OM373210	FS241	China	2018	GII.P31
1439	OM373317	FS257	China	2018	GII.P31
1440	OM373532	FS273	China	2018	GII.P31
1441	OM373624	FS290	China	2018	GII.P31
1442	OM373643	FS303	China	2018	GII.P31
1443	OM373654	FS480	China	2019	GII.P31
1444	OM386670	FS578	China	2019	GII.P31
1445	OM386814	FS686	China	2019	GII.P31
1446	OM386843	FS759	China	2019	GII.P31
1447	OM980238	3915VLC	Spain	2019	GII.P31
1448	OM980239	3973VLC	Spain	2019	GII.P31
1449	OM980240	4008ALC	Spain	2019	GII.P4
