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canadian Immunohistochemistry Quality control

Assessor's report for cIQc Run 30: ER, PR and HER2

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Assessment performed on Tuesday, July 23, 2013, at St. Paul's Hospital

Overview

Similar to Run 22, participating laboratories were asked to stain a tissue microarray consisting of nine formalin-fixed, paraffin-embedded cell lines. Two cores from each cell line were included on the tissue microarray. ER, PR and HER2 mRNA expression levels were previously quantified by RT-PCR, providing an independent method of assessment to be used as a reference (R1) in the study.

Overall, self-assessments from participating labs were good. If slides were returned to cIQc in time for the assessment meeting in Vancouver, were blindly reviewed by two assessors (NM and JG). For Labs 148, 155 and 172, all cores stained for ER and PR were re-assessed due to the unexpectedly high proportion of unsatisfactory cores originally reported by self-assessment. Independent review led to infrequent alteration of original self-reported results for certain discordant cores due to 1) an obvious data entry error, 2) contamination from potential transfer of cells during coring and TMA construction or 3) a core score was deemed to be discordant between self-assessment and final cIQc review and re-classified as either positive or negative.

ER: Cores 2, 5, 7, 11, 14 and 16 were comprised of ER positive cell lines based on mRNA expression levels and immunohistochemistry in most participating labs. Slides were unavailable for re-assessment from Labs 124, 136 and 159. Only cytoplasmic staining (not nuclear staining) was noted in Core 2 from Labs 155, 156, 167 and 198. Therefore, Core 2 was confirmed to be false negative against the reference result in Labs 155, 156, 167, 177 and 198 by independent review. For Core 11, false-negative ER staining was also observed from Labs 155, 156, 167, 177, 180, 187 and 198. A majority of these false-negative cores possessed cytoplasmic background staining that ranged from weak to strong. In general, Cores 2 and 11 were noted by the assessors to be potential indicators of sensitivity of ER staining in participating lab.

Based on self-assessment, Labs 122, 159 and 188 showed more frequent false-positive staining of ER negative cell lines, indicating a potential specificity issue. However, microscopic contamination from transfer of cells during TMA construction was suspected to be responsible for false-positive staining observed in Cores 10, 12, 13 and 15, which each possessed few positive cells restricted to the periphery. As a result, these cores originally scored by self-assessment as ER positive in a group of labs were re-classified as unsatisfactory for evaluation after independent review and excluded from the further analysis.

Table with 18 rows (Cores) and 31 columns (Labs). Legend: P Positive, N Negative, U Unsatisfactory.

Overall Run 30 Conclusions

In general, our second attempt to use cell lines for breast cancer biomarker proficiency testing was successful, providing further encouraging results and revealing potential caveats of the approach. Please note that Supplementary Tables 1 to 3 summarizing kappa agreement values, sensitivity and specificity of each participating laboratory can be found at the end of this document. Quality control methodologies of immunohistochemical assessment are evolving, and numeric results should be interpreted with this reservation. Annual summary statistics may become more valid and precise, as the assessment sample size increases for each laboratory.

Your regular participation in cIQc is greatly appreciated and we look forward to working with you and the Canadian Association of Pathologists – Association Canadienne des Pathologistes in the future as we continue to improve our external quality assurance services.

Table S1. ER descriptive statistics based on corrected self-assessments

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	Cohen's kappa
101	18	100	18	18/18 (100%)	1	1	1
102	18	100	18	18/18 (100%)	1	1	1
103	18	100	18	18/18 (100%)	1	1	1
105	18	100	18	18/18 (100%)	1	1	1
106	18	100	18	18/18 (100%)	1	1	1
107	18	100	18	18/18 (100%)	1	1	1
109	18	100	18	18/18 (100%)	1	1	1
111	18	100	18	18/18 (100%)	1	1	1
112	18	100	18	18/18 (100%)	1	1	1
113	18	100	18	18/18 (100%)	1	1	1
114	18	100	18	18/18 (100%)	1	1	1
115	18	100	18	18/18 (100%)	1	1	1
116	18	100	18	18/18 (100%)	1	1	1
117	18	100	18	18/18 (100%)	1	1	1
119	18	100	18	18/18 (100%)	1	1	1
120	18	94.44	17	17/17 (100%)	1	1	1
122	18	100	18	15/18 (83%)	1	0.75	0.67
123	18	94.44	17	17/17 (100%)	1	1	1
124	18	100	18	16/18 (89%)	0.67	1	0.73
125	18	100	18	18/18 (100%)	1	1	1
126	18	100	18	18/18 (100%)	1	1	1
127	18	100	18	18/18 (100%)	1	1	1
128	18	100	18	18/18 (100%)	1	1	1
129	18	100	18	18/18 (100%)	1	1	1
132	18	100	18	18/18 (100%)	1	1	1
133	18	100	18	18/18 (100%)	1	1	1
134	18	100	18	18/18 (100%)	1	1	1
135	18	100	18	18/18 (100%)	1	1	1
136	18	100	18	17/18 (94%)	0.83	1	0.87
138	18	100	18	18/18 (100%)	1	1	1
139	18	100	18	18/18 (100%)	1	1	1
141	18	100	18	18/18 (100%)	1	1	1
143	18	100	18	18/18 (100%)	1	1	1
144	18	100	18	18/18 (100%)	1	1	1
145	18	83.33	15	15/15 (100%)	1	1	1
147	18	83.33	15	15/15 (100%)	1	1	1
148	18	100	18	18/18 (100%)	1	1	1
149	18	100	18	18/18 (100%)	1	1	1
150	18	88.89	16	16/16 (100%)	1	1	1
151	18	100	18	18/18 (100%)	1	1	1
152	18	100	18	18/18 (100%)	1	1	1
153	18	100	18	18/18 (100%)	1	1	1
155	18	72.22	13	11/13 (85%)	0.67	1	0.68
156	18	88.89	16	13/16 (81%)	0.67	0.9	0.59
157	18	100	18	18/18 (100%)	1	1	1
159	18	88.89	16	13/16 (81%)	1	0.7	0.64
160	18	88.89	16	16/16 (100%)	1	1	1
161	18	83.33	15	14/15 (93%)	1	0.89	0.86
162	18	100	18	18/18 (100%)	1	1	1
163	18	77.78	14	14/14 (100%)	1	1	1
164	18	88.89	16	16/16 (100%)	1	1	1
165	18	100	18	18/18 (100%)	1	1	1
167	18	100	18	16/18 (89%)	0.67	1	0.73
168	18	100	18	18/18 (100%)	1	1	1
170	18	100	18	18/18 (100%)	1	1	1
172	18	100	18	18/18 (100%)	1	1	1
173	18	100	18	18/18 (100%)	1	1	1
175	18	100	18	18/18 (100%)	1	1	1
177	18	100	18	16/18 (89%)	0.67	1	0.73
178	18	88.89	16	16/16 (100%)	1	1	1
179	18	100	18	18/18 (100%)	1	1	1
180	18	100	18	17/18 (94%)	0.83	1	0.87
183	18	100	18	18/18 (100%)	1	1	1
184	18	94.44	17	17/17 (100%)	1	1	1
186	18	100	18	18/18 (100%)	1	1	1
187	18	100	18	17/18 (94%)	0.83	1	0.87
188	18	100	18	14/18 (78%)	1	0.67	0.57
189	18	100	18	18/18 (100%)	1	1	1
190	18	100	18	18/18 (100%)	1	1	1
191	18	100	18	18/18 (100%)	1	1	1
192	18	100	18	18/18 (100%)	1	1	1
194	18	88.89	16	16/16 (100%)	1	1	1
198	18	100	18	16/18 (89%)	0.67	1	0.73
199	18	100	18	18/18 (100%)	1	1	1
200	18	100	18	18/18 (100%)	1	1	1
202	18	100	18	18/18 (100%)	1	1	1

Table S2. PR descriptive statistics based on corrected self-assessments

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	Cohen's kappa
101	18	100	18	18/18 (100%)	1	1	1
102	18	100	18	18/18 (100%)	1	1	1
103	18	100	18	18/18 (100%)	1	1	1
105	18	100	18	18/18 (100%)	1	1	1
106	18	100	18	18/18 (100%)	1	1	1
107	18	100	18	18/18 (100%)	1	1	1
109	18	100	18	18/18 (100%)	1	1	1
111	18	100	18	18/18 (100%)	1	1	1
112	18	100	18	18/18 (100%)	1	1	1
113	18	100	18	18/18 (100%)	1	1	1
114	18	100	18	18/18 (100%)	1	1	1
115	18	88.89	16	15/16 (94%)	1	0.9	0.87
116	18	100	18	18/18 (100%)	1	1	1
117	18	100	18	18/18 (100%)	1	1	1
119	18	100	18	18/18 (100%)	1	1	1
120	18	100	18	18/18 (100%)	1	1	1
122	18	100	18	18/18 (100%)	1	1	1
123	18	88.89	16	16/16 (100%)	1	1	1
124	18	100	18	18/18 (100%)	1	1	1
125	18	100	18	18/18 (100%)	1	1	1
126	18	100	18	18/18 (100%)	1	1	1
127	18	100	18	18/18 (100%)	1	1	1
128	18	100	18	18/18 (100%)	1	1	1
129	18	100	18	17/18 (94%)	1	0.92	0.88
132	18	100	18	18/18 (100%)	1	1	1
133	18	100	18	18/18 (100%)	1	1	1
134	18	100	18	18/18 (100%)	1	1	1
135	18	100	18	18/18 (100%)	1	1	1
136	18	100	18	18/18 (100%)	1	1	1
138	18	100	18	18/18 (100%)	1	1	1
139	18	100	18	18/18 (100%)	1	1	1
141	18	100	18	18/18 (100%)	1	1	1
143	18	100	18	18/18 (100%)	1	1	1
145	18	83.33	15	15/15 (100%)	1	1	1
146	18	100	18	18/18 (100%)	1	1	1
147	18	100	18	18/18 (100%)	1	1	1
149	18	100	18	18/18 (100%)	1	1	1
150	18	94.44	17	16/17 (94%)	1	0.91	0.88
151	18	100	18	18/18 (100%)	1	1	1
152	18	100	18	18/18 (100%)	1	1	1
153	18	100	18	18/18 (100%)	1	1	1
155	18	100	18	17/18 (94%)	1	0.92	0.88
156	18	77.78	14	14/14 (100%)	1	1	1
157	18	77.78	14	14/14 (100%)	1	1	1
159	18	83.33	15	10/15 (67%)	1	0.44	0.39
160	18	83.33	15	15/15 (100%)	1	1	1
161	18	66.67	12	12/12 (100%)	1	1	1
162	18	100	18	18/18 (100%)	1	1	1
163	18	83.33	15	13/15 (87%)	1	0.78	0.74
164	18	94.44	17	17/17 (100%)	1	1	1
165	18	100	18	16/18 (89%)	1	0.83	0.77
167	18	100	18	18/18 (100%)	1	1	1
168	18	100	18	18/18 (100%)	1	1	1
170	18	100	18	18/18 (100%)	1	1	1
172	18	100	18	18/18 (100%)	1	1	1
173	18	100	18	15/18 (83%)	1	0.75	0.67
175	18	100	18	18/18 (100%)	1	1	1
177	18	100	18	18/18 (100%)	1	1	1
178	18	100	18	18/18 (100%)	1	1	1
179	18	100	18	18/18 (100%)	1	1	1
183	18	100	18	18/18 (100%)	1	1	1
184	18	94.44	17	17/17 (100%)	1	1	1
186	18	100	18	16/18 (89%)	1	0.83	0.77
187	18	100	18	18/18 (100%)	1	1	1
188	18	100	18	18/18 (100%)	1	1	1
189	18	100	18	18/18 (100%)	1	1	1
190	18	100	18	18/18 (100%)	1	1	1
191	18	100	18	18/18 (100%)	1	1	1
192	18	83.33	15	15/15 (100%)	1	1	1
194	18	94.44	17	17/17 (100%)	1	1	1
198	18	100	18	18/18 (100%)	1	1	1
199	18	100	18	18/18 (100%)	1	1	1
200	18	94.44	17	17/17 (100%)	1	1	1
202	18	100	18	18/18 (100%)	1	1	1

Table S3. HER2 descriptive statistics based on corrected self-assessments

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	Cohen's kappa
101	18	100	18	18/18 (100%)	1	1	1
102	18	100	18	18/18 (100%)	1	1	1
103	18	100	18	18/18 (100%)	1	1	1
105	18	100	18	18/18 (100%)	1	1	1
106	18	100	18	18/18 (100%)	1	1	1
107	18	100	18	18/18 (100%)	1	1	1
109	18	100	18	18/18 (100%)	1	1	1
110	18	100	18	18/18 (100%)	1	1	1
111	18	100	18	18/18 (100%)	1	1	1
112	18	100	18	18/18 (100%)	1	1	1
113	18	100	18	18/18 (100%)	1	1	1
114	18	100	18	18/18 (100%)	1	1	1
115	18	100	18	18/18 (100%)	1	1	1
116	18	100	18	18/18 (100%)	1	1	1
117	18	100	18	18/18 (100%)	1	1	1
119	18	100	18	18/18 (100%)	1	1	1
120	18	94.44	17	17/17 (100%)	1	1	1
123	18	100	18	18/18 (100%)	1	1	1
124	18	100	18	18/18 (100%)	1	1	1
125	18	100	18	18/18 (100%)	1	1	1
126	18	100	18	18/18 (100%)	1	1	1
127	18	100	18	18/18 (100%)	1	1	1
129	18	100	18	18/18 (100%)	1	1	1
133	18	100	18	18/18 (100%)	1	1	1
135	18	100	18	18/18 (100%)	1	1	1
136	18	83.33	15	15/15 (100%)	1	1	1
138	18	100	18	18/18 (100%)	1	1	1
139	18	77.78	14	14/14 (100%)	1	1	1
145	18	83.33	15	15/15 (100%)	1	1	1
147	18	100	18	18/18 (100%)	1	1	1
149	18	100	18	18/18 (100%)	1	1	1
150	18	94.44	17	17/17 (100%)	1	1	1
151	18	100	18	18/18 (100%)	1	1	1
152	18	100	18	18/18 (100%)	1	1	1
153	18	100	18	18/18 (100%)	1	1	1
155	18	83.33	15	15/15 (100%)	1	1	1
156	18	100	18	18/18 (100%)	1	1	1
157	18	83.33	15	15/15 (100%)	1	1	1
160	18	94.44	17	17/17 (100%)	1	1	1
161	18	83.33	15	15/15 (100%)	1	1	1
162	18	88.89	16	16/16 (100%)	1	1	1
164	18	100	18	18/18 (100%)	1	1	1
167	18	100	18	18/18 (100%)	1	1	1
170	18	100	18	18/18 (100%)	1	1	1
175	18	100	18	18/18 (100%)	1	1	1
179	18	100	18	18/18 (100%)	1	1	1
181	18	100	18	18/18 (100%)	1	1	1
186	18	100	18	18/18 (100%)	1	1	1
187	18	100	18	18/18 (100%)	1	1	1
188	18	88.89	16	16/16 (100%)	1	1	1
189	18	100	18	18/18 (100%)	1	1	1
190	18	100	18	18/18 (100%)	1	1	1
191	18	100	18	18/18 (100%)	1	1	1
194	18	100	18	18/18 (100%)	1	1	1
198	18	100	18	18/18 (100%)	1	1	1
199	18	100	18	18/18 (100%)	1	1	1
200	18	94.44	17	17/17 (100%)	1	1	1
202	18	100	18	18/18 (100%)	1	1	1