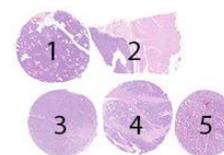


Material

The slide to be stained for SYP comprised:

1. Pancreas, 2. Colon, 3. Small cell lung carcinoma (SCLC), 4. Colon adenocarcinoma, 5. Neuroendocrine tumour



All tissues were fixed in 10% neutral buffered formalin.

Criteria for assessing SYP staining as optimal included:

- A strong, distinct cytoplasmic staining reaction of virtually all endocrine islet cells in the pancreas.
- A moderate to strong, distinct cytoplasmic staining reaction of neuroendocrine cells, ganglion cells and axons of the nerve plexus in the colon.
- A weak to moderate staining reaction of scattered goblet cells in the colon mucosa[#].
- An at least weak to moderate, distinct, cytoplasmic staining reaction of nerve fibers intermingling between exocrine cells in the pancreas and of peripheral nerves situated in lamina propria mucosa of the colon.
- An at least moderate, distinct, cytoplasmic staining reaction of virtually all neoplastic cells of the SCLC.
- A strong, distinct cytoplasmic staining reaction of virtually all neoplastic cells of the neuroendocrine tumour.
- No staining of neoplastic cells in the colon adenocarcinoma.

A weak to moderate cytoplasmic staining reaction of the exocrine pancreatic epithelial cells was accepted.

[#] Following the recommendations given by the International Ad Hoc Expert Committee (Appl Immunohistochem Mol Morphol. 2015 Jan;23(1):1-18.) strictly, the majority of goblet cells should display a weak to moderate staining intensity. This criterion was not in this run applied, since virtually no laboratory was able to obtain this reaction pattern.

Participation

Number of laboratories registered for SYP, run 52	317
Number of laboratories returning slides	308 (97%)

Results

308 laboratories participated in this assessment. 230 (75%) of these achieved a sufficient mark (optimal or good). Table 1 summarizes antibodies (Abs) used and assessment marks (see page 2).

The most frequent causes of insufficient staining were:

- Inefficient HIER (too short heating time or use of a non-alkaline buffer)
- Too low concentration of the primary antibody
- Less successful Ready-to-use (RTU) systems (PA0299/Leica and 760-4595/Ventana)
- Use of less sensitive detection systems
- Unexplained technical issues

Performance history

This was the sixth NordiQC assessment of SYP. The overall pass rate decreased compared to previous run 43 (2015) (see Table 2).

Table 2. **Proportion of sufficient results for SYP in the six NordiQC runs performed**

	Run 18 2006	Run 22 2008	Run 29 2010	Run 37 2013	Run 43 2015	Run 52 2018
Participants, n=	94	112	151	214	243	308
Sufficient results	68%	58%	55%	58%	82%	75%

Conclusion

The mAb clones **27G12**, **BS15**, **DAK-SYNAP** and **Snp88** and the rmAb clones **MRQ-40** and **SP11** could all be used to obtain an optimal staining reaction for SYP. Irrespective of clone applied, HIER in an alkaline buffer was mandatory for an optimal staining reaction, and concentration of the primary Ab must be carefully calibrated. The RTU systems IR660/GA660 (Agilent/Dako) based on the mAb DAK-SYNAP were the most successful assays obtaining a pass rate of 100%. The RTU systems PA0299 (Leica), based on the mAb 27G12, and 760-4595 (Roche/Ventana), based on the rmAb MRQ-40, both provided a low pass rate. No technical parameters could be identified explaining the relative inferior performance obtained with

these two assays. The use of 3-step polymer/multimer based detection systems, regardless of assay type applied, provided the highest proportion of sufficient and optimal results. Colon is still the most recommendable positive tissue control for SYP. Nerves of lamina propria muscularis must show a strong staining reaction while endocrine cells of the mucosa and nerve fibres of the lamina propria mucosa must show an at least weak to moderate staining reaction. In this assessment, only scattered goblet cells displayed the expected weak to moderate staining reaction.

Table 1. **Antibodies and assessment marks for SYP, run 52**

Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff. ¹	Suff. OPS ²
mAb clone 27G12	64	Leica/Novocastra						
	1	Biocare Medical						
	1	Monosan	13	36	15	3	73%	83%
	1	KliniPath						
mAb clone BS15	1	Nordic Biosite	1	0	0	0	-	-
mAb clone DAK-SYNAP	21	Agilent/Dako	12	6	1	2	86%	88%
mAb clone SNP88	7	Biogenex	1	2	4	0	43%	-
mAb clone SY38 ³	2	Dako	0	0	1	1	-	-
rmAb clone MRQ-40	6	Cell Marque	1	4	1	0	83%	-
rmAb clone SP11	11	Thermo/Neomarkers						
	5	Spring Bioscience						
	1	Abcam	6	5	7	0	61%	64%
	1	Invitrogen						
pAb 336A	1	Cell Marque	0	1	0	0	-	-
pAb RB-1461	1	Thermo/Neomarkers	0	0	0	1	-	-
Ready-To-Use antibodies								
mAb clone 27G12 PA0299	13	Leica/Novocastra	0	6	5	2	46%	-
mAb clone 27G12 PA0299 ⁴	2	Leica/Novocastra	0	0	2	0	-	-
mAb clone DAK-SYNAP IR660	31	Agilent/Dako	16	15	0	0	100%	100%
mAb clone DAK-SYNAP IR660 ⁴	19	Agilent/Dako	8	11	0	0	-	-
mAb clone DAK-SYNAP GA660	5	Agilent/Dako	3	2	0	0	100%	100%
mAb clone DAK-SYNAP GA660 ⁴	4	Agilent/Dako	4	0	0	0	-	-
mAb clone BS15 8453-C010	1	Sakura FineTek	1	0	0	0	-	-
mAb clone SNP88 AM363-10M ⁴	1	Biogenex	0	0	1	0	-	-
mAb clone SY38 IR/IS776 ³	1	Dako	0	1	0	0	-	-
rmAb MRQ-40 760-4595	43	Ventana/Cell Marque	6	22	13	2	65%	90%
rmAb clone MRQ-40 336R	12	Cell Marque	2	4	3	3	-	-
rmAb clone SP11 790-4407	48	Ventana	25	14	7	2	81%	96%
rmAb clone SP11 KIT-0022	1	Maixin	1	0	0	0	-	-
rmAb clone SP11 RMPD018	1	Diagnostic Biosystem	0	0	1	0	-	-
rmAb clone EP158 MAD-000685QD	2	Master Diagnostica	0	1	1	0	-	-
Total	308		100	130	62	16	-	
Proportion			33%	42%	20%	5%	75%	

1) Proportion of sufficient stains (optimal or good).

2) Proportion of sufficient stains with optimal protocol settings only, see below.

3) Product discontinued.

4) Ready-to-use product developed for a specific semi/fully automated platform by a given manufacturer but inappropriately applied by laboratories on other non-validated semi/fully automatic systems or used manually.

Detailed analysis of SYP, Run 52

The following protocol parameters were central to obtain optimal staining:

Concentrated antibodies

mAb clone **27G12**: Protocols with optimal results were all based on HIER using Target Retrieval Solution (TRS) pH 9 (3-in-1) (Dako) (3/11)*, Cell Conditioning 1 (CC1; Ventana) (7/32) or Bond Epitope Retrieval Solution 2 (BERS2; Leica) (3/15) as retrieval buffer. The mAb was typically diluted in the range of 1:25-1:100 depending on the total sensitivity of the protocol employed. Using these protocol settings, 43 of 52 (83%) laboratories produced a sufficient staining result (optimal or good).

* (number of optimal results/number of laboratories using this HIER buffer).

mAb clone **BS15**: One protocol with an optimal result was based on HIER in PT module for 20 min. using Tris-EDTA/EGTA pH 9 as retrieval buffer. The mAb was diluted 1:300 using a 3-step polymer-based detection system and performed on the Autostainer, LabVision.

mAb clone **DAK-SYNAP**: Protocols with optimal results were all based on HIER using TRS pH 9 (3-in-1) (Dako) (6/9), CC1 (Ventana) (3/7), BERS2 (Leica) (2/3) or Tris-EDTA/EGTA pH 9 (1/2) as retrieval buffer. The mAb was typically diluted in the range of 1:50-1:100 depending on the total sensitivity of the protocol employed. Using these protocol settings, 14 of 16 (88%) laboratories produced a sufficient staining result.

mAb clone **SNP88**: One protocol with an optimal result was performed on the Bond platform (Leica) using HIER in BERS2 (Leica) for 30 min. The mAb was diluted 1:50 using Bond Refine as detection system.

rmAb clone **MRQ-40**: One protocol with an optimal result was performed on the Benchmark Ultra platform (Ventana) using HIER in CC1 for 64 min. The rmAb was diluted 1:250 using Ultraview with amplification as detection system.

rmAb clone **SP11**: Protocols with optimal results were all based on HIER using CC1 (Ventana) (4/12) or Tris-EDTA/EGTA pH 9 (2/3) as retrieval buffer. The mAb was diluted in the range of 1:25-1:100 depending on the total sensitivity of the protocol employed. Using these protocol settings, 9 of 14 (64%) laboratories produced a sufficient staining result.

Table 3. Proportion of optimal results for SYP for the most commonly used antibodies as concentrates on the 4 main IHC systems*

Concentrated antibodies	Dako Autostainer Link / Classic		Dako Omnis		Ventana BenchMark XT / Ultra		Leica Bond III / Max	
	TRS pH 9.0	TRS pH 6.1	TRS pH 9.0	TRS pH 6.1	CC1 pH 8.5	CC2 pH 6.0	ER2 pH 9.0	ER1 pH 6.0
mAb clone 27G12	2/3**	0/1	1/8 (13%)	-	7/31 (23%)	-	3/10 (30%)	0/2
mAb clone DAK-SYNAP	2/4	-	2/2	-	3/6 (50%)	-	2/2	-
rmAb clone SP11	0/1	-	-	0/1	4/11 (36%)	-	-	-

* Antibody concentration applied as listed above, HIER buffers and detection kits used as provided by the vendors of the respective systems.

** (number of optimal results/number of laboratories using this buffer)

Ready-To-Use antibodies and corresponding systems

mAb clone **DAK-SYNAP**, product no. **IR660**, Dako, Autostainer+/Autostainer Link:

Protocols with optimal results were typically based on HIER in PT-Link using TRS pH 9 (3-in-1) (efficient heating time 10-20 min. at 97°C), 20-30 min. incubation of the primary Ab and EnVision FLEX/FLEX+ (K8000/K8002) as detection systems. Using these protocol settings, 29 of 29 (100%) laboratories produced a sufficient staining result.

mAb clone **DAK-SYNAP**, product no. **GA660**, Dako, Omnis:

Protocols with optimal results were typically based on HIER using TRS High pH 9 (GV804) (efficient heating time 30 min. at 97°C), 25 min. incubation of the primary Ab and EnVision FLEX+ (GV800/GV823+GV821) as detection system. Using these protocol settings, 3 of 3 (100%) laboratories produced a sufficient staining result (all assessed as optimal).

rmAb clone **MRQ-40**, product no. **760-4595**, Ventana, BenchMark XT, GX, ULTRA:

Protocols with optimal results were typically based on HIER using CC1 (efficient heating time 24-76 min.), 32-80 min. incubation of the primary Ab and UltraView (760-500) + amplification kit (760-080) or OptiView (760-700) as detection systems. Using these protocol settings, 19 of 21 (90%) laboratories produced a sufficient staining result.

rmAb clone **SP11**, product no. **790-4407**, Ventana, BenchMark XT, GX, ULTRA:
 Protocols with optimal results were typically based on HIER using CC1 (efficient heating time 32-76 min.), 32-72 min. incubation of the primary Ab and UltraView (760-500) + amplification kit (760-080) or OptiView (760-700) +/- amplification (760-099/860-099) as detection systems. Using these protocol settings, 22 of 23 (96%) laboratories produced a sufficient staining result.

Table 4 summarizes the proportion of sufficient and optimal marks for the most commonly used RTU systems. The performance was evaluated both as "true" plug-and-play systems performed strictly accordingly to the vendor recommendations and by laboratory modified systems changing basal protocol settings. Only protocols performed on the specific IHC stainer device are included.

Table 4. **Proportion of sufficient and optimal results for SYP for the most commonly used RTU IHC systems**

RTU systems	Recommended protocol settings*		Laboratory modified protocol settings**	
	Sufficient	Optimal	Sufficient	Optimal
Leica BOND MAX/III mAb 27G12 PA0299	40% (2/5)	0% (0/5)	50% (4/8)	0% (0/8)
Dako AS mAb DAK-SYNAP IR660	100% (14/14)	36% (5/14)	100% (17/17)	65% (11/17)
Dako Omnis mAb DAK-SYNAP GA660	3/3	3/3	2/2	0/2
VMS Ultra/XT/GX rmAb MRQ-40 760-4595	0/3	0/3	69% (27/39)	15% (6/39)
VMS Ultra/XT/GX rmAb SP11 790-4407	0/4	0/4	89% (39/44)	57% (25/44)

* Protocol settings recommended by vendor – Retrieval method and duration, Ab incubation times, detection kit, IHC stainer/equipment.

** Significant modifications: retrieval method, retrieval duration and Ab incubation time altered >25%, detection kit – only protocols performed on the specified vendor IHC stainer were included.

Comments

In concordance with the previous NordiQC assessments for SYP, the prevalent feature of an insufficient staining result was a too weak or completely false negative staining reaction of cells and structures expected to be demonstrated. This pattern was observed in 96% of the insufficient results (75 of 78). The remaining insufficient results were characterized by poor signal-to-noise ratio and/or false positive staining reaction compromising interpretation of the specific reactions.

Virtually all participating laboratories were able to stain SYP in cells with high-level expression as pancreatic endocrine cells and neoplastic cells of the neuroendocrine tumour (tissue core no. 5), whereas demonstration of SYP in endocrine cells of the colon crypts, in nerve fibers of the pancreas or in the lamina propria mucosa of the colon was more challenging and could only be demonstrated when applying optimized and appropriate protocol settings.

Optimal staining results could be obtained with the mAbs clones 27G12, BS15, DAK-SYNAP and SNP88 and the rmAb clones MRQ-40 and SP11 (see Table 1). Irrespective of the clone applied, HIER in an alkaline buffer was mandatory for optimal performance.

The mAb clones 27G12 and DAK-SYNAP was the most widely used antibodies for demonstration of SYP. Used as a concentrate in a laboratory developed (LD) assay, mAb clone 27G12 gave an overall pass rate of 73% (49 of 67). Although, as shown in Table 3, optimal results could be obtained on all four main IHC platforms, Omnis (Dako), Autostainer (Dako), Bond (Leica) and BenchMark (Ventana), the proportion of optimal results was low (e.g. 13% on the Omnis, Dako). As mentioned in the previous report (Run 43), the choice of detection system and titer of the primary Ab could significantly influence the overall performance of the analyses. In this assessment using the mAb 27G12 within a LD-assay, all protocols (100%, 13 of 13) giving an optimal mark were applying a 3-step multimer/polymer detection system (e.g. OptiView +/- amplification or Bond Refine). The average working dilution for mAb clone 27G12 was 1:57 (range 1:25 to 100). In comparison, and in the group of protocols assessed as insufficient (borderline or poor), the proportion of laboratories using a 3-step multimer/polymer was only 55% (11 of 20) and the average working dilution was 1:95 (range 1:10 to 200). Based on these observations and provided that efficient HIER in alkaline buffers has been performed, it is advisable to use a relative high concentration of the primary Ab in combination with a highly sensitive 3-step detection system with or without amplification.

The mAb DAK-SYNAP used within a LD-assay, gave an overall pass rate of 86% (18 of 21) of which 57% (12 of 21) were assessed as optimal. Also, mAb DAK-SYNAP provided optimal results on the four main IHC platforms (see Table 3). As for mAb 27G12, identical technical parameters influenced the performance of the mAb DAK-SYNAP and therefore, it is recommendable to use a sensitive 3-step detection system (with or without amplification) and carefully calibrate the titer of the primary Ab in relation to critical staining

indicators (e.g. endocrine cells in the colon crypts, peripheral nerves in lamina propria mucosa or goblet cells in colon epithelium).

As reported in the previous run 43, the mAb clone SNP88 occasionally gave an aberrant granular cytoplasmic staining reaction. In this run 52, this pattern was seen in 38% (3 of 8) of the submitted slides and especially pancreatic exocrine cells displayed this strong aberrant granular staining intensity. This atypical pattern is caused by the Mouse Ascites Golgi (MAG) reaction in blood type A tissue as described in the previous report.

The rmAb SP11 used within a LD-assay, gave an overall pass rate of 61% (11 of 18) of which 33% (6 of 18) were assessed as optimal. No significant technical parameters could be identified distinguishing insufficient from sufficient results. However, there was a tendency towards using higher concentrations of primary Ab (average working dilution of 1:64) in protocols assessed as optimal compared to protocols giving an insufficient mark (average working dilution of 1:84).

60% (184 of 308) of the laboratories used a Ready-To-Use (RTU) system for SYP. In this assessment, the RTU systems IR/GA660 based on mAb clone DAK-SYNAP (Dako) was the most successful assays for demonstration of SYP and provided a pass rate of 100% (36 of 36) of which 50% (18 of 36) were optimal. For the RTU system IR660 (Autostainer), both vendor and laboratory modified protocol settings could be used to produce an optimal result (see Table 4), but the proportion of optimal results was significant higher using laboratory modified protocol settings, typically substituting Envision Flex with Envision Flex+ as detection system.

The Ventana RTU system for the BenchMark IHC platform based on rmAb clone MRQ-40 (760-4595) provided an overall pass rate of 65% (28 of 43) and only 14% (6 of 43) were assessed as optimal. Compared to the results obtained in run 43, providing a pass rate of 97% (30 of 31) of which 74% (23 of 31) were optimal, this was a significant decline in the overall performance. The specific causes for this decrease in performance is difficult to identify as participants were applying similar protocol settings in both assessments for SYP.

The number of participants using laboratory modified protocol settings (see Table 4) may indicate that the assay is challenging. None of the 3 laboratories using the recommended protocol settings, provided by the company, could produce a sufficient result. The vast majority of laboratories modified their protocol settings on important parameters, providing an overall pass rate of 69% (27 of 39) of which 15% (6 of 39) were assessed as optimal. The overall performance was influenced by the choice of detection system.

Applying optimal protocol settings (see above), and using UltraView (760-500) + amplification kit (760-080) or OptiView (760-700) as detection systems, the pass rate was 90% (19 of 21) of which 24% (5 of 21) were optimal. In comparison, and applying exactly the same protocol settings, except for the use of UltraView without amplification as the detection system, the pass rate was only 29% (5 of 17) of which 6% (1 of 17) were optimal. One protocol assessed as optimal using the low sensitive detection system Ultraview, incubated in primary Ab for 120 min.

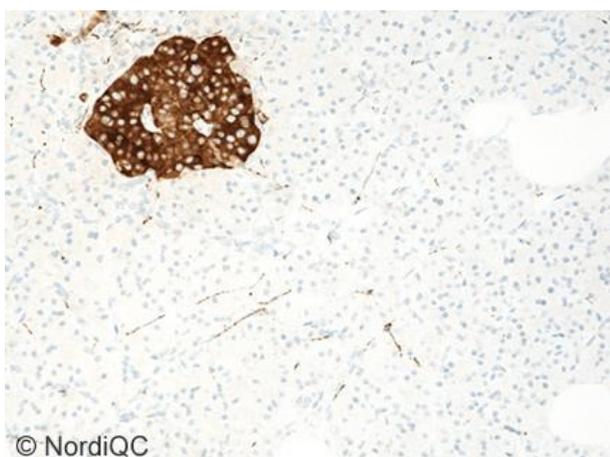
The Ventana RTU system based on rmAb clone SP11 (790-4407) provided an overall pass rate of 81% (39 of 48) of which 52% (25 of 48) were assessed as optimal. Optimal results could only be obtained by use of laboratory modified protocol settings (see Table 4) and best results was achieved applying a high sensitive detection system. Using optimal protocol settings (see above) and applying UltraView as the detection system, the pass rate was only 38% (3 of 8) and none (0 of 8) were assessed as optimal. Using exactly the same protocol settings except for the application of UltraView (760-500) + amplification kit (760-080) or OptiView (760-700) with or without amplification (760-099 / 860-099) as detection systems, the pass rate was 96% (22 of 23) of which 74% (15 of 23) were optimal.

The RTU system PA02999 based on mAb clone 27G12 (Leica) was used by 13 laboratories and as RTU system provided the lowest number of sufficient results. An overall pass rate of 46% (6 of 13) was seen and none (0 of 13) were optimal. Although applying protocol settings providing optimal results in previous assessments, the causes for the overall low performance in this run is unclear.

This was the sixth assessment of SYP in NordiQC (see Table 2). Although not using the recommendations strictly given by the International Ad Hoc Expert Committee (Appl Immunohistochem Mol Morphol. 2015 Jan;23(1):1-18.) (see criteria for assessing SYP staining as optimal) the pass rate dropped to 75% compared to a pass rate of 82% in run 43, 2015. Among laboratories participating for the first time (n=94), the pass rate was 63%. Although this was lower than the overall pass rate, it could not explain the overall decline in pass rate, since the pass rate among labs that also participated in run 43 (n=214) was 78%. However, unsolved problems with the RTU systems based on the mAb 27G12 (Leica) and rmAb MRQ-40 (Ventana) together with poorly calibrated LD-assay may account for the overall lower pass rate. Importantly, and provided that efficient HIER in alkaline buffer and careful calibration of primary Ab has been performed, the use of high sensitive 3-step polymer/multimer detection systems may improve the performance of the respective LD-assays or RTU systems.

Controls

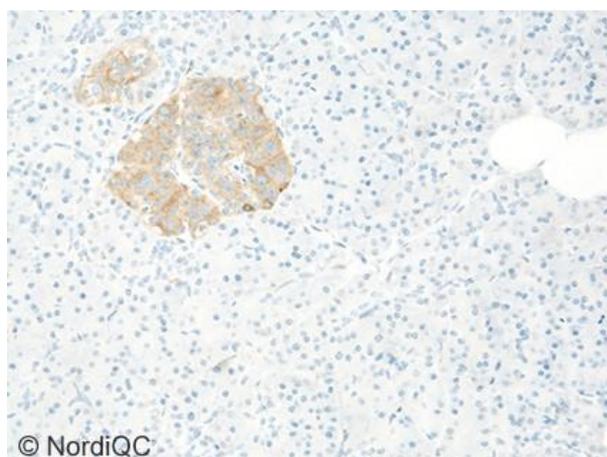
Colon is recommended as control for detection of SYP. The protocol must be calibrated to give an intense staining reaction of the axons of the Auerbach's and Meissner's plexus with a high-level expression of SYP. The endocrine cells of the mucosa and the peripheral nerves situated in lamina propria mucosa must show an at least weak to moderate staining reaction. In the former run 43, detection of the majority of epithelial goblet cells (weak to moderate intensity) was recommended as critical staining quality indicator for an optimal calibrated protocol. In this run, and in protocols assessed as optimal, only scattered goblet cells displayed this staining pattern. No staining must be seen in smooth muscle cells. From the recommendations of the international IHC ad hoc committee, pancreas (specifically Langerhans islets) is also recommended as positive tissue control. For this reason pancreas tissue was included in this run. Islet cells were in this run positive in both sufficient and insufficient staining reactions (although the staining intensity was weaker in insufficient staining reactions). However, peripheral nerve fibres intermingling between the exocrine cells were shown to be an excellent critical staining quality indicator. In this assessment, and if these nerve fibres were unstained, the protocols provided too low sensitivity causing false negative results. In addition, and since most other cells and structures in pancreas do not express synaptophysin, pancreas may be an easy control to interpret.



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Fig. 1a (x200)

Optimal staining of SYP in the pancreas using the rmAb clone SP11 (RTU 790-4407, Ventana), HIER in CC1 (64 min.) and OptiView (3-step multimer, Ventana) as detection system. Virtually all endocrine islet cells show a strong and distinct cytoplasmic staining reaction, and peripheral nerve fibres intermingling between exocrine cells displays a weak to moderate staining intensity. Same protocol used in Figs. 2a - 5a.

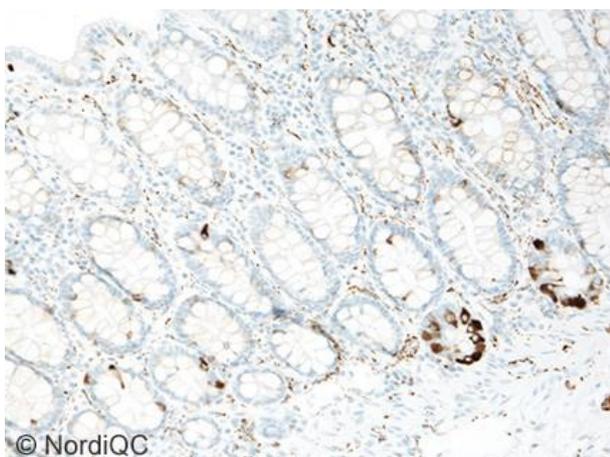


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Fig. 1b (x200)

Insufficient staining of SYP in the pancreas using a protocol with too low sensitivity – same field as in Fig. 1a.

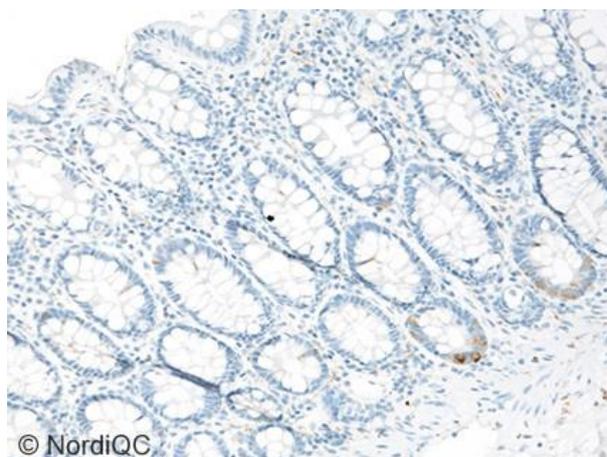
The protocol was based on the rmAb clone SP11 as concentrate, HIER in CC1 (64 min.) and the less sensitive UltraView (2-step multimer, Ventana) as the detection system. Same protocol used in Figs. 2b - 5b. The intensity of the endocrine cells is significantly reduced and the peripheral nerve fibres are completely negative. Compare with Fig. 1a.



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Fig. 2a (x200)

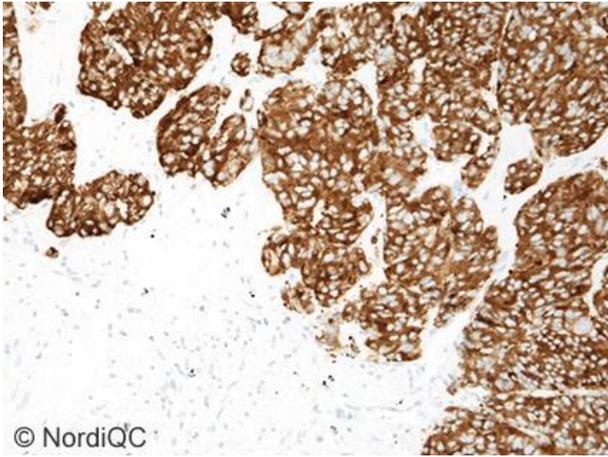
Optimal staining of SYP in the colon using same protocol as in Fig. 1a. The peripheral nerves in lamina propria mucosa show a weak to moderate staining intensity and neuroendocrine cells of the colon epithelium displays a strong, distinct cytoplasmic staining reaction. Scattered goblet cells show a weak to moderate cytoplasmic staining reaction.



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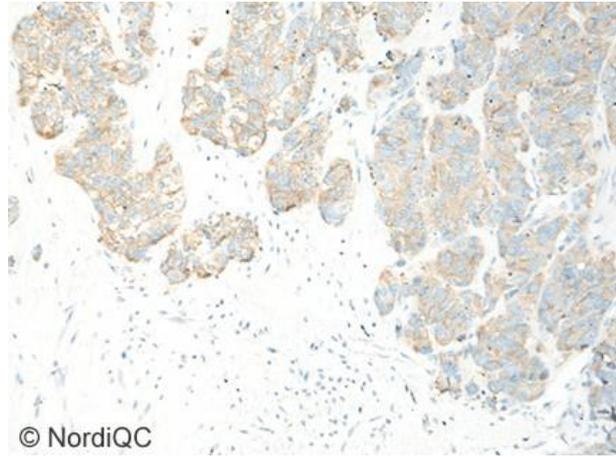
Fig. 2b (x200)

Insufficient staining of SYP in the colon using same protocol as in Fig. 1b – same field as in Fig. 2a. The peripheral nerves in lamina propria mucosa are virtually all negative or only faintly demonstrated, and proportion/staining intensity of the neuroendocrine cells is reduced. No staining reaction is seen in the goblet cells.



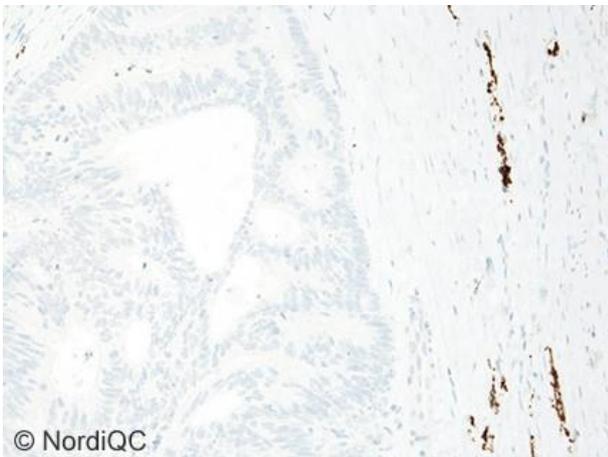
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Fig. 3a (x200)
Optimal staining of SYP in the SCLC using same protocol as in Figs. 1a and 2a. Virtually all neoplastic cells show a strong and distinct staining reaction. No background staining is seen.



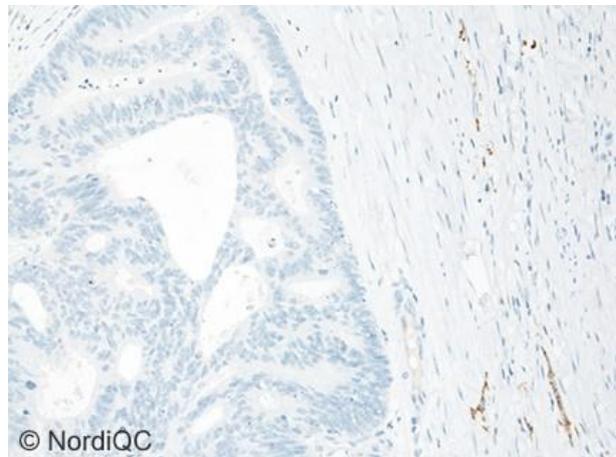
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Fig. 3b (x200)
Insufficient staining of SYP in the SCLC using same protocol as in Figs. 1b and 2b - same field as in Fig. 3a. The neoplastic cells display a too weak staining intensity.



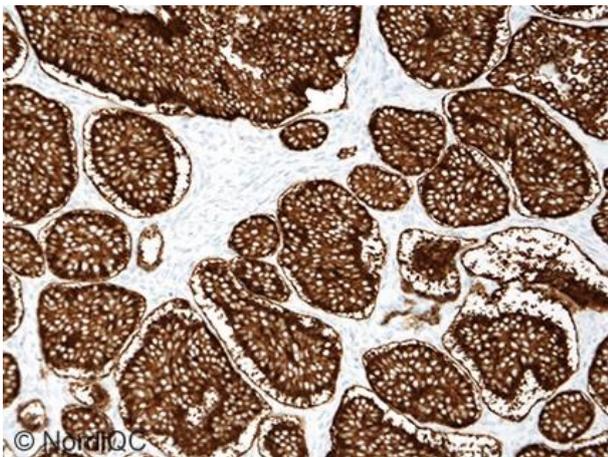
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Fig. 4a (x200)
Optimal staining of SYP in the colon adenocarcinoma using same protocol as in Figs. 1a - 3a. As expected, no staining of neoplastic cells is seen. The peripheral nerves in the stromal compartment show a strong and distinct cytoplasmic staining reaction.



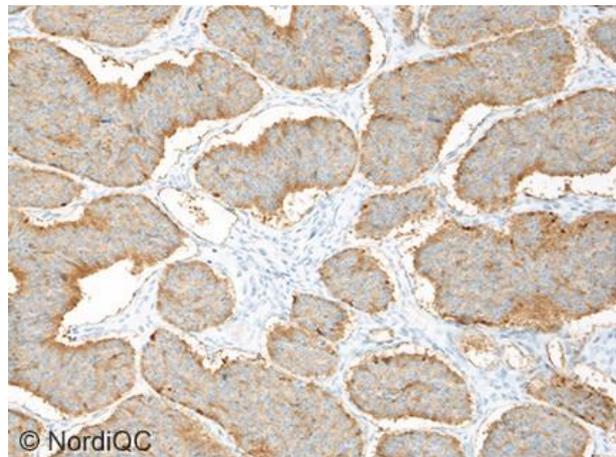
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Fig. 4b (x200)
Insufficient staining of SYP in the colon adenocarcinoma using same protocol as in Figs. 1b - 3b - same field as in Fig. 4a. The neoplastic cells are negative, but the peripheral nerves in the stromal compartment only display a faint to weak staining reaction.



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Fig. 5a. (x200)
Optimal staining of SYP in the neuroendocrine tumour using same protocol as in Figs. 1a - 4a. All neoplastic cells are strongly stained.



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Fig. 5b. (x200)
Insufficient staining of SYP in the neuroendocrine tumour - same field as in Fig. 5a. Although the neoplastic cells display moderate staining intensity, the protocol provides to low sensitivity - compare with Fig. 1a - 5b.

MB/LE/MV/RR 22.03.2018