



The role of immunochemistry in the SDHx mutations in pheochromocytomas and paragangliomas

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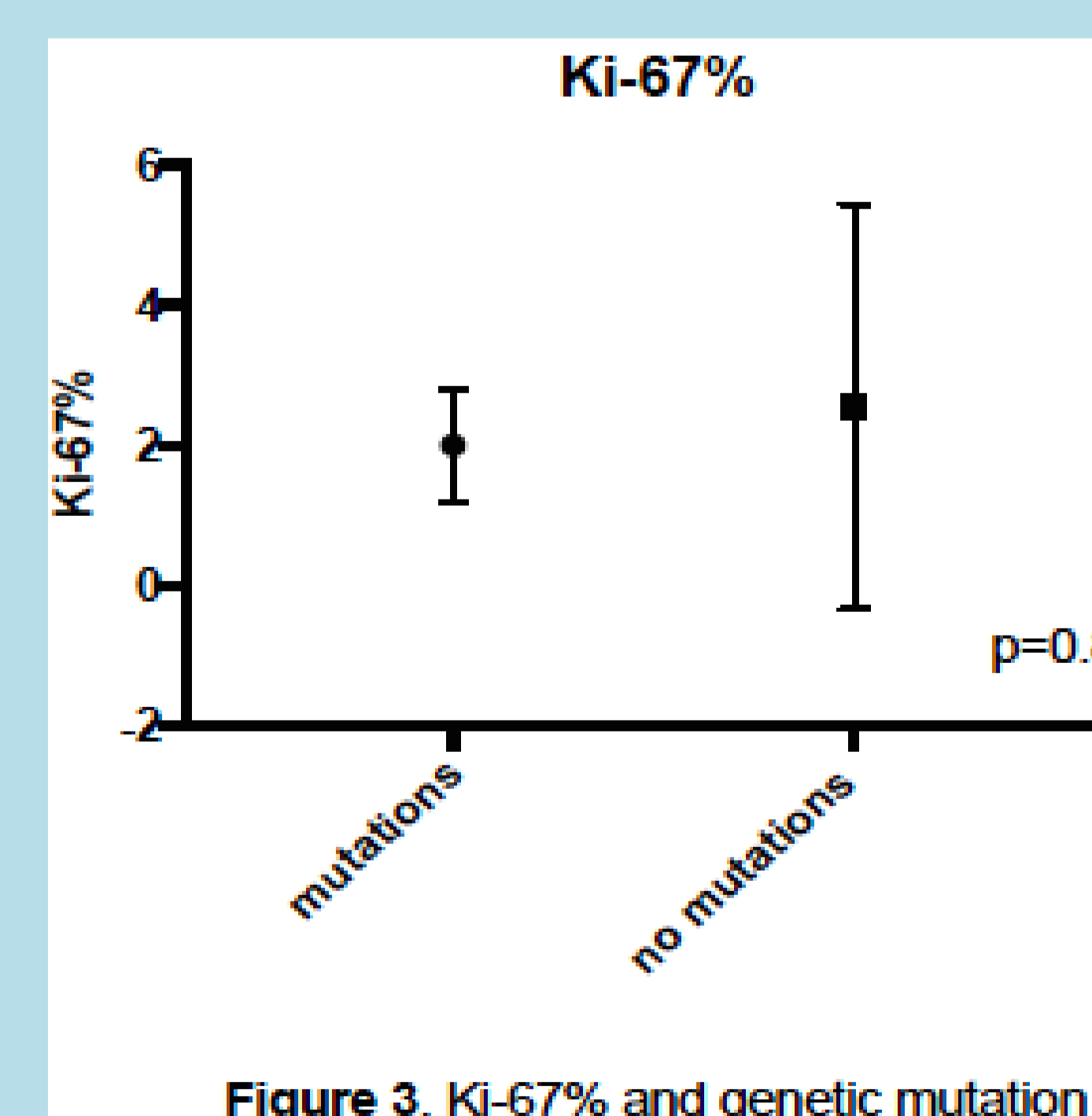
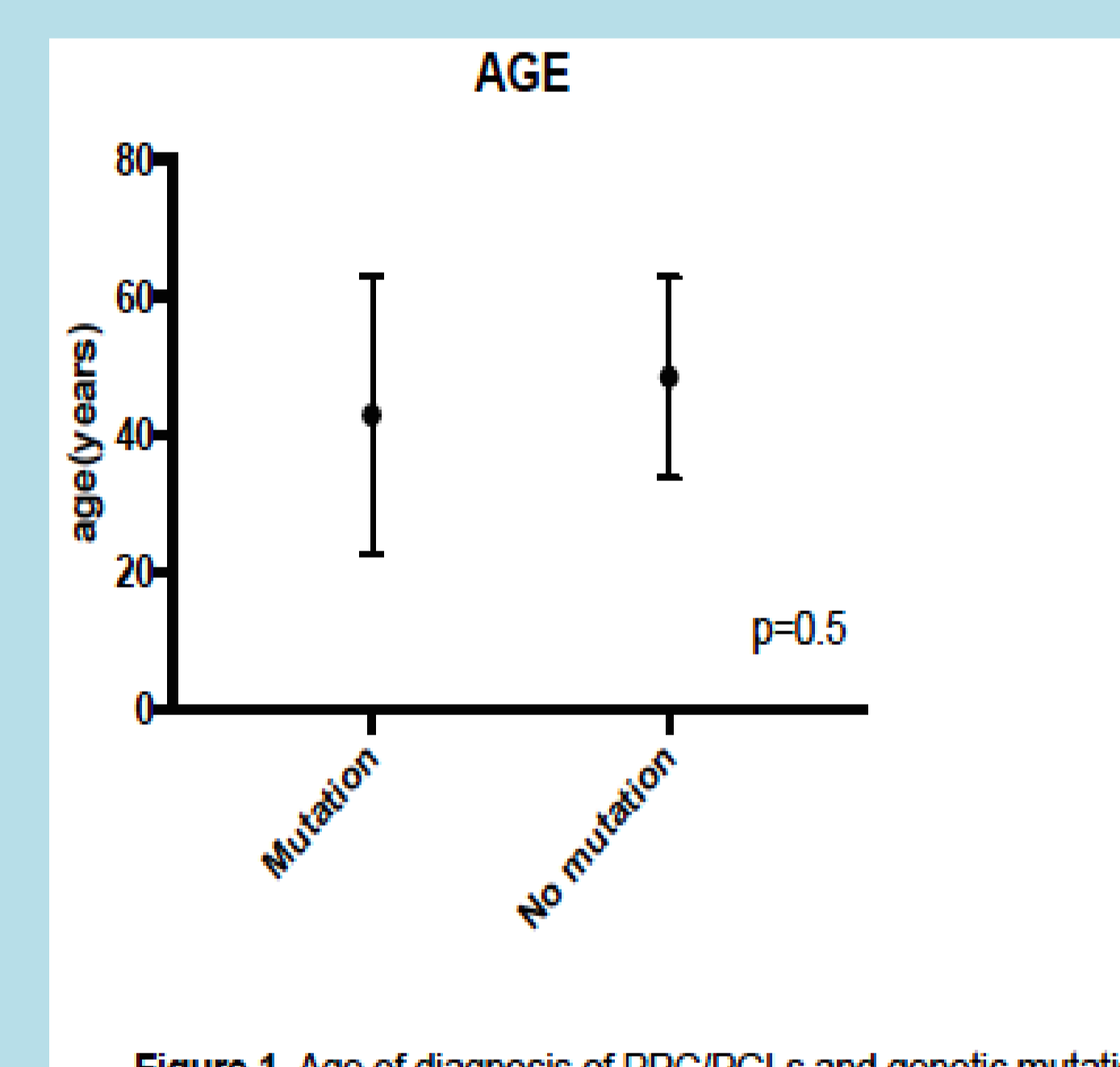
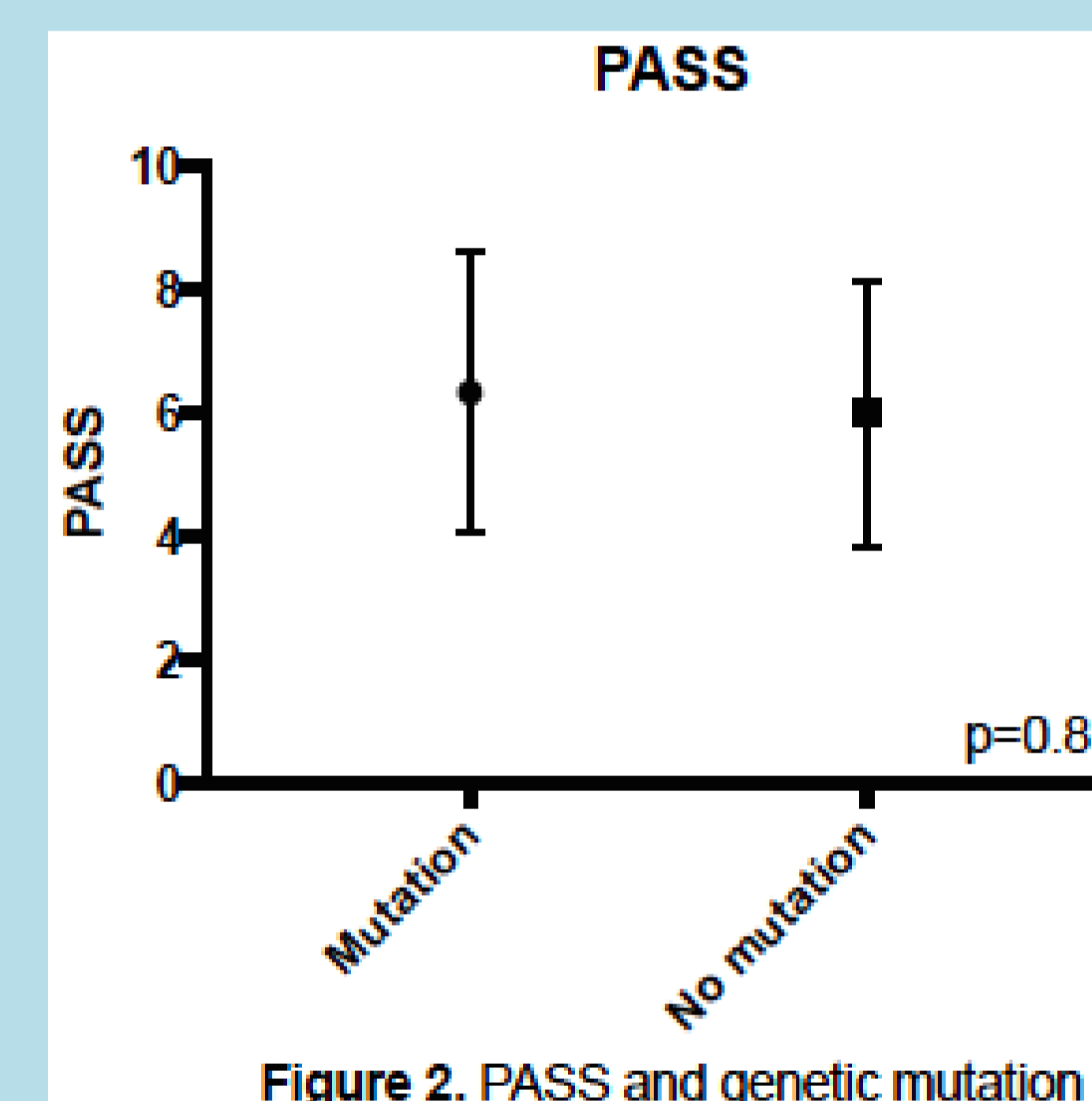
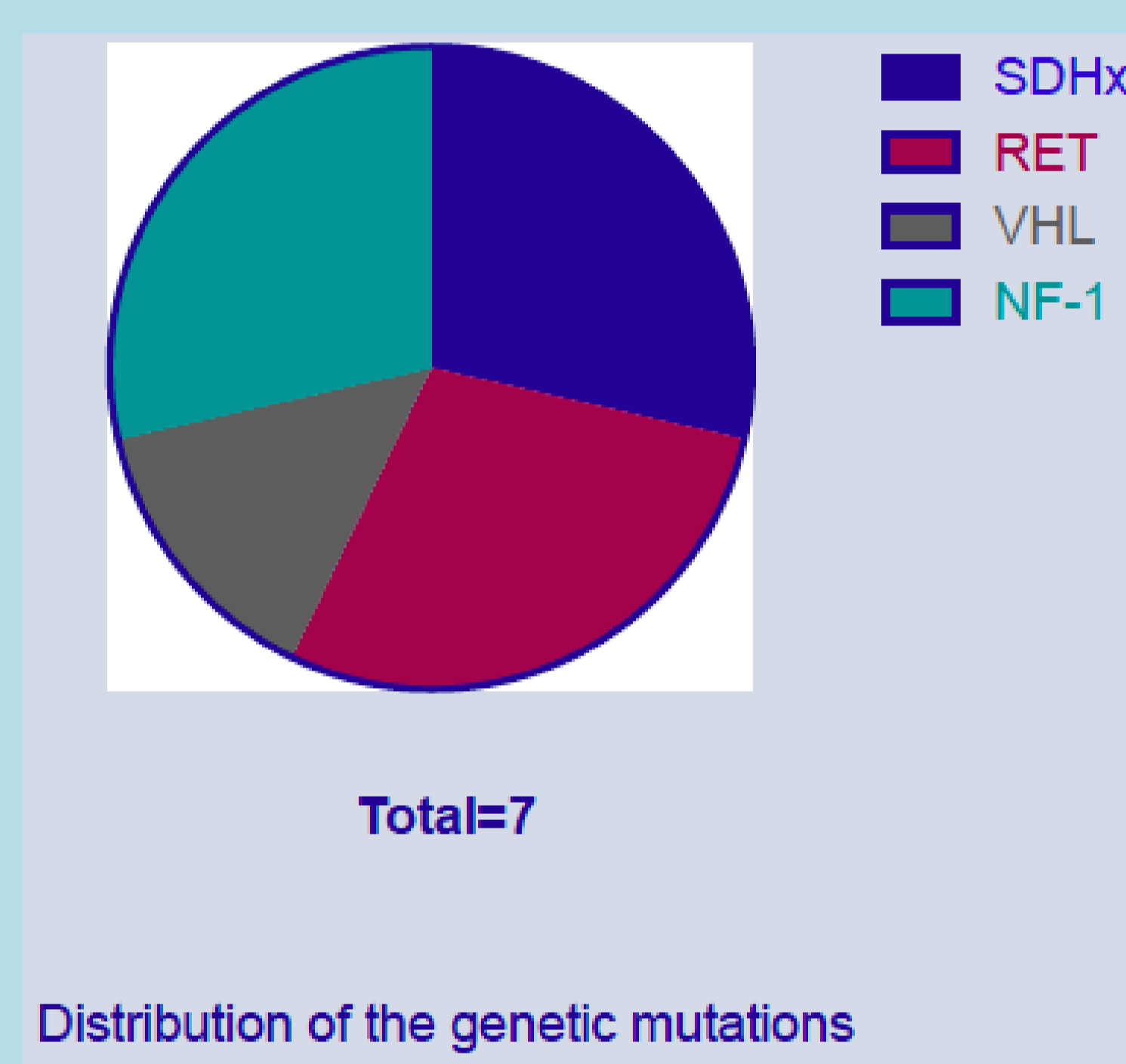
Introduction: Early detection of succinate dehydrogenase complex (SDH) mutations in patients with pheochromocytoma and paraganglioma (PPC/PGL) has important implications as when present the risk of malignancy is increased. The use of negative immunohistochemical (IHC) staining for SDH subunit B, D, A (SDHB/-D/-A) has been proposed as an indicator of SDHs mutation and as an effective substitute for the high-cost genetic screening of all of these genes.

Methods: We have performed SDHB/-D/-A and Ki-67% immunohistochemical staining in a series of 29 paraffin embedded PPCs/PGLs specimens. Screening for point mutations by direct Sanger sequencing was performed in germline DNA from patients with potential aggressive (PASS>6) PPC or metastatic PPCs at the initial diagnosis or in cases of PGLs.

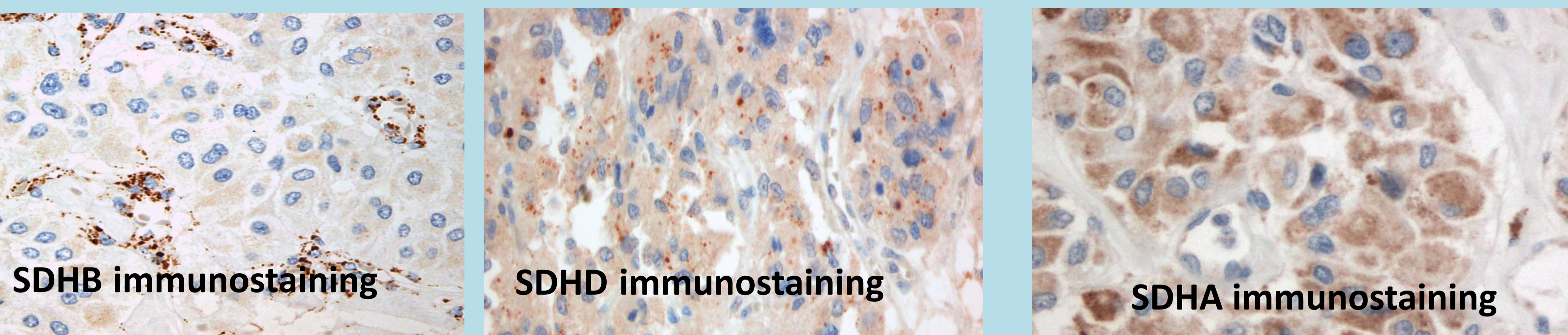
Results: Twenty-six cases with PPCs and 3 with PGLs were enrolled (18 females). Three cases were metastatic at diagnosis whereas two developed metastases during follow up. Ten cases (40%) had a PASS >6. Mean Ki-67% was 2% for cases with mutation and 2.6% for cases without mutations (p=0.8). Genetic testing for germline analysis had previously been performed in 21 cases and positive results were found in 7 cases (1 case was found positive for SDHB mutation, 1 for familial SDHD, 2 for RET, 2 for NF1 and 1 for VHL mutation) **Table 1**. The patient with the SDHB germinal mutation exhibited negative SDHB and positive SDHD/-A staining pattern. The patient with the SDHD germinal mutation exhibited negative SDHB/-D and positive SDHA staining pattern. Cases with RET, NF1 and VHL germline mutation as well as those without any mutations exhibited positive SDHB/-A and negative SDHD immunostaining.

Characteristics of the studied population	
N	29
Sex(f/m)	18/11
Age(median,yrs)	49.5
PPC/PGLs	26/3
Secretion	15(52%)
Size>5 cm	9(31%)
PASS>6	10(34.5%)
Follow-up(months)	72
Genetic mutation	7/21(33.3%)
-SDH family	2
-RET	2
-VHL	1
-NF-1	2
Metastatic disease	5(17%)
Mortality	1(0.3%)

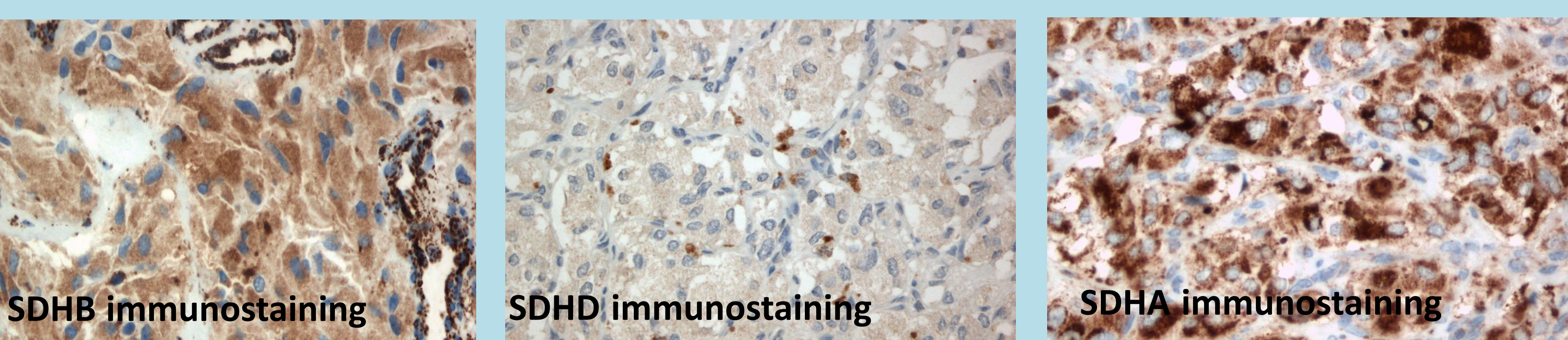
Table 1



The patient with SDHB genetic mutation



The patient with SDHD genetic mutation



Discussion: Our results are in agreement with previous series which have shown that SDHB/-D/-A immunohistochemical analysis could be a low cost technique to predict the presence of SDHx mutations. SDHB immunochemistry when used as a guide to genetic testing could potentially reduce the effort, time and costs of testing among patients with PPC/PGLs.

Bibliography: Castelblanco E, Endocr Pathol, 2013; Menara M, JCEM, 2015