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Calreticulin is Associated with Clinical Characteristics in Pancreatic Neuroendocrine Tumors

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BACKGROUND

Following IHC of CALR, H-scoring was performed by a pathologist. H-scoring was validated by MIF of the same tissue, wherein random-forest machine learning (ML) classifiers were employed to classify cells. ML classifiers were trained to distinguish between pNET cells and tumor stroma using approximately 30% of cells for the respective cell population of interest in each TMA core. Pearson's correlations were used to evaluate the relationship between H-scoring and mean fluorescent intensity in tumor cells. H-scoring was then evaluated for a relationship with clinical variables, including tumor grade and metastatic status (both lymphatic and distant). 111 resected pNET samples were analyzed.

METHODS

CALR MIF was performed for 40/89 patients. CALR H-scoring and IF were highly correlated ($r = 71$ [95% CI 50-83]; $p < 0.0001$). CALR expression was significantly higher in pNETs compared to normal pancreatic islets ($p < 0.0001$), as well as in primary pNETs compared to distant metastatic pNETs ($p = 0.02$). There was however no difference in CALR expression based on tumor grade (0.82) or N stage (0.58).

RESULTS

CALR MIF was performed for 40/111 patients. CALR H-scoring and IF were highly correlated ($r = 71$ [95% CI 50-83]; $p < 0.0001$). CALR expression differed significantly between pNETs and normal pancreatic islets ($p < 0.0001$), approached significance by N stage ($p = 0.07$), but did not differ by M stage ($p = 0.72$) or tumor grade ($p = 0.78$).

CALR H Score (mean ± sd)				p value
Tumor/Islet	Tumor (n=111) 217±95	Islet(n=17) 53±51		< 0.0001*
Grade	G1 (n=51) 213±101	G2 (n=52) 218±92	G3 (n=6) 241±73	0.82
M Stage	M0 (n=63) 232±86	M1 (n=38) 186±105	Mx (n=10)	0.02*
N Stage	N0 (n=62) 219±96	N1 (n=26) 232±85	Nx (n=23)	0.58

CONCLUSIONS

CALR expression is increased in pNETs compared to normal islets and may be decreased in cases of distant metastatic disease. Future studies will aim to examine these relationships in a larger cohort with more diverse clinical outcome to better define this relationship.

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