Germline mutation spectrum of neuroendocrine tumors

Yuting Sun[a], Huijing Tan[a], Lin Dong[a], Liming Jiang[a], Hong Zhao[a], Jianming Ying[a], Yihebali Chi[a]

[a] National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; Chinese Neuroendocrine Tumor Society (CNETS)

Background:

Neuroendocrine tumors (NETs) are rare and highly heterogeneous tumors. Some specific hereditary syndromes enhance the incidence of NETs, suggesting that germline variation may contribute to neuroendocrine tumorigenesis. However, germline genetic variants in Chinese NET patients remain unclear.

Methods:

This study included histologically confirmed NET patients treated at our center from 2020 to 2023. Germline DNA extracted from saliva or blood samples was analyzed using next-generation sequencing and targeted sequencing.

Results:

Of 225 Chinese NET patients, 59 (26.2%) cases had germline mutations. Among them, pancreas (27.1%, 16/59), mediastinum (27.1%, 16/59) and intestine (22.0%, 13/59) were the top 3 primary tumor locations. 32/59 (54.2%) germline variants were classified as pathogenic or likely pathogenic, while the remaining 27 (45.8%) individuals had variations of uncertain significance. The most common pathogenic/likely pathogenic mutated gene was MEN1, accounting for 4.0% (9/225) of the total, followed by PALB2 (1.3%, 3/225), VHL (0.9%, 2/225), RAD50 (0.9%, 2/225), SDHB (0.9%, 2/225) and other infrequent genes (such as CHEK2, MUTYH, RET etc.).

Conclusions

Approximately one-fourth of NET patients have germline mutation. We present the germline mutation spectrum of neuroendocrine tumors in the Chinese population.

Keywords

germline mutation, neuroendocrine tumors, genetic.

Future Directions for Research:

- Confirm gene function by mutant analysis

Contact: Yuting Sun, sunyt99@hotmail.com

Characteristics		Total (n = 59)
Age (years)	Median (range)	42(21-67)
Sex	Male	35 (59.3%)
	Female	24 (40.7%)
Histology	G1	12 (20.3%)
	G2	41(69.5%)
	G3	5 (8.5%)
	Unknown	1 (1.7%)
Tumor location	Pancreas	16 (27.1%)
	Mediastinum	16 (27.1%)
	Intestine	13 (22.0%)
	Stomach	5 (8.5%)
	Retroperitoneum	3 (5.1%)
	Other	2 (3.4%)
	Unknown	4 (6.8%)
Family history	Yes	23 (39.0%)
	No	36 (61.0%)
Metastasis	Yes	24 (40.7%)
	No	35 (59.3%)
SSTR2	Positive	34 (57.7%)
	Negative	12 (20.3%)
	Unknown	13 (22.0%)

Table 1. Baseline characteristics of all germline variants.

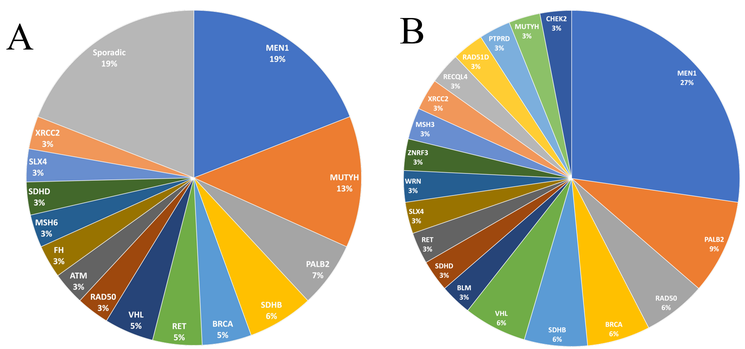

Figure 1. The genetic mutation spectrum of all germline variants (A) and pathogenic or likely pathogenic variants (B) .