

215P - Somatic mutations and gene expression of neuroendocrine pathways in aggressive and nonaggressive breast cancer

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Conclusions

Neuroendocrine pathways, particularly glucocorticoid pathway, play a role in breast cancer prognosis through differential mutations and expression.

Background

Neuroendocrine pathways are involved in essential steps of cancer progression.

Aim

To examine whether neuroendocrine pathways are differentially mutated and expressed in tumor tissue by comparing breast cancer patients with poor and favorable prognosis.

Methods

Extreme case-control study. Breast cancer patients with poor invasive disease-free survival (iDFS) and favorable iDFS were matched on molecular subtype, identified from the Breast Cancer Cohort at West China Hospital (WCH) and The Cancer Genome Atlas (TCGA). Whole exome sequencing (WES) and RNA sequencing (RNA-seq) were performed for tumor and paired normal breast tissues. Pathway somatic mutation burden and gene expression in relation to breast cancer iDFS were analyzed using the logistic regression and global test, respectively.



Results

Table 1. The associations between tumor mutation burden (TMB) of neuroendocrine pathways and breast cancer invasive disease-free survival

Pathway	Mutation	WCH + TCGA	WCH	TCGA
No. of patients		416	192	224
Odds ratio				
Adrenergic	Any	1.16 (0.74, 1.81)	2.01 (1.06, 3.8)	0.66 (0.34, 1.29)
	TMB	1.07 (0.91, 1.24)	1.28 (1.02, 1.59)	0.89 (0.7, 1.12)
Glucocorticoid	Any	1.66 (1.07, 2.58)	1.81 (0.95, 3.44)	1.57 (0.84, 2.95)
	TMB	1.17 (1.02, 1.35)	1.22 (0.99, 1.51)	1.12 (0.91, 1.38)
Dopaminergic	Any	1.07 (0.69, 1.66)	1.84 (0.95, 3.56)	0.7 (0.37, 1.33)
	TMB	1.02 (0.89, 1.17)	1.2 (0.98, 1.46)	0.88 (0.72, 1.08)
Serotonergic	Any	1.04 (0.66, 1.62)	1.74 (0.9, 3.36)	0.61 (0.32, 1.18)
	TMB	1.02 (0.89, 1.18)	1.2 (0.98, 1.47)	0.85 (0.68, 1.05)
Cholinergic	Any	1.59 (1.01, 2.53)	2.75 (1.42, 5.32)	0.87 (0.44, 1.72)
	TMB	1.14 (0.97, 1.34)	1.33 (1.06, 1.67)	0.95 (0.74, 1.21)

No mutation was used as the reference. Logistic regression models were adjusted for cohort membership, age at diagnosis, menopausal status at diagnosis, molecular subtype, and cancer stage.

Table 2. The associations of neuroendocrine pathway gene expression in tumor and matched normal breast tissues with breast cancer invasive disease-free survival

Pathway	Tumor			Normal
	WCH + TCGA	WCH	TCGA	WCH
No. of patients	407	185	222	142
P values				
Adrenergic	0.084	0.162	0.073	0.764
Glucocorticoid	0.028	0.085	0.046	0.701
Dopaminergic	0.132	0.437	0.103	0.788
Serotonergic	0.014	0.114	0.062	0.713
Cholinergic	0.096	0.155	0.071	0.625

Global tests were adjusted for cohort membership, age at diagnosis, menopausal status at diagnosis, molecular subtype, and cancer stage.

Translational Relevance

This study adds to the underlying mechanisms linking glucocorticoid pathway to breast cancer prognosis. If the function role is confirmed, it may provide important implications for developing novel therapeutic targets for breast cancer.

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