

STEM CELL EVALUATION BY ALDH1A1 EXPRESSION IN OVARIAN EPITHELIAL TUMORS

Thesis

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ABSTRACT

Background: Increasing evidence has proposed that tumors contain tumors initiating cells or cancer stem cells (CSCs) that are responsible for its progression and relapse. Aldehyde dehydrogenase 1A1 (ALDH1A1) has recently been identified as a marker for cancer stem cells in some human malignancies including ovarian epithelial cancer.

Aim of Work: The assessment of immuno-histochemical expression of ALDH1A1 in epithelial ovarian tumors, tracking stem cells during ovarian cancer development and its correlation with the clinic-pathological features of such tumors.

Methods: This study consisted of 42 cases of ovarian epithelial tumors, classified as 14 cases of benign cystadenomas, 14 cases of borderline tumors and 14 cases of carcinomas. Immuno-histochemical reactions were carried out by using ALDH1A1 monoclonal antibody. Cases were classified into two groups, low ALDH1 expression and high ALDH1 expression.

Results: Immuno-histochemical staining of ALDH1A1 displayed a heterogeneous expression pattern, with differences in the distribution and intensity of positivity. High ALDH1 expression was detected in 26 cases (62%) out of the forty-two studied cases of ovarian tumors. The positivity of ALDH1 was significantly higher in the malignant tumors (86%) than in benign and borderline tumors (50%) (p value = 0.025). There was a significant correlation between ALDH1 expression score and the tumor grade (p value = 0.05) where the highest expression of ALDH1 was detected among high grade tumors; grades II & III (100%). More expression of ALDH1A1 was noticed in cases with advanced stage but without statistically significant relation (P = 0.42). Highest ALDH1A1 expression was noticed in cases of serous type tumors (71%) and endometrioid type tumors (100%), although it doesn't reach statistical significance.

Conclusion: ALDH1A1 expression was significantly higher in malignant than benign and borderline tumors and showed significant correlation to prognostically poor parameters in malignant tumors, and thus can be a prognostic indicator in malignant ovarian tumors and a target for further therapy.

Key Words: Cancer stem cells, ALDH1A1, ovarian epithelial tumors.

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LIST OF ABBREVIATIONS

AACR	: American Association for Cancer Research Workshop
ABC	: Avidin biotin complex
A-catenin	: Alpha- catenin
AI	: Auto-implant
ALDH	: Aldehyde dehydrogenase
ALDH1	: Class 1 of the ALDH family
ALDH1A1	: Aldehyde dehydrogenase isoform 1A1
APC	: Adenomatous polyposis coli gene
APST	: Atypical proliferative serous tumor
ASC	: Adipose derived stem cells
ASCs	: Human adipose derived stem cells
BM	: Bone marrow
BPH	: Benign prostatic hyperplasia
BRCA1	: Breast Cancer 1
BRCA2	: Breast Cancer 2
CD 133	: Cell membrane differentiation antigen 133
CD 34	: Cell membrane differentiation antigen 34
CD 44	: Cell membrane differentiation antigen 44
CICs	: Cancer initiating cells
CSCs	: Cancer stem cells
CTNNB	: Catenin beta
EOC	: Epithelial ovarian carcinoma
ESS	: Edessy stem cell score
FC	: Flow cytometry
FIGO	: International Federation of Gynecology and Obstetrics
GOG	: Gynecologic Oncology Group
GSCs	: Germ line stem cells

H&E	: Hematoxylin and Eosin
IHC	: Immunohistochemistry
I-MBOT	: Mucinous Borderline Ovarian Tumors of Intestinal Type
KRAS	: Kirsten rat sarcoma viral oncogene homolog
LMP	: Low malignant potential
LOH	: Loss of heterozygosity
MBOTs	: Mucinous borderline ovarian tumors
MBTs	: Mucinous borderline tumors
N.C.I	: National Cancer Institute
Oct 4	: Octamer-binding transcription factor 4
OSCs	: Ovarian stem cells
OSE	: Ovarian surface epithelium
P53	: Protein 53
PIK3CA	: Phosphoinositide 3-kinase catalytic subunit alpha
PP	: Pseudomyxoma Peritonei
PTEN	: Phosphatase and tensin homolog
SBOT-MP	: Serous borderline ovarian tumors, micropapillary patterns
SBOTs	: Serous Borderline Ovarian Tumors
SBTs	: Serous borderline tumors
SCs	: Stem cells
SD	: Standard deviation
SLMNs	: Sarcoma-like mural nodules
SP	: Side population
SPSS	: Statistical package for social science
STIC	: Serous Tubal Intraepithelial Carcinoma
WB	: Western blot
WHO	: World Health Organization

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INTRODUCTION