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Original Article

Expression and clinical significance of chromatin remodeling component ARID1A in epithelial ovarian cancer

Liya Qiu[1,2,3*], Jiena Zhou[1,2,4*], Jinfei Tong[1,2], Xudong Ma[1,2], Hailan Yu[1,2], Jianhua Yang[1,2]

[1]Assisted Reproduction Unit, Department of Obstetrics and Gynecology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China; [2]Key Laboratory of Reproductive Dysfunction Management of Zhejiang Province, Hangzhou, Zhejiang Province, China; [3]Department of Obstetrics and Gynecology, Taizhou Women and Children's Hospital, Taizhou, Zhejiang Province, China; [4]Department of Obstetrics and Gynecology, Yaojiang Township Central Hospital, Zhuji, Zhejiang Province, China. [*]Equal contributors and co-first authors.

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Abstract: AT-rich interactive domain 1A (ARID1A) is frequently mutated in ovarian cancers, and deletion of ARID1A is associated with poor prognosis in various type of tumors, so this study aimed to investigate the expression level of ARID1A in epithelial ovarian cancer (EOC) and to analyze its correlation with pathological characteristics and survival. The study took place in the Sir Run Shaw Hospital, School of Medicine, Zhejiang University from 2015 to 2018. After protocol revision and approval by Human Research Ethical Committee of the Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, we obtained EOC pathological specimens from 57 epithelial ovarian cancers, 20 borderline ovarian tumors, and 21 benign ovarian tumors. We used Fisher's exact and χ^2 tests to analyze the relationship between clinicopathological parameters and ARID1A expression. The Kaplan-Meier method was used to analyze survival. The results showed that positive ARID1A expression was observed in 47.4% of EOC tissues, 42.9% of borderline ovarian tumor tissues, and 5.0% of benign ovarian tumor tissues. The expression level of ARID1A was significantly upregulated in EOC compared with benign ovarian tumor ($P < 0.001$). The aberrant expression of ARID1A in EOC was notably associated with FIGO stage ($P = 0.024$), CA199 levels ($P = 0.019$), and CEA levels ($P = 0.011$). Moreover, ARID1A expression was markedly increased in serous ovarian carcinoma compared with other types of EOC ($P = 0.013$). According to TCGA, in the Caucasian population, the prognosis of serous ovarian cancer in patients with higher or lower expression of ARID1A mRNA is better than serous ovarian cancer in patients with normal ARID1A expression ($P < 0.05$). All of These data showed that ARID1A has different roles in the occurrence and development of different pathological types of EOC. Moreover, ARID1A shows a dose-effect relationship and may exhibit both anticancer and carcinogenic effects.

Keywords: Epithelial ovarian cancer, ARID1A, SWI/SNF complex, immunohistochemistry, prognosis

Introduction

Ovarian cancer is the second most common cancer in the female genital tract system and remains the most lethal gynecological malignancy worldwide. Despite significant progress in the understanding of ovarian cancer genetics, a cure remains elusive due to a lack of insight into the underlying molecular mechanisms of this disease [1-4]. Ovarian cancer has heterogeneous histology and it can be classified into three groups: epithelial, germ cell, and stromal cell tumors [5, 6]. Most ovarian cancers (≥ 90%) are epithelial ovarian cancers (EOCs). EOCs can be divided into Type I and Type II tumors [7, 8]. Type I tumors include endometrioid, clear cell, mucinous, and low-grade serous carcinomas and it is often associated with a precursor lesion [9]. According to the International Federation of Gynecology and Obstetrics (FIGO) staging criteria, the prognosis of patients with early-stage (I and II) epithelial ovarian cancer is better than that of patients with advanced-stage (III and IV). The

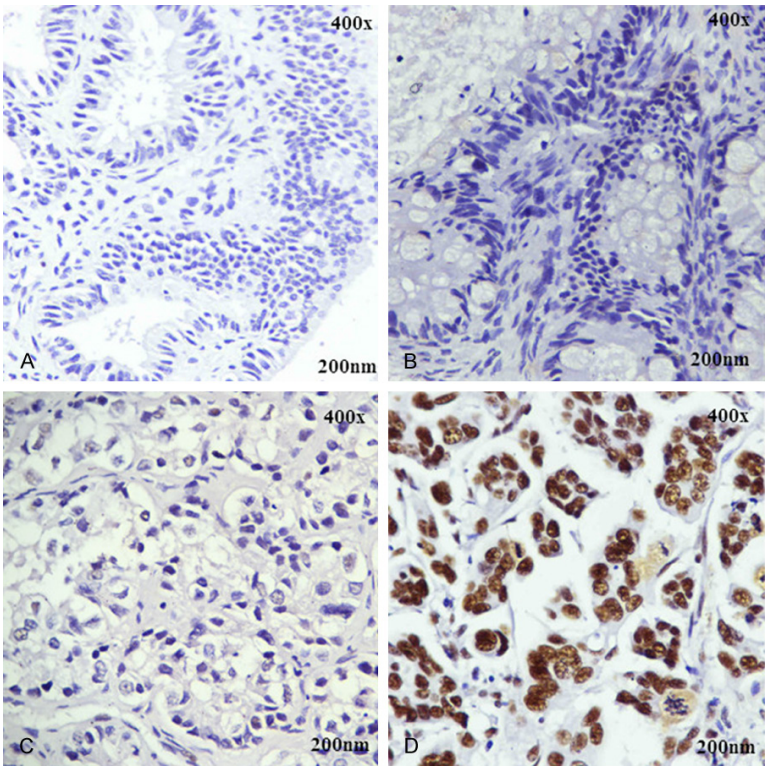

Figure 1. ARID1A protein expression analyzed with immunohistochemistry (magnification ×400). Immunohistochemical staining showed a strong nucleus staining of ARID1A in the serous ovarian cancer samples (A). In contrast, ARID1A immunoreactivity was negative or weakly observed in clear cell (B), Endometrioid (C) and Mucinous samples (D).

5-year survival rate in patients with early-stage can be increased to 60%-90% [10]. Therefore, an in-depth analysis of the pathogenesis and prognostic factors of ovarian cancer will provide a strong basis for early diagnosis and proper treatment.

Epigenetics refers to all the inheritable regulatory modes that affect the gene expression without altering DNA sequences. Previous studies have confirmed that epigenetic modification plays a vital role in stem cell differentiation, early embryonic development, and the occurrence and development of many diseases. In oncological research, epigenetic modification is closely related to proto-oncogene activation, tumor suppressor gene inactivation, damage repair defects, and differentiation of cancer stem cells. Among the epigenetic mechanisms in cancer, chromatin remodeling of complex genes has been found in multiple types of cancers. A clear example of the link between chromatin remodeling and cancer is SMARCB1/SNF5/INI1/BAF47, which is the core component of SWI/SNF chromatin remodeling complex, and ARID1A is one of them [11]. AT-rich interactive domain 1A (ARID1A) is a crucial member of the ARID family of proteins and encodes a subunit of the SWI/SNF non-fermentable chromatin remodeling family [12, 13]. Recent studies demonstrated that ARID1A is frequently mutated in some types of cancers, such as ovarian, kidney, mammary, and gastric cancers [14-16]. The mutation rates of ARID1A are significantly high in gynecologic cancers, approximately 46% in ovarian clear cell carcinomas and 30% in endometrioid carcinomas [17, 18]. However, ARID1A mutations have not been detected in high-grade serous carcinoma and mucinous carcinoma [19, 20].

Current studies have focused on the occurrence of mutant ovarian clear cell carcinoma and endometrioid carcinomas, but few studies have been conducted on serous carcinoma. We hypothesized that ARID1A expression correlates with tumorigenesis in patients with EOCs. In the present study, we investigated the expression pattern of the ARID1A in EOCs, borderline ovarian tumor, benign ovarian tumor specimens, and analyzed the correlation between its expression and clinical pathologic parameters. Furthermore, we evaluated the prognostic value of ARID1A in patients with EOC.

Materials and methods

Patient tissue selection

The study took place in the Sir Run Shaw Hospital, School of Medicine, Zhejiang University from 2015 to 2018. After protocol revision and approval by Human Research Ethical Committee of the Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, we ob-

Table 1. Association analyses between the expression levels of ARID1A and the clinicopathological characteristics of epithelium ovarian carcinoma patients

Variables	No.	Expression		X^2	*p*-value
		Low	High		
Age (yrs.)					
< 55	35 (60.7%)	19	16	0.100	0.752
≥ 55	22 (39.3%)	11	11		
Tumor size (cm)					
≤ 5	14 (24.6%)	10	4	2.63	0.105
> 5	43 (75.4%)	20	23		
Histologic type					
serous	37 (64.9%)	15	22	6.184	0.013[a,*]
clear cell	8 (14.0%)	7	1		
Endometrioid	3 (5.3%)	2	1		
Mucinous	4 (7.0%)	4	0		
Adeno	5 (8.8%)	2	3		
Clinical Stage/FIGO stage					
I/II	28 (49.1%)	19	9	5.117	0.024[*]
III/IV	29 (50.9%)	11	18		
Histologic grade					
G1/G2	12 (21.1%)	4	8	2.271	0.132
G3	45 (78.9%)	26	19		
Lymph node metastasis					
no	36 (63.3%)	22	14	2.818	0.093
yes	21 (36.8%)	8	13		
Ascites (mL)					
≤ 500	44 (77.2%)	22	22	0.536	0.464
> 500	13 (22.8%)	8	5		
Two tumor models					
I Type	21 (36.8%)	14	7	2.627	0.105
II Type	36 (63.3%)	16	20		
CA125 (U/mL)					
< 35	6	3	3	0.04	1.000[b]
≥ 35	46	25	21		
CA199 (IU/mL)					
< 37	40	18	22	5.458	0.019[b,*]
≥ 37	12	10	2		
CEA (ng/mL)					
< 3	45	21	24	6.933	0.011[b,*]
≥ 3	7	7	0		

Abbreviations: G1 = well-differentiated; G2 = moderately differentiated; G3 = poorly differentiated. [a]serous ovarian carcinoma vs other ovarian carcinomas; [b]there were 5 cases with missing data, and deletion was performed at the time of Statistics; [*]significant.

tained EOC pathological specimens from 57 epithelial ovarian cancers, 20 borderline ovarian tumors, and 21 benign ovarian tumors. After informed consent approval, these specimens were surgically treated. All the specimens were from patients over 18 years old who did not undergo radiotherapy, chemotherapy, or targeted therapy before surgery, and had adequate clinical data. Qualified gynecology pathologists evaluated all the tissue specimens and slides.

Immunohistochemistry

The IHC study was carried out on formalin-fixed, paraffin-embedded, 4-μm-thick tissue sections. The sections were treated with 3% hydrogen peroxide to inhibit endogenous peroxidase activity using standard procedures. Sections were incubated with antibody against ARID1A (ab182560; 1:1,000, Abcam), overnight at 4°C after antigen retrieval in a sodium citrate buffer. Slides were incubated with biotinylated species-specific secondary antibodies (GTVisionTM III Detection System/Mo&Rb, Gene technology company) for 60 minutes, and then exposed to avid in-biotin-peroxidase complex. Sections were treated with 0.02% diaminobenzidine (DAB) as a chromogen, and counterstained with hematoxylin. Finally, the sections were washed, followed by dehydration and sealing.

Interpretation of IHC expression patterns for various proteins

The intensity of staining was evaluated as follows: 0 = no staining; 1 = weak staining; 2 = moderate staining; and 3 = strong staining. The percentage of staining was given the following scores: 1) 0%-25%; 2) 25%-50%; 3) 51%-75%; and 4) 75%-100%. The final score was obtained by multiplying the scores on staining reaction and staining intensity (range 0-12). Scores of 0-6 were categorized as ARID1A low expression while scores of 6-12 were categorized as ARID1A high expression (**Figure 1**).

Table 2. Spearman analysis of the correlation between ARID1A and clinicopathological characteristics

Variables	ARID1A expression level Spearman correlation	*p*-value
Age	0.156	0.246
Height	0.064	0.638
Weight	0.056	0.680
BMI	0.061	0.652
Number of pregnancies	0.012	0.929
Number of births	-0.101	0.461
Menarche	0.012	0.932
Menopause	0.151	0.270
Menopause length	0.183	0.173
Tumor size	-0.061	0.652
Clinical Stage	0.381	0.003*
Histologic grade	0.186	0.166
Lymph node metastasis	0.239	0.074
Ascites	-0.138	0.307
CA125 (U/mL)	0.083	0.557
CA199 (IU/mL)	-0.158	0.282
CEA (ng/mL)	-0.441	0.001*
AFP (ng/mL)	-0.06	0.671

*Significant.

Statistical analysis

The correlations between the ARID1A expression levels and clinicopathological parameters were examined using the χ^2 test or Fisher exact test, as appropriate. The Rank sum test was applied to quantitative data not suitable for the chi-square test and without normal distribution. Correlation analysis was conducted using the Spearman rank correlation test. Survival analysis was performed using the Kaplan-Meier method, and the differences in survival rates were assessed with the log-rank test. Two-sided *P* values less than 0.05 were considered statistically significant. All the statistical analyses were performed using the SPSS version 22.0 software (SPSS, Chicago, IL).

Results

The expression of ARID1A protein in ovarian cancer is higher than in normal epithelial and ovarian cysts

The high expression rate of ARID1A in epithelial ovarian cancer, borderline ovarian tumor, and the benign ovarian tumor was 47.4% (27/57), 42.9% (9/21), and 5.0% (1/20), respectively. The difference between these three groups was statistically significant ($P < 0.001$). The expression intensities of ARID1A in epithelial ovarian cysts were significantly lower than in cancer ($P < 0.001$), and borderline epithelial ovarian tumor tissues ($P = 0.003$).

ARID1A expression and its association with the clinicopathological features of EOCs

We studied the ARID1A clinicopathology correlation. The expression of ARID1A protein in epithelial ovarian cancer was associated with FIGO stage ($P = 0.024$), CA199 level ($P = 0.019$), and CEA (Carcinoembryonic antigens) levels ($P = 0.011$). There was a negative relationship between the levels of ARID1A protein expression and CEA levels (rs = 0.381, $P = 0.001$). The expressions of ARID1A in serous ovarian carcinoma expression was significantly higher than in other types of epithelial ovarian cancer ($P = 0.013$). The expression levels of ARID1A protein in epithelial ovarian cancer were not associated with age, ascites, and CA125 level (**Tables 1** and **2**).

Since the expression of ARID1A in serous ovarian cancer and other types of ovarian cancer are significantly different (**Table 1**), we divided the samples into serous ovarian cancer and other types of epithelial ovarian cancer for further analysis. An interesting finding was that ARID1A expression in other types of ovarian cancers is positively correlated with the patient's height (**Tables 3** and **4**).

Next, we divided 57 cases of epithelial ovarian cancer in Type I and Type II. In Type I, the expression levels of ARID1A protein were significantly associated with clinical stage, histologic grade, and lymphatic metastasis of ovarian cancer. ARID1A was positively correlated with clinical stage, histologic grade, lymph node metastasis, and negatively correlated with serum CEA levels. In Type II, the expression levels of ARID1A protein were significantly correlated with obesity and negatively correlated with serum CEA level (**Tables 5** and **6**).

Relationship between ARID1A mRNA expression and prognosis of serous ovarian cancer

We extracted data related to the prognosis of serous ovarian cancer (SOC) from the TCGA database, downloaded from Oncomine (https://www.oncomine.org). This database

Table 3. Association analyses between the expression levels of ARID1A and the clinicopathological characteristics of serous and other Histologic type ovarian carcinoma patients

Variables	Serous					Other EOCs				
	NO.	Low	High	X^2	p	No.	Low	High	X^2	*p*-value
Age (y)										
< 55	21	8	13	0.120	0.729	14	11	3	0.317	0.613
≥ 55	16	7	9			6	4	2		
BMI (kg/m^2)										
≤ 24	27	13	14	2.399	0.153	11	9	2	0.606	0.617
> 24	10	2	8			9	6	3		
Tumor size (cm)										
≤ 5	10	6	4	2.153	0.258	4	4	0	1.667	0.530
> 5	27	9	18			16	11	5		
Clinical Stage/FIGO stage										
I/II	10	5	5	0.509	0.708	18	14	4	0.741	0.447
III/IV	27	10	17			2	1	1		
Histologic grade										
G1/G2	30	14	16	2.469	0.204	15	12	3	0.800	0.560
G3	7	1	6			5	3	2		
Lymph node metastasis										
no	17	8	9	0.554	0.457	19	14	5	0.351	1.000
yes	20	7	13			1	1	0		
Ascites (mL)										
≤ 500	29	12	17	0.039	1.000	15	10	5	2.222	0.266
> 500	8	3	5			5	5	0		
CA125 (U/mL)										
< 35	2	0	2	1.46	0.502*	4	3	1	0.000	1.000
≥ 35	30	13	17			16	12	4		
CA199 (IU/mL)										
< 37	27	9	18	3.809	0.132*	13	9	4	0.659	0.613
≥ 37	5	4	1			7	6	1		
CEA (ng/mL)										
< 3	30	11	19	3.118	0.157*	15	10	5	2.222	0.266
≥ 3	2	2	0			5	5	0		

Abbreviations: G1 = well-differentiated; G2 = moderately differentiated; G3 = poorly differentiated. *There were 5 cases with missing data, and deletion was performed at the time of Statistics.

contains the gene expression data of ovarian cancer and normal tissues. We performed a Kaplan-Meier analysis on 479 Caucasian patients with serous ovarian cancer. According to the expression of ARID1A mRNA, they were divided into three groups: the first 15% were low expression group, the middle expression group was 15%-35% (ARID1A mRNA expression was similar to the normal ovary), and the high expression group was 35%-100%. The results showed that there was a notable correlation between the survival rates of ovarian cancer patients with high and low expression of ARID1A and those with a medium expression of ARID1A ($P < 0.05$). The 5-year productivity of patients with high expression of arid1a was 24.395%, that of patients with low expression of arid1a was 30.304%, and that of patients with normal expression was 12.104%, as shown in **Figure 2C**.

Discussion

The results of this study showed that the protein expression levels of ARID1A were negatively correlated with serum CEA in epithelial ovari-

Table 4. Serous vs. other EOCs, Spearman analysis of the correlation between ARID1A and clinicopathological characteristics

Variables	Serous		Another EOCs	
	Spearman correlation	*p*-value	Spearman correlation	*p*-value
Age	-0.159	0.348	0.382	0.096
Height	-0.091	0.594	0.597	0.005*
Weight	0.155	0.361	0.318	0.172
BMI	0.219	0.194	0.145	0.542
Number of pregnancies	-0.319	0.055	0.255	0.278
Number of births	-0.282	0.095	0.007	0.978
Menarche	-0.091	0.591	-0.191	0.419
Menopause	-0.017	0.921	0.291	0.227
Menopause length[a]	-0.187	0.267	0.488	0.029*
Tumor size	0.074	0.663	0.187	0.430
Clinical Stage	0.249	0.138	0.104	0.661
Histologic grade	0.278	0.096	0.142	0.550
Lymph node metastasis	0.112	0.508	-0.233	0.322
Ascites	-0.042	0.805	-0.267	0.255
CA125 (U/mL)	-0.151	0.411[b]	0.137	0.564
CA199 (IU/mL)	0.032	0.868[b]	-0.048	0.849
CEA (ng/mL)	-0.288	0.110[b]	-0.632	0.003*

[a]Menopause length = Menopause age-Menarche age. [b]There were 5 cases with missing data, and deletion was performed at the time of Statistics. *Significant.

an cancer patients. CEA is the product of carcinoembryonic antigen 5 genes. CEA has seven extracellular immunoglobulin domains and one glycosyl-phosphatidylinositol (GPI) anchor, which might explain why soluble CEA can be detected in serum [21]. CEA was initially considered a tumor marker in colon cancer, but later, it was found to be highly expressed in many other tumors [22, 23]. CEA is expressed in normal epithelial cells, especially those found on the apical surface of the gastrointestinal epithelium. Other studies have shown that CEA is one of the cell component inhibited in the differentiation of normal digestive epithelial cells but reappears in the malignant cells through inhibited dedifferentiation [22, 24]. So far, this protein has been found only in primate species.

Studies have shown that ARID1A is highly expressed in early embryos and embryonic stem (ES) cells. The embryos of ARID1A-deficient mice stagnated at 6.5 days of development, and the detection showed that the mesoderm cells were utterly deficient. The pluripotency and self-renewal ability of ES cells lacking ARID1A was severely impaired and began to differentiate into primitive endodermal-like cells. It was also found that ARID1A is a maintenance factor of ES cells [25]. ARID1A regulates the expression of many genes during early embryonic development. The lack of ARID1A results in the change of ES cells gene expression profile. The expression of stem cells self-renewal genes such as Sox2, Ufl, and Oct4 is decreased. Simultaneously, the expression of development-related genes such as Gata4, Gata6, Tnt2, and Myl3 is upregulated [25]. Another study showed that ARID1A expression decreased during embryonic stem cell differentiation.

The ovarian surface has no mature epithelial tissue. In contrast, the immature cells on the ovarian surface are germinal layer cells reserved to the mesodermal coelomic epithelium. Epithelial hyperplasia can form various kinds of epithelial tumors differentiated from the Müllerian tubal epithelium. Their histological morphology and structure simulate the histological properties of Müllerian tubal epithelial differentiation, such as serous tumors simulating oviductal epithelium, endometrioid tumors and clear cell carcinomas simulating endometrial epithelium, and mucinous cervical epithelium. Brenner tumor simulates cervicovaginal and vaginal fornix epithelium. Therefore, we speculate that ARID1A may be associated with ovarian cancer differentiation.

Our study showed that ARID1A was associated with FIGO staging, indicating that ARID1A may be involved in tumorigenesis. Since the proposal of the dualistic model of ovarian cancer back in 2004, more than ten years have been spent in studying the molecular genetic typing of ovarian cancer to establish a more accurate molecular typing than binary typing. When the cases were divided into two types, the expression of ARID1A protein in Type I was positively correlated to clinical stage, histologic grade, lymph node metastasis, and negatively correlated with serum CEA. The expression of ARID1A protein in Type II was significantly cor-

Table 5. Association analyses between the expression levels of ARID1A and the clinicopathological characteristics of epithelium ovarian carcinoma patients in two tumor models

Variables	Type I					Type II				
	No.	Low	High	X^2	*P*-value	NO.	Low	High	X^2	*P*-value
Age (yrs.)										
< 55	16	10	6	0	1.000	19	9	10	0.066	0.797
≥ 55	8	5	3			14	6	8		
BMI (kg/m^2)										
≤ 24	16	9	7	0.8	0.657	22	13	9	4.95	0.026*
> 24	8	6	2			11	2	9		
Tumor size (cm)										
≤ 5	5	4	1	0.825	0.615	9	6	3	2.246	0.239
> 5	19	11	8			24	9	15		
Clinical Stage/FIGO stage										
I/II	15	12	3	5.227	0.036*	13	7	6	0.609	0.435
III/IV	9	3	6			20	8	12		
Histologic grade										
G1/G2	10	3	7	7.726	0.010*	2	1	1	0.018	1.000
G3	14	12	2			31	14	17		
Lymph node metastasis										
no	18	14	4	7.17	0.015*	18	8	10	0.016	1.000
yes	6	1	5			15	7	8		
Ascites (mL)										
≤ 500	18	10	8	1.481	0.351	26	12	14	0.024	1.000
> 500	6	5	1			7	3	4		
CA125 (U/mL)										
< 35	5	3	2	0.077	1.000[a]	1	0	1	0.842	1.000[a]
≥ 35	18	12	6			28	13	15		
CA199 (IU/mL)										
< 37	17	9	8	2.272	0.191	23	9	14	2.758	0.153[a]
≥ 37	7	6	1			5	4	1		
CEA (ng/mL)										
< 3	20	11	9	2.88	0.259	25	10	15	3.877	0.087[a]
≥ 3	4	4	0			3	3	0		

Abbreviations: G1 = well-differentiated; G2 = moderately differentiated; G3 = poorly differentiated. [a]There were 1-5 cases with missing data, and deletion was performed at the time of Statistics. *Significant.

related with obesity and negatively correlated with serum CEA. Based on these findings, we believe that ARID1A is more closely correlated with the occurrence and development of Type I ovarian cancer.

Some studies have tried to analyze the prognostic significance of ARID1A mutations, transcript levels or protein loss in different cancers and single cancer subtypes, but no consistent relationship between ARID1A mutation or expression and prognosis has been found [14, 26-34]. Our study showed that when the expression of ARID1A mRNA in epithelial ovarian cancer was different from normal ARID1A mRNA expression, the prognosis of serous ovarian cancer patients was better. In other words, patients with the same ARID1A expression and normal ovarian epithelium had the worst prognosis. This is inconsistent with previous study that found ARID1A is not related to ovarian cancer prognosis. This may be because, in previous studies, the expression of ARID1A was divided into high and low groups, and the absence of ARID1A expression was used to evaluate the correlation with progno-

Table 6. Spearman analysis of the correlation between ARID1A and clinic pathological in two tumor models

Variables	Type I		Type II	
	Spearman correlation	*P*-value	spearman correlation	*P*-value
Age	0.333	0.112	-0.044	0.807
Height	0.042	0.845	-0.031	0.863
Weight	-0.217	0.308	0.282	0.112
BMI	-0.307	0.145	0.314	0.076
Number of pregnancies	0.04	0.853	-0.089	0.624
Number of births	0.184	0.389	-0.332	0.059
Menarche	0.317	0.131	-0.245	0.170
Menopause	0.328	0.117	-0.032	0.863
Menopause length	0.3	0.154	0.049	0.788
Tumor size	0.048	0.824	-0.057	0.753
Clinical Stage	0.459	0.024*	0.269	0.130
Histologic grade	0.52	0.009*	-0.139	0.441
Lymph node metastasis	0.471	0.020*	0.050	0.783
Ascites	-0.254	0.232	-0.016	0.929
CA125 (U/mL)	0.274	0.205[a]	-0.116	0.550[a]
CA199 (IU/mL)	-0.200	0.373	-0.049	0.811[a]
CEA (ng/mL)	-0.466	0.022*	-0.455	0.015*,[a]

[a]There were 1-5 cases with missing data, and deletion was performed at the time of Statistics. *Significant.

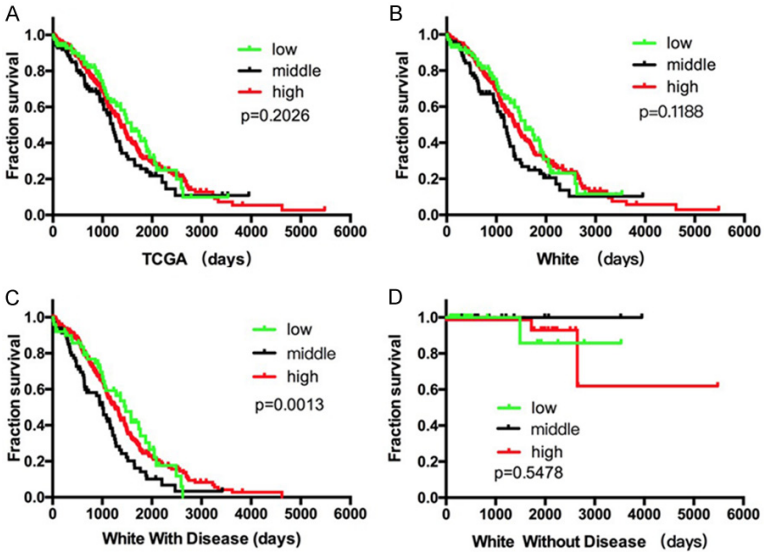

Figure 2. Kaplan-Meier survival curves for all Race. A. And only White. B. According to various AT-rich interactive domain 1A (ARID1A) mRNA expression patterns. C. Survival curves of with disease survival of ARID1A in White person (P = 0.0013). D. Survival curves of without disease survival of ARID1A in White person (P = 0.5478).

sis, while the expression of ARID1A was not compared with normal ovarian epithelium (need reference support). The prognosis of patients with high expression of ARID1A in serous ovarian cancer was better, suggesting that ARID-1A may have an anti-cancer effect, which is consistent with previous studies. However, it cannot explain why patients with low expression of ARID1A have a better prognosis. This raises an interesting question about the dual function of ARID1A: is it an anti-cancer or pro-cancer gene? This may also be due to different mutation patterns among different cancer subtypes, which determine different tissue-specific mutation effects. On the other hand, it also illustrates the challenge of distributing the mechanical introduction of many mutations identified by cancer genome sequencing. At the same time, it once again illustrates the complexity of Epigenetics.

In conclusion, ARID1A is associated with the occurrence and development of epithelial ovarian cancer and affects the prognosis of serous ovarian cancer. However, ARID1A might have multiple roles and exhibit dose-effects during these processes. Meanwhile, ARID1A, a regulatory subunit of SWI/SNF complex, might determine the pathological classification of ovarian cancers and promote the differentiation of germinal epithelial cells towards different directions.

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Disclosure of conflict of interest

None.

Address correspondence to: Jianhua Yang, Assisted Reproduction Unit, Department of Obstetrics and Gynecology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China; Key Laboratory of Reproductive Dysfunction Management of Zhejiang Province, No.3 Qingchun East Road, Hangzhou 310016, Zhejiang Province, China. Tel: +86-13989816498; E-mail: yjh2006@zju.edu.cn

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