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Original article

Estimate Expression Levels of LPA Receptor 1, and LPA Receptor 2 Genes Epithelial Ovarian Cancer Cell Lines Using qPCR and Immunocytochemistry Approach

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Abstract
Epithelial ovarian carcinoma accounts for the highest number of mortalities among patients with ovarian cancer. However, the molecular mechanisms fundamental to Epithelial Ovarian Cancer (EOC) tumorigenesis are presently ambiguous. In this study, a Real-time–quantitative polymerase Chain Reaction(RT-qPCR) was selected to manipulate Lipoprotein Receptor 1(LPAR1), and Lipoprotein Receptor 2 (LPAR2) gene expression in ovarian cancer cell lines. Immunocytochemical staining was used to examine the expression of LPAR1, 2 in Ovarian Adenocarcinoma W42 (OAW42) and Cystadenocarcinoma Ovary(SKOV3), which are ovarian cancer cell lines, and using Human Ovarian Surface Epithelium Cell (HOSEpiC) as a negative, which was created, from human ovarian surface epithelial cells. The results established that LPAR1, 2 expressions were upregulated in OAW42 and SKOV3 when using the qPCR technique to assist, however, the immunocytochemistry results showed the expression of LPAR1, and LPAR2 in the OAW42 SKOV3and HOSEpiC which is indicated that both of LPAR1 and LPAR2 are not good biomarkers to detect the Epithelial Ovarian Cancer at an early stage. In conclusion, the results of the present study indicate the correlation between LPAR1 and LPAR2 does not serve as biomarkers or diagnostic targets in EOC on the other hand, using qPCR and Immunocytochemistry (ICC) techniques is considered good tools to use.
Keywords: LPAR1, LPAR2, Ovarian Cancer, Immunocytochemistry, qRT-PCR.

Introduction

Ovarian cancer is becoming a gynaecological disease with a high mortality rate regarding the incidence ratio which is increased steadily for both endometrial and cervical cancer, so it is considered one of the most common gynaecological diseases globally [1-5] and is accounted for just 2.5% of all female cancer cases [6]. Further, ovarian neoplasm includes various histopathologic entities and the perfect treatment is based on the classification of the precise tumour type, for instance, epithelial ovarian cancer is considered the most malignant ovarian carcinoma which is accounted for (~80%) [7-9]. A confident diagnosis of ovarian carcinoma usually arises at advanced stages despite research on ovarian cancer has realized some improvement. Also, the natural topography of the ovarian cancer location occurs deeply in the pelvic cavity [2,11]. Due to, there being no noticeable signs of ovarian carcinoma in the early stages, which obstructs the subsequent treatment [12], early recognition and management become serious objectives for the rescue of ovarian cancer patients [2,13].

LPA was first implicated in human carcinogenesis once elevated in the ascetic fluid of ovarian cancer patients [14-17], it has many roles in controlling ovarian cancer proliferation, cell survival, angiogenesis, and metastasis as an autocrine factor [17,18]. Also, it can release in ovarian cancer patient's plasma [18]. It is presented in the blood serum at concentrations of 2–20 µM and has been shown to stimulate the proliferation of ovarian cancer cells, surge resistance to chemotherapy, stimulation of Dinucleotide Acid (DNA) synthesis, cytoskeleton restructuring, cell survival, drug resistance, cell adhesion, migration, cytokine production, and ion transport [14,19-21] and as mentioned by Kraft that LPA is mostly transcribed in the liver [22]. Despite the coagulation process and normal constituent of serum; LPA can form and be released by Activated platelets, it is usually found only at very low levels in whole blood or fresh platelet-poor plasma from healthy individuals [15, 23]. The fatty acid chain that LPA consists of could link to the glycerol backbone during various chemical linkages which leads to the creation of different subclasses such as [alkyl (A-LPA), acyl, and alkenyl (An-LPA)] [24].

LPA occurs as phospholipid activates distinct members of the endothelial differentiation gene (Edg) which is the subfamily of G protein-coupled receptors (GPCRs) to support multiple cellular responses [25]. Further, LPA and other phospholipids play roles in stimulating the expression of [interleukin 8] in ovarian cancer which probably could be produced by cancer cells and migrates from the peritoneal cavity to the circulation similar to another marker i.e. Carcinogenic Antigen 125 (CA125) [26,27]. Due to specific G protein-coupled receptors (GPCRs) are a supervisor to mediate the biological function of extracellular LPA which includes Edg- 2/ LPA1, Edg-4/LPA2, and Edg-7/LPA3, that belong to the endothelial differentiation gene (Edg) family [28-30], so LPA interacts with specific cell surface G- protein-coupled receptors of the endothelial

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differentiation gene (Edg2) [31] and (Edg4) [29] Subfamily which considers specific LPA receptors present on many cell types; various cellular responses will happen and these responses occur as follow: (i) stimulation of cell proliferation by increasing cell cycle progression, [32] inhibiting apoptosis, inhibition of cell differentiation,(iii) stimulation of tumour cell invasion [33].
Since the invention of LPA1 via Cognate cell surface receptors in 1996 [28]; resulted in the identification of two extra closely related receptors (LPA2, LPA3), also, the recent identification of two more, slightly divergent, receptors (LPA4 and LPA5). All these five receptors are classified as type I, rhodopsin-like G protein-coupled receptors (GPCRs) which contrast whereas, they conflict downstream signalling pathways, and tissue distribution [34]. On the other hand, they have reported the GPCRs GPR23/p2y9 (LPA4) [32], GPR92/93 (LPA5) [35, 36] GPR87/95 (LPA6) [36, 37], p2y5 [38] and p2y10 [39] to be new, non-Edg family LPA receptors that have little sequence homology to LPA1–3, these new receptors still with an unknown mechanism [20, 40, 41]. Using LPA as a biomarker for early detection of ovarian cancer is still not approved and it is under investigation to recognize the efficacy of LPA [15, 42]. On the opposite, another study confirmed the relationship between ovarian cancer tumorigenicity aggressiveness and LPA receptors [20, 43]. This study will investigate the expressions of LPAR1, and LPAR2 Table 2.1 in human ovarian epithelial cancer cells comparing and using the normal epithelial ovarian cell line as an internal negative control.

Material and Methods

RNA extraction, cDNA synthesis, and quantitative real-time reverse transcriptase-PCR (RT-PCR)

After cell culture procedures for SKOV-3, OAW42 in DMED, and HOSEpiC Ovarian Basal Medium with Inducers and Components (OBMiC)media, according to the Roche kit, isolated total RNA from cultured cells, which are suited for $1x10^6$, and we followed these steps, which are approved by Roche Company. Also, concerning the manufacturer's instructions. cDNA was synthesized using the First Strand cDNA Synthesis Kit (Roche) and followed the manufacturer's instructions. Quantitative real-time PCR was done using a Roche LightCycler 480(for software Version 1.2.9.11) system using a KAPA SYBR® FAST for ABI Prism® PCR Mix (2X) (Kapa Biosystems), according to the manufacturer's datasheet and was optimized for all primer combinations was used to perform qRT-PCR reactions and followed by a dissociation (melt) curve analysis. The quantitative real-time PCR conditions were 50°C (2 min), 95°C (10 min), 40 cycles of 95°C (15 s), and 60°C (1min). Primers obtained from (Inqapa Company). The Relative Expression Software Tool Pair Wise Fixed Reallocation Randomisation Test © software (REST®) was used to analyze the qPCR data through the ΔΔCt method which was used to obtain the relative quantification. GAPDH and HPRT were used as internal control genes whereas normal ovarian (HOSEpiC) RNA as an internal control sample. HOSEpiC cell line purchased from (Inqapa Company).

Immunocytochemistry of LPAR1, and LPAR2

To frequently and dependably estimate LPAR1, and LPAR2 expression for diagnostic and molecular research motivation, a routine process for ICC of LPAR1, and LPAR2 in a Para-formaldehyde-fixed cell line was needed to achieve the protein expression of these genes by using a new, highly specific mouse monoclonal which is Anti-GFRA1 antibody (1:500 dilution) and at the Histology Laboratory at Tygerberg Hospital in a Leica Bond Auto Stainer (Leica) all staining, washing, and antibody incubations were performed. The antibodies used were obtained from Abcam: LPAR1 (Anti-EDG2 antibody ab84788), (1:50); and LPAR2 (PAB24995) (1:50), Immunocytochemistry for LPAR1 and LPAR2 was done showed Leica Bond Auto Stainer (Leica) following the common protocol of the manufacturer. The technician (Reggie Williams) carried out all analyses of immunocytochemical staining and photos.

Results and Discussions

The results were statistically tested by graph pad prism 7 and the Relative Expression Software Tool Pair Wise Fixed Reallocation Randomisation Test © software (REST®) Results are given as cross point (Cp) values Differences between normal and cancer cells were considered significant at P<.05.

RT-qPCR result

To investigate the sensitivity of the method based on cross point (Cp) values, calibration curves were prepared for LPA1 and LPA2 cDNAs from known quantities of cDNA (each diluted 10-fold from 105 to 102 copies of cDNA per reaction mixture). All calibration curves showed correlation coefficients >0.99, indicating an accurate log-linear relation. The detection limit using the specific primers was the same (10 copies of cDNA) for all the target genes. First, we examined the expression of LPA1, and LPA2 mRNA in 2 human ovarian cancer cells, Skov-3, and OAW42 using a normal human ovarian cell line (HOSEpiC) as an internal negative control. SKOV-3, OAW42 cell lines, expressed significant levels of LPAR1, and LPAR2.
Table 1 shows the primer efficiency (E), slope, and R2 value for each primer pair as calculated using Pair Wise Fixed Reallocation Randomisation Test © software. An E value of two indicates 100% primer efficiency and an R^2 value of 0.99 indicates a good correlation between Ct and sample concentration in HOSEpiC, SKOV-3, and OAW42. expressed significant levels of LPAR1, and LPAR2.

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Table 1. Primer efficiency (E), slope, and R2 value for each primer pair as calculated using

Gene	HOSEPiC			SKOV3			OAW42		
	slope	Efficiency (%)	R2	slope	Efficiency (%)	R2	Slope	Efficiency (%)	R2
GAPDH	-3.4	96.84	0.99	-3.34	99.25	1	-3.37	98.03	0.99
HPRT	-3.38	97.63	1	-3.36	98.44	0.99	-3.39	97.24	1
LPAR1	-3.34	99.25	0.99	-3.37	98.03	1	-3.4	96.84	0.99
LPAR2	-3.46	94.54	0.99	-3.44	95.3	0.99	-3.39	97.24	1

An E value of two indicates 100% primer efficiency and an R2 value of 0.99 indicates a good correlation between Ct and sample concentration in HOSEPiC, SKOV3, and OAW42 cells.

The Ct values of the HKGs (GAPDH and HPRT) as measured in both the control cell line (HOSE) and the cancer cell lines (SKOV-3 and OAW42) were for the Ct value of HPRT1 expression was found to be relatively more stable for the 3 cell lines evaluated compared against GAPDH which was highly unstable expressed gene in the three different cell lines so, for this reason, the HPRT p-values were used to interpret the expression of genes. Relative to GAPDH, the expression of LPAR1 mRNA was high in SKOV-3 cells (2.86-fold change; Figure 1), but it was very low in OAW42 cells (0.03-fold change; Figure 3). However, relative to HPRT, there was a 3.05-fold increased expression of LPAR1 mRNA in SKOV-3 cells (Figure 2) and a -5.4-fold change (downregulated expression) in OAW42 (Figure 4) with parallel p=0.01 in both cell types. Figure 2 shows a 5-fold increased LPAR2 mRNA expression in SKOV-3 cells, relative to HPRT, whereas expression of this candidate gene in OAW42 cells is upregulated 2.3-fold (Figure 4). Despite the significant increase in the relative density of LPAR2 (5-fold change; p=0.01) in SKOV-3 cells (Figure 2), the relative density of LPAR2 in OAW42 cells was significantly decreased by 0.6-fold (p=0.02; Figure 4).

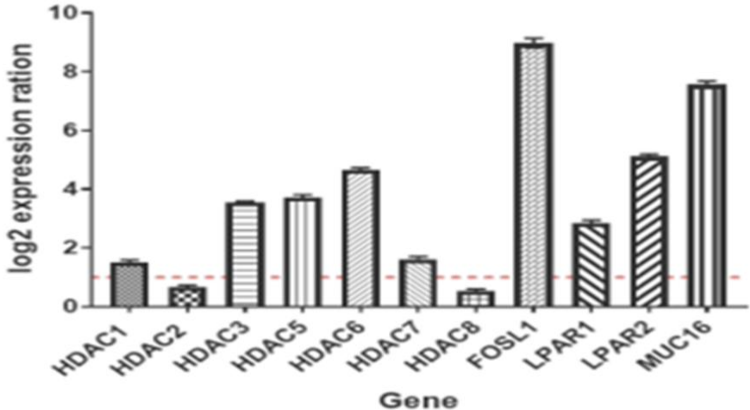

Figure 1. Expression of LPAR1 and LPAR2 relative to GAPDH in SKOV3 cells

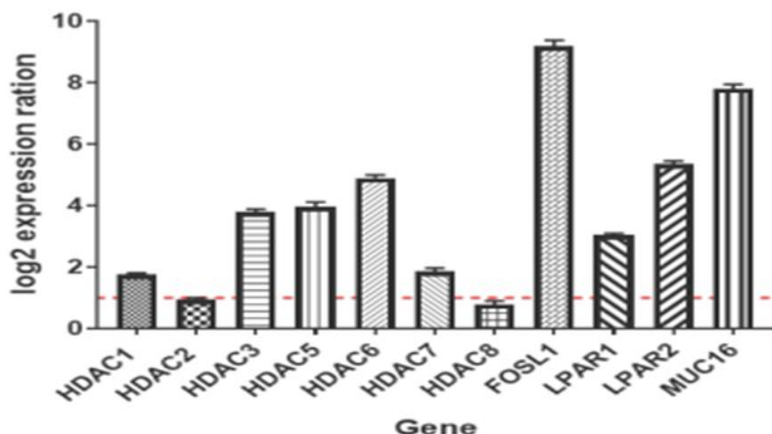

Figure 2. Expression of LPAR1 and LPAR2 relative to HPRT in SKOV3 cells

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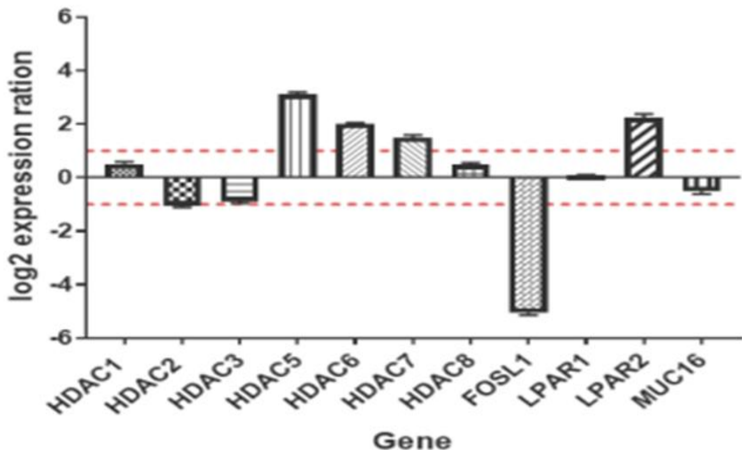

Figure 3: Expression of LPAR1 and LPAR2 relative to GAPDH in OAW42 cells

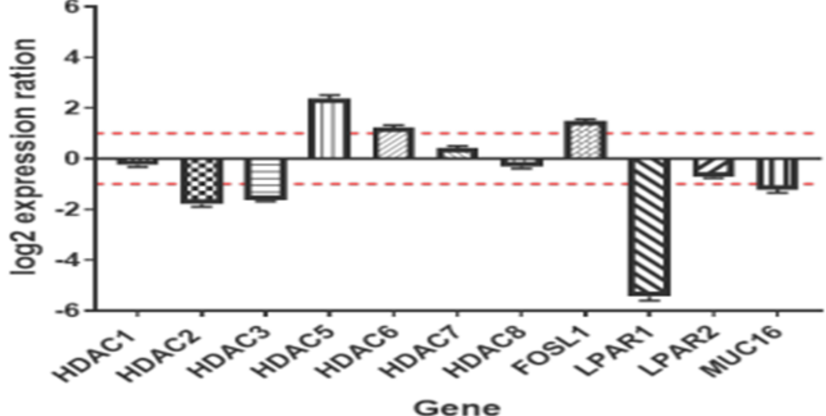

Figure 4. Expression of LPAR1 and LPAR2 relative to HPRT in OAW42 cells

Immunocytochemistry result

LPAR1 shows low cytoplasmic expression in SKOV-3 and OAW42 cells, which is indicated by the light brown colour intensity in their cytoplasm. High expression of LPAR1 was observed in the HOSEPiC nucleus, as indicated by the dark-intensity stain of the HOSEPiC cytoplasm (Figure 5).

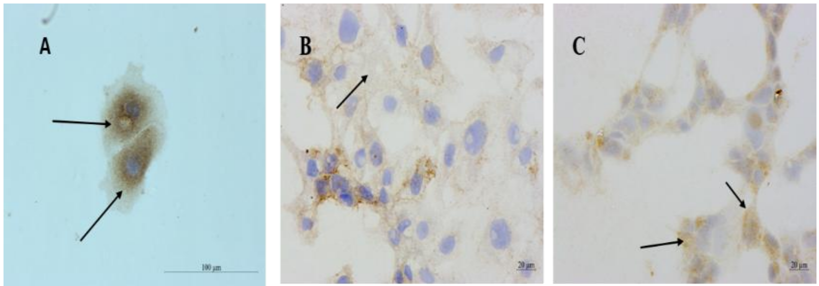

Figure 5: ICC analysis of LPAR1 expression in HOSEpiC, SKOV3, and OAW42 stained with hematoxylin and eosin (H&E). A, B, and C show in HOSEpiC, SKOV3, and OAW42 cells cytoplasm, respectively, and stained with H&E and the LPAR1 antibody. The dark purple stain represents the nuclei, while the brown stain represents LPAR2. The black arrows point to the localization of LPAR2. Images taken at 20 X magnification

LPAR2 protein expression exhibited upregulation in the cytoplasm of HOSEpiC cells while being downregulated in OAW42 and SKOV3 cells, as evidenced by the light staining intensity observed in their cytoplasm (Figure 2). Additionally, analysis of HDAC5 expression revealed higher expression levels in the cytoplasm of SKOV3 cells, with a moderate to strong presence in HOSEpiC cells, whereas its expression was significantly lower in OAW42 cells. Comparatively, HDAC6 protein staining intensity was more pronounced in both OAW42 and HOSEpiC cell cytoplasm, whereas SKOV3 cells exhibited only moderate intensity (Figure 6). These findings suggest distinct regulatory patterns for LPAR2, HDAC5, and HDAC6 across different ovarian cell lines, which may reflect their varying roles in ovarian cancer biology and progression.

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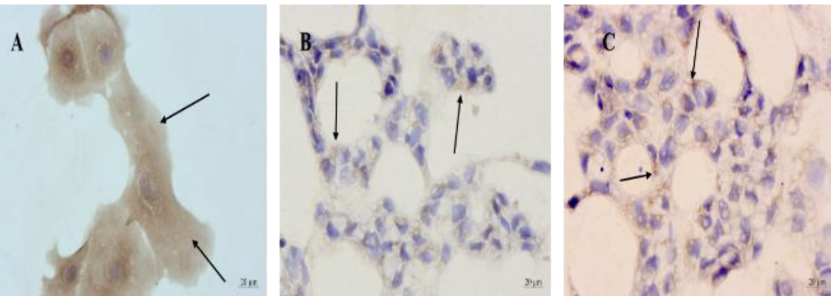

Figure 6: ICC analysis of LPAR2 expression in HOSEPiC, OAW42, and SKOV3 stained with hematoxylin and eosin (H&E). A, B, and C show in HOSEPiC, OAW42, and SKOV3 cells cytoplasm, respectively, and stained with H&E and the LPAR2 antibody. The dark purple stain signifies the nuclei, while the brown stain represents LPAR2. The black arrows point to the localization of LPAR2. Images were taken at 20 X magnification.

Discussion

Although the different expression of the candidate 'genes that achieved using the quantitative real-time RT-PCR method, the immunocytochemistry conducted used to quantify, LPA1, and LPA2 mRNA in epithelial ovarian cancer (OAW42 and SKOV-3) and normal ovarian epithelium (HOSEPiC), this approach is a fast and sensitive technique to quantify gene expression and needs smaller quantities of mRNA ovarian cells than common approaches. The results obtained with real-time RT-PCR were reliable with our previous data obtained by immunocytochemistry analysis According to our qRT-PCR results for LPAR1 was up-regulated normalized to HPRT in SKOV-3 and OAW42 (Figures 2 and 4) respectively, that supports the Human Protein Atlas database (Figure 7) which uses as a reference to confirm all human genes and protein expression in all cancer tissues [44, 45]. In addition, LPAR2 had a high expression in SKOV-3 which agreed with HPA but LPAR2 expressed low in OAW42 which is dissimilar to HPA data (Figure 8, 9).

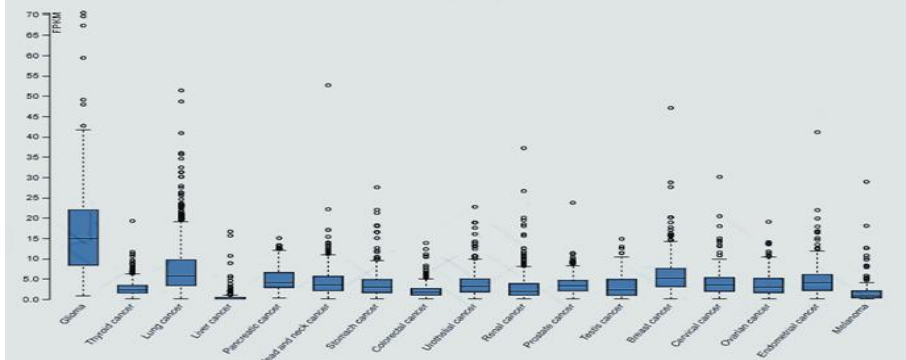

Figure 7. Expression in selected cancer types

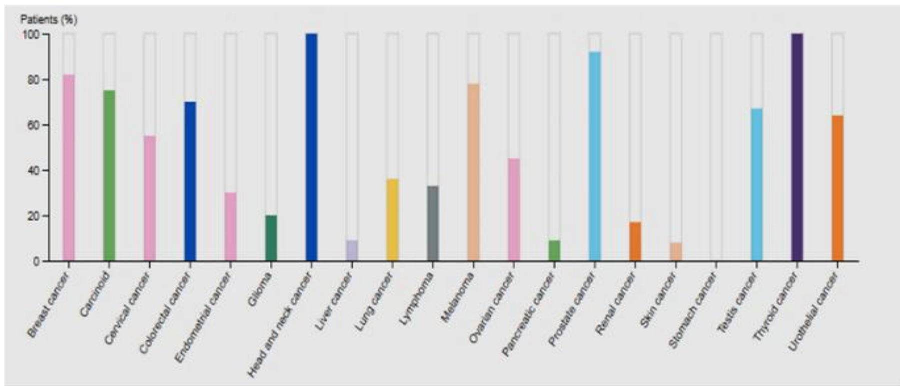

Figure 8. LPAR2 expression in all cancer types.

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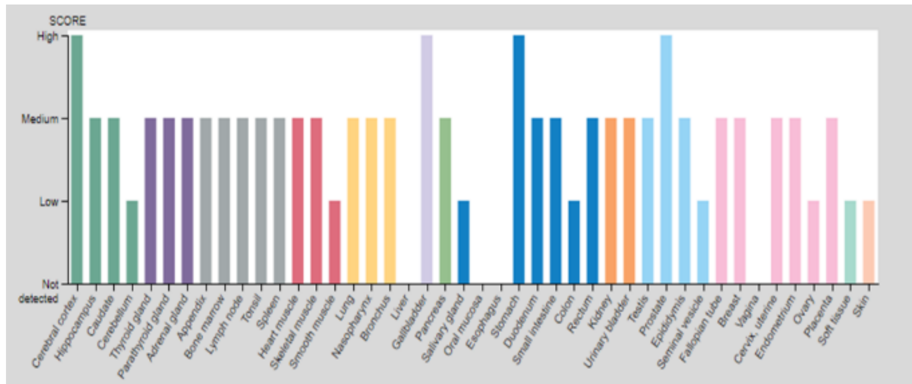
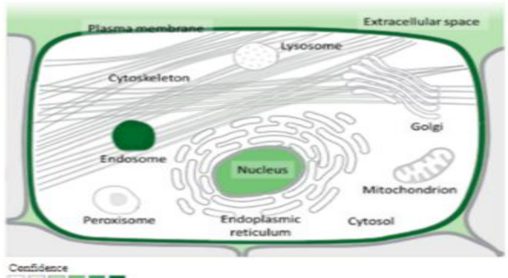


Figure 9. Protein expression overview of LPAR2 with score HPA database

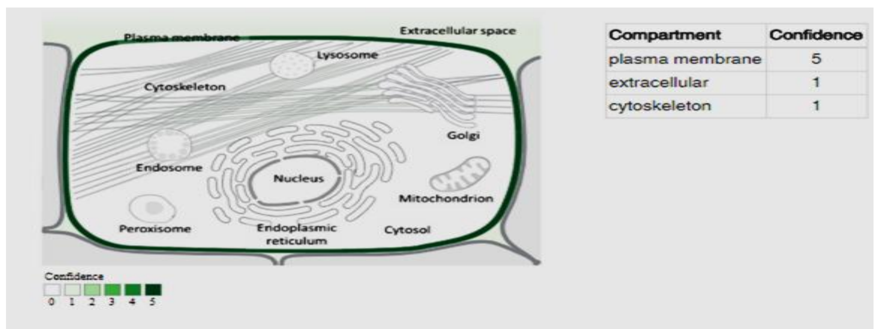
Regarding LPAR1 and LPAR2 protein expression as analyzed via immunocytochemistry (ICC), LPAR1 exhibited low-intensity cytoplasmic staining in both OAW42 and SKOV3 cells. However, due to the lack of available Human Protein Atlas (HPA) data, confirmation of LPAR1 expression in cancerous tissues remains inconclusive, as its analysis is still pending (https://www.proteinatlas.org/ENSG00000198121-LPAR1/pathology). Similarly, LPAR2 demonstrated low-intensity cytoplasmic staining in OAW42 and SKOV3 cells (Figure 5), whereas both LPAR1 and LPAR2 were found to be expressed in the cytoplasm of normal epithelial ovarian cells (HOSEpiC).

Comparative analysis with the GeneCards database [47-49] indicates that LPAR1 is predominantly localized in the endosome, plasma membrane, and nucleus, while LPAR2 is mainly expressed in the plasma membrane (Figure 6). These findings suggest that, while LPAR1 and LPAR2 are present in ovarian cancer cell lines, their cytoplasmic localization in normal epithelial ovarian cells (HOSEpiC) limits their specificity as cancer biomarkers. Further studies are required to elucidate their precise functional roles and potential implications in ovarian cancer pathogenesis.



Compartment	Confidence
plasma membrane	5
endosome	5
nucleus	3
extracellular	2
cytoskeleton	1

Figure 10. LPAR1 localization in the normal cell



Compartment	Confidence
plasma membrane	5
extracellular	1
cytoskeleton	1

Figure 11. LPAR2 localization in the normal cell

Conclusion

Ovarian cancer remains one of the most lethal gynaecological malignancies, and the identification of reliable biomarkers for early detection and disease progression remains a critical challenge. Due to the inherent heterogeneity of epithelial ovarian cancer (EOC), gene expression patterns vary across different cell lines, necessitating comprehensive investigations to assess their diagnostic and prognostic value. The present study aimed to evaluate the expression of LPA receptor genes, LPAR1 and LPAR2, in ovarian cancer cell lines using qPCR and immunocytochemistry (ICC) techniques. The findings revealed that while LPAR1 and LPAR2 were upregulated in ovarian cancer cell lines SKOV3 and OAW42, their expression was also detected in normal ovarian surface epithelial cells (HOSEpiC), thereby limiting their specificity as exclusive biomarkers

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for EOC.
Although these genes exhibit altered expression in malignant ovarian cells, their presence in non-cancerous cells suggests that LPAR1 and LPAR2 alone are insufficient as definitive diagnostic markers for early-stage EOC detection. The study highlights the complexity of ovarian cancer pathophysiology, where molecular markers may serve functional roles in both normal and cancerous cells, rather than acting as unique disease indicators. Nevertheless, qPCR and ICC techniques proved to be effective molecular tools for analyzing gene expression, reinforcing their applicability in ovarian cancer research.
To enhance the clinical utility of these findings, future studies should expand the scope of investigation by evaluating LPAR1 and LPAR2 expression in patient-derived plasma samples to determine their potential role as circulating biomarkers. Additionally, integrating these genes with a broader panel of molecular markers associated with EOC progression and metastasis may provide more robust diagnostic correlations. Further research should also focus on elucidating the downstream signaling pathways of LPAR1 and LPAR2 in ovarian cancer to understand their functional significance in tumour development, progression, and therapeutic targeting.
Ultimately, while LPAR1 and LPAR2 alone may not serve as standalone biomarkers for early EOC detection, their role in ovarian cancer biology warrants further investigation, particularly in combination with other molecular signatures. A multi-marker approach, alongside advanced genomic and proteomic techniques, may provide a more comprehensive framework for improving early detection, prognostic assessment, and targeted therapeutic strategies in EOC.

Conflict of interest. Nil

References

1. David M, Machuca-Gayet I, Kikuta J, Ottewell P, Mima F, Leblanc R, et al. Lysophosphatidic acid receptor type 1 (LPA1) plays a functional role in osteoclast differentiation and bone resorption activity. Journal of Biological Chemistry 2014, 289(10):6551-6564.
2. Zhang H-F, Hu P, Fang S-Q: Understanding the role of CD44V6 in ovarian cancer. Oncology Letters 2017, 14(2):1989-1992.
3. Zhang X, Ng W-L, Wang P, Tian L, Werner E, Wang H, et al. microrna-21 modulates the levels of reactive oxygen species by targeting SOD3 and tnfα. Cancer research 2012, 72(18):4707-4713.
4. Goff BA, Mandel LS, Melancon CH, Muntz HG: Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. Jama 2004, 291(22):2705-2712.
5. Flam F, Einhorn N, Sjövall K: Symptomatology of ovarian cancer. European Journal of Obstetrics and Gynecology and Reproductive Biology 1988, 27(1):53-57.
6. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2018. CA: a cancer journal for clinicians 2018, 68(1):7-30.
7. Moolenaar WH, van Meeteren LA, Giepmans BN: The ins and outs of lysophosphatidic acid signaling. Bioessays 2004, 26(8):870-881.
8. Morgan RJ, Alvarez RD, Armstrong DK, Boston B, Burger RA, Chen L, et al. Epithelial ovarian cancer. Journal of the National Comprehensive Cancer Network 2011, 9(1):82-113.
9. Chan JK, Cheung MK, Husain A, Teng NN, West D, Whittemore AS, et al. Patterns and progress in ovarian cancer over 14 years. Obstetrics & Gynecology 2006, 108(3, Part 1):521-528.
10. 10.Jemal A, Siegel R, Xu J, Ward E: Cancer statistics, 2010. CA: a cancer journal for clinicians 2010, 60(5):277-300.
11. Ouyang Y-B, Lu Y, Yue S, Giffard RG: mir-181 targets multiple Bcl-2 family members and influences apoptosis and mitochondrial function in astrocytes. Mitochondrion 2012, 12(2):213-219.
12. Webb PM, Purdie DM, Grover S, Jordan S, Dick M-L, Green AC: Symptoms and diagnosis of borderline, early and advanced epithelial ovarian cancer. Gynecologic oncology 2004, 92(1):232-239.
13. Singer CF, Tea M-K, Pristauz G, Hubalek M, Rappaport C, Riedl C, Helbich T: Guideline for the prevention and early detection of breast and ovarian cancer in HIGH-RISK patients, particularly in women from HBOC (hereditary breast and ovarian cancer) families. Wiener klinische Wochenschrift 2012, 124(9-10):334-339.
14. Xu Y, Fang X, Casey G, Mills G: Lysophospholipids activate ovarian and breast cancer cells. Biochemical Journal 1995, 309(Pt 3):933.
15. Xu Y, Shen Z, Wiper DW, Wu M, Morton RE, Elson P, et al. Lysophosphatidic acid as a potential biomarker for ovarian and other gynecologic cancers. Jama 1998, 280(8):719-723.
16. Mills GB, May C, mcgill M, Roifman CM, Mellors A. A putative new growth factor in ascitic fluid from ovarian cancer patients: identification, characterization, and mechanism of action. Cancer research 1988;48(5):1066-1071.
17. Baker DL, Morrison P, Miller B, Riely CA, Tolley B, Westermann AM, et al. Plasma lysophosphatidic acid concentration and ovarian cancer. Jama 2002, 287(23):3081-3082.
18. Xiao Y, Chen Y, Kennedy AW, Belinson J, Xu Y: Evaluation of plasma lysophospholipids for diagnostic significance using electrospray ionization mass spectrometry (ESI-MS) analyses. Annals of the New York Academy of Sciences 2000, 905(1):242-259.
19. Mills GB, Moolenaar WH: The emerging role of lysophosphatidic acid in cancer. Nature Reviews Cancer 2003, 3(8):582.

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https://doi.org/10.54361/ajmas.258139

20. Yu S, Murph MM, Lu Y, Liu S, Hall HS, Liu J, et al. Lysophosphatidic acid receptors determine tumorigenicity and aggressiveness of ovarian cancer cells. JNCI: Journal of the National Cancer Institute 2008, 100(22):1630-1642.
21. Xu Y, Gaudette DC, Boynton JD, Frankel A, Fang X-J, Sharma A, et al. Characterization of an ovarian cancer activating factor in ascites from ovarian cancer patients. Clinical Cancer Research 1995, 1(10):1223-1232.
22. Kraft H, Menzel H, Hoppichler F, Vogel W, Utermann G: Changes of genetic apolipoprotein phenotypes caused by liver transplantation. Implications for apolipoprotein synthesis. The Journal of Clinical Investigation 1989, 83(1):137-142.
23. Choi JW, Herr DR, Noguchi K, Yung YC, Lee C-W, Mutoh T, et al. LPA receptors: subtypes and biological actions. Annual review of pharmacology and toxicology 2010, 50:157-186.
24. Shen Z, Wu M, Elson P, Kennedy AW, Belinson J, Casey G, Xu Y: Fatty acid composition of lysophosphatidic acid and lysophosphatidylinositol in plasma from patients with ovarian cancer and other gynecological diseases. Gynecologic oncology 2001, 83(1):25-30.
25. Moolenaar WH: Development of our current understanding of bioactive lysophospholipids. Annals of the New York Academy of Sciences 2000, 905(1):1-10.
26. Fang X, Yu S, Bast RC, Liu S, Xu H-J, Hu S-X, et al. Mechanisms for lysophosphatidic acid-induced cytokine production in ovarian cancer cells. Journal of Biological Chemistry 2004, 279(10):9653-9661.
27. Fritsche HA, Bast RC: CA 125 in ovarian cancer: advances and controversy. In.: Clinical Chemistry; 1998.
28. Hecht JH, Weiner JA, Post SR, Chun J: Ventricular zone gene-1 (vzg-1) encodes a lysophosphatidic acid receptor expressed in neurogenic regions of the developing cerebral cortex. The Journal of Cell Biology 1996, 135(4):1071-1083.
29. An S, Bleu T, Hallmark OG, Goetzl EJ: Characterization of a novel subtype of human G protein-coupled receptor for lysophosphatidic acid. Journal of Biological Chemistry 1998, 273(14):7906-7910.
30. Bandoh K, Aoki J, Hosono H, Kobayashi S, Kobayashi T, Murakami-Murofushi K, et al. Molecular cloning and characterization of a novel human G-protein-coupled receptor, EDG7, for lysophosphatidic acid. Journal of Biological Chemistry 1999, 274(39):27776-27785.
31. An S, Dickens MA, Bleu T, Hallmark OG, Goetzl EJ: Molecular cloning of the human Edg2 protein and its identification as a functional cellular receptor for lysophosphatidic acid. Biochemical and biophysical research communications 1997, 231(3):619-622.
32. Noguchi K, Ishii S, Shimizu T. Identification of p2y9/GPR23 as a novel G protein-coupled receptor for lysophosphatidic acid, structurally distant from the Edg family. Journal of Biological Chemistry 2003, 278(28):25600-25606.
33. Moolenaar WH, Kranenburg O, Postma FR, Zondag GC. Lysophosphatidic acid: G-protein signaling and cellular responses. Current opinion in cell biology 1997, 9(2):168-173.
34. Fan Q, Cai Q, Xu Y. FOXM1 is a downstream target of LPA and YAP oncogenic signaling pathways in high-grade serous ovarian cancer. Oncotarget 2015, 6(29):27688.
35. Kotarsky K, Boketoft Å, Bristulf J, Nilsson NE, Norberg Å, Hansson S, et al. Lysophosphatidic acid binds to and activates GPR92, a G protein-coupled receptor highly expressed in gastrointestinal lymphocytes. Journal of Pharmacology and Experimental Therapeutics 2006, 318(2):619-628.
36. Lee C-W, Rivera R, Gardell S, Dubin AE, Chun J: GPR92 as a new G12/13-and Gq-coupled lysophosphatidic acid receptor that increases camp, LPA5. Journal of Biological Chemistry 2006, 281(33):23589-23597.
37. Tabata K-i, Baba K, Shiraishi A, Ito M, Fujita N: The orphan GPCR GPR87 was deorphanized and shown to be a lysophosphatidic acid receptor. Biochemical and biophysical research communications 2007, 363(3):861-866.
38. Pasternack SM, von Kügelgen I, Al Aboud K, Lee Y-A, Rüschendorf F, Voss K, Hillmer AM, Molderings GJ, Franz T, Ramirez A: G protein-coupled receptor P2Y5 and its ligand LPA are involved in the maintenance of human hair growth. Nature Genetics 2008, 40(3):329.
39. Murakami M, Shiraishi A, Tabata K, Fujita N: Identification of the orphan GPCR, P2Y 10 receptor as the sphingosine-1-phosphate and lysophosphatidic acid receptor. Biochemical and biophysical research communications 2008, 371(4):707-712.
40. Mcintyre TM, Pontsler AV, Silva AR, Hilaire AS, Xu Y, Hinshaw JC, et al. Identification of an intracellular receptor for lysophosphatidic acid (LPA): LPA is a transcellular pparγ agonist. Proceedings of the National Academy of Sciences 2003, 100(1):131-136
41. Zhang C, Baker DL, Yasuda S, Makarova N, Balazs L, Johnson LR, et al. Prestwich GD: Lysophosphatidic acid induces neointima formation through pparγ activation. Journal of Experimental Medicine 2004, 199(6):763-774.
42. Sutphen R, Xu Y, Wilbanks GD, Fiorica J, Grendys EC, lapolla JP, et al. Lysophospholipids are potential biomarkers of ovarian cancer. Cancer Epidemiology and Prevention Biomarkers 2004, 13(7):1185-1191.
43. Murph MM, Nguyen GH, Radhakrishna H, Mills GB: Sharpening the edges of understanding the structure/function of the LPA1 receptor: expression in cancer and mechanisms of regulation. Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids 2008, 1781(9):547-557.
44. Fagerberg L, Hallström BM, Oksvold P, Kampf C, Djureinovic D, Odeberg J, et al. Analysis of the human tissue-specific expression by genome-wide integration of transcriptomics and antibody-based proteomics. Molecular & Cellular Proteomics 2014, 13(2):397-406.
45. Paik Y-K, Jeong S-K, Omenn GS, Uhlen M, Hanash S, Cho SY, et al. The Chromosome-Centric Human Proteome Project for cataloging proteins encoded in the genome. Nature Biotechnology 2012, 30(3):221.

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المستخلص

يشكل سرطان المبيض الظهاري أعلى عدد من الوفيات بين مرضى سرطان المبيض. ومع ذلك، فإن الآليات الجزيئية الأساسية لتكوين الورم في سرطان المبيض الظهاري غامضة في الوقت الحالي. في هذه الدراسة، تم اختيار تفاعل البوليميراز المتسلسل الكمي في الوقت الحقيقي للتلاعب بتعبير جين مستقبل البروتين الدهني 1 ومستقبل البروتين الدهني 2 في سلالات خلايا سرطان المبيض. تم استخدام التلوين المناعي الكيميائي لفحص تعبير جين مستقبل البروتين الدهني 1، 2 في سرطان المبيض الغدي وسرطان المبيض الكيسي، وهما سلالات خلايا سرطان المبيض، واستخدام خلايا ظهارة سطح المبيض البشرية كصورة سلبية، والتي تم إنشاؤها، من الخلايا الظهارية سطح المبيض البشرية. أثبتت النتائج أن تعبيرات جين مستقبل البروتين الدهني 1و 2 قد ارتفعت في سرطان المبيض الغدي و وسرطان المبيض الكيسي عند استخدام تقنية البوليميراز المتسلسل الكمي في الوقت الحقيقي للمساعدة، ومع ذلك، أظهرت نتائج المناعة الخلوية التعبير عن جين مستقبل البروتين الدهني و جين مستقبل البروتين الدهني 2 في سرطان المبيض الغدي وسرطان المبيض الكيسي و خلايا ظهارة سطح المبيض البشرية مما يشير إلى أن كل من جين مستقبل البروتين الدهني 1و جين مستقبل البروتين الدهني 2 ليسا مؤشرين حيويين جيدين للكشف عن سرطان المبيض الظهاري في مرحلة مبكرة. وفي الختام، تشير نتائج الدراسة الحالية إلى أن الارتباط بين جين مستقبل البروتين الدهني 1و جين مستقبل البروتين الدهني 2 لا يعمل كمؤشرات حيوية أو أهداف تشخيصية في سرطان المبيض الظهاري من ناحية أخرى، يعتبر استخدام تقنيات تفاعل البوليميراز المتسلسل الكمي في الوقت الحقيقي و الكيمياء المناعية الخلوية كأدوات جيدة للاستخدام.

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