Common Dysregulated Genes in Endometriosis and Malignancies

Genes comuns desregulados em endometriose e doenças malignas

Daniel Blasioli Dentillo[1] Juliana Meola[1] Rui Alberto Ferriani[2] Julio César Rosa-e-Silva[3]

[1] Department of Gynecology and Obstetrics, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo – USP, Ribeirão Preto, SP, Brasil
[2] Human Reproduction Sector, Department of Gynecology and Obstetrics, Faculdade de Medicina de Ribeirão Preto, USP, Ribeirão Preto, SP, Brasil
[3] Gynecology Surgery Sector, Department of Gynecology and Obstetrics, Faculdade de Medicina de Ribeirão Preto, USP, Ribeirão Preto, SP, Brasil

Address for correspondence Daniel Blasioli Dentillo, PhD, Departamento de Ginecologia e Obstetrícia, Hospital das Clínicas da FMRP-USP, Avenida Bandeirantes, 3900, 8° andar, Monte Alegre, Ribeirão Preto, SP, Brasil 14049-900 (e-mail: danieldentillo@usp.br).

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Abstract

Several authors have investigated the malignant transformation of endometriosis, which supports the hypothesis of the pre-neoplastic state of endometriotic lesions, but there are few data about the pathways and molecular events related to this phenomenon. This review provides current data about deregulated genes that may function as key factors in the malignant transition of endometriotic lesions. In order to do so, we first searched for studies that have screened differential gene expression between endometriotic tissues and normal endometrial tissue of women without endometriosis, and found only two articles with 139 deregulated genes. Further, using the PubMed database, we crossed the symbol of each gene with the terms related to malignancies, such as *cancer* and *tumor*, and obtained 9,619 articles, among which 444 were studies about gene expression associated with specific types of tumor. This revealed that more than 68% of the analyzed genes are also deregulated in cancer. We have also found genes functioning as tumor suppressors and an oncogene. In this study, we present a list of 95 informative genes in order to understand the genetic components that may be responsible for endometriosis' malignant transformation. However, future studies should be conducted to confirm these findings.

Keywords

- cancer
- endometriosis
- gene expression

Resumo

Vários autores têm estudado transformações malignas em endometriose que suportam a hipótese de um estado pré-neoplásico das lesões endometrióticas; contudo, existem poucos dados sobre as vias e eventos moleculares relacionados a este fenômeno. Esta revisão fornece dados atuais sobre genes desregulados que possam funcionar como fatores-chave para a transição maligna das lesões endometrióticas. Assim, inicialmente, estudos de expressão gênica diferencial em larga escala

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comparando tecido endometriótico e endométrio normal de mulheres sem endometriose foram procurados, e apenas dois artigos com 139 genes desregulados foram obtidos. Posteriormente, usando o banco de dados do PubMed, foram cruzados os símbolos de cada gene com termos relacionados à malignidade, como *câncer* e *tumor*, e 9.619 artigos foram obtidos, dos quais 444 eram estudos sobre expressão de genes associados a tipos específicos de tumor. Isto revela que mais de 68% dos genes analisados eram também desregulados em câncer. Também foram encontrados genes que funcionam como supressor tumoral e um oncogene. Este estudo apresenta uma lista de 95 genes informativos para compreender os componentes genéticos que possam ser responsáveis por transformações malignas na endometriose. Contudo, estudos futuros são necessários para confirmar estes achados.

Palavras-chave
- câncer
- endometriose
- expressão gênica

Introduction

Endometriosis is a chronic gynecological disorder that affects nearly 10% of women in reproductive age worldwide.[1] It is characterized by the existence of endometrial tissue outside the uterus, mainly ovary and pelvic peritoneum, and is related to pelvic pain and infertility symptoms in great part of the patients.[2,3] Although endometriosis is considered a benign disease, it shares some biological characteristics with cancer, like cell invasion, expansion of new blood vessels, unrestrained growth, resistance to apoptosis, potential to metastasize and occurrence of chronic inflammation.[4,5]

Several investigations have focused on the malignant transformation of ectopic endometrial tissue, supporting the hypothesis of its pre-neoplastic state, predominantly in the ovary.[6–18] Studies have revealed that endometriotic lesions in endometriosis-associated ovarian cancer (and tumor) may go through multistep transition stages, from typical to atypical endometriosis, and then to carcinoma.[19,20] It has also been documented that the two major cancer histotypes related to the malignization of ovarian endometriosis are endometrioid and clear cell carcinomas,[21] and serous and mucinous carcinomas are encountered less frequently.[22,23] Even though rare, the occurrence of the malignant transformation of endometriosis in other organs such as the colon and the rectum is reported,[24,25] including cases like endometriosis-associated abdominal wall cancer, which shows aggressiveness and poor prognosis.[21]

Regarding the frequency, some authors have estimated the overall risk of 1% for the development of neoplasms from endometriotic tissue, but this percentage is supposed to be higher, since there are few studies of cancer arising from endometriosis available.[14,22] Besides, a great limitation to calculate the real risk of endometriosis' progression to malignancy is associated with the rigorous histopathological criteria used to characterize this transition: proof of endometriotic foci close to the tumor; the carcinoma must arise from endometriosis, and not invade it from other sources; presence of tissue resembling endometrial stroma surrounding characteristic glands; and morphological demonstration of continuity between benign and malignant tissues within endometriosis.[26,27] Rarely all these stringent features are fulfilled, leading to the underestimation of the malignant conversion of endometriotic tissue.[28] Moreover, another aggravating condition is that cancerous tissue probably destroys endometriotic foci, removing the histological evidence of endometriosis' transformation to cancer.[28,29]

Currently, molecular events that would clarify endometriosis transformation into cancer are being researched. It is believed that epigenetic processes and somatic genetic changes in endometriotic implants could initiate tumorigenesis.[5,30–32] Gogusev et al[33,34] showed that ectopic endometrium in peritoneal implants and ovarian endometrioma have gain and loss of certain chromosomal regions that harbor genes representative of those involved in malignancies, such as oncogenes and tumor suppressors. However, the real frequency of these alterations and which genes really contribute to the benign–malign phenomenon in endometriosis remain unknown.[28]

The aim of this review is to identify in the literature deregulated genes in endometriotic lesions that may be involved with cancer pathways, explain malign transition from endometriosis, and bring new insights about the origin and development of endometriosis itself.

Methods

We performed two rounds of searches based on the survey of data available in PubMed (from 1985 to 2015) from articles published in English only.

In the first round, we used the terms *gene expression* and *endometriosis*. The inclusion criteria were studies that have screened global differential gene expression (individual studies of a single gene expression were not included) and those that have compared endometriotic tissues and normal endometrial tissues of women without endometriosis. We did not consider the comparison between ectopic and eutopic endometria of women with endometriosis since these tissues share biochemical and functional changes that are not detected in the endometria of women without endometriosis.[35] We excluded from our search works in which: a) the absence and presence of endometriosis were not confirmed

by laparoscopy; and b) the patients had undergone hormonal therapy prior to the sample collection.

In the second round, we crossed the symbol of each selected gene from the papers obtained in the first search with the terms: *cancer*, *tumor*, *endometrioid carcinoma*, *clear cell carcinoma*, *serous carcinoma*, *mucinous carcinoma*, *oncogene,* and *tumor suppressor gene*. We just considered cancers and tumors in female organs, and genes with altered expression in both endometriosis and cancer. Genetic polymorphisms were not considered.

Results

In the first search, we excluded 843 articles because we found just 2 studies that satisfied the established criteria.[36,37] Honda et al[36] defined the profile of gene expression by serial analysis of gene expression (SAGE) using ovarian lesions as samples, and showed 34 deregulated genes. In another work published by our group,[37] we utilized samples of peritoneal lesions and ovarian endometriotic tissues and defined 105 deregulated genes using rapid subtraction hybridization (RaSH). *ITGB1*, which encodes the integrin β-1 subunit, is the unique gene shared by both analyzed articles. In the two investigations, the control group of women and the endometriosis patients were at the proliferative phase of the menstrual cycle.

In the second search, we obtained 9,619 articles that resulted from the match of each gene symbol with the specific terms. Among these articles, 444 of them were studies about gene expression associated with different types of tumor (►**Table 1**). We found that more than 68% of the genes deregulated in endometriosis were also deregulated in cancer.

The list of genes with deregulated expression in the major cancer histotypes related to the malignization of endometriosis is the following: clear cell carcinoma (*LDHA*, *RHOC*, *ILK*, *HLA-DRA*, *MMP2*, *ACTN4*); endometrioid carcinoma (*ILK*, *HLA-DRA*, *MMP2*, *MMP7*, *ANAXA2*); serous carcinoma (*CRABP2*, *RHOC*, *SPARC*, *SP1*, *ILK*, *MMP2*, *MMP7*, *HLA-DRA*, *ACTN4*, *IGF2*, *ANAXA2*); and mucinous carcinoma (*SP1*, *ILK*, *HLA-DRA*). We have also found in the literature *ENO1*, *TXNIP* and *SPARC* acting as tumor suppressor genes and *ID2* acting as an oncogene.

Discussion

The investigations about the development of cancer from endometriosis initiated with Sampson (1925).[26] Since then, some publications and case reports have documented cancerous tissues forming within endometriotic lesions.[24,38–44]

The majority of works that have tried to comprehend the malignant progression of endometriosis refers to the ovary, which is responsible for 80% of cases.[45] It is estimated that ovarian cancer develops in 1 to 5% of cases of ovarian endometriosis (10 to 20% endometrioid carcinoma and less than 5% clear cell carcinoma histotypes).[4,22,46] Nevertheless, if we take into account histological transition from benign to malign endometriosis, according to the description of Sampson[26] and Scott,[27] its prevalence is estimated as 0.9%. Apparently, in patients with endometriosis the ovaries are more susceptible to malignization.[47,48] Findings from ultrasound assessment of carcinomas forming in endometrioid cysts point to some characteristics that are indicative of malignant transformation in the ovaries,[49] where a continuum of typical and atypical endometriosis with transition to an invasiveness condition was already found.[50] Indeed, the calculated risk of women developing ovarian cancer is two times higher compared with the general population, and after a follow-up period of over 10 years, this risk may increase 4.2-fold.[4,17] Although the ovary is the most affected organ by endometriosis-originated tumors, reports have recently showed that endometriosis is a risk factor for the development of endometrial cancer.[48,51]

Even if infrequently, there have been reports of extraovarian sites affected by malignant transition from endometriotic implants. The organs most usually affected are the rectovaginal septum, the vagina, the urinary bladder and the colorectum (the last corresponding to 5%), but alterations in the pelvic ligaments, the umbilicus, the abdominal wall, the cervix, and the uterine tubes were also reported. However, no risk of ectopic endometrium conversion to cancer in these locations has been calculated.[21,22,52,53]

The predicted incidence for ovarian and extraovarian malignization in endometriosis is an underestimate. Some of the reasons for this are: difficulty to fulfill Sampson's and Scott's criteria; excision of endometriotic foci is generally complete, and atypical unidentified lesions may be absent after surgery; the emerging cancerous cells can obliterate endometriotic lesions, removing the signs of a clear transition of a benign to a malignant condition; some endometriotic tissues are never treated surgically: they are only partially resected, preventing extensive sampling performance; and the number of investigations about the transition between endometriosis and cancer is insufficient until now.[14,22,28,47,54]

Even so, the cancerous potential of endometriosis should be carefully analyzed, for malignancy is often not recognized until a precise pathologic examination of the extirpated specimen.[54] Besides, in some cases malignancy can occur in residual remnant derived from an inadequate total endometriotic foci removal surgery.[55] In this way, most specifically for ovarian endometriosis, it is essential to run a detailed inspection and an effective surgical intervention, as epithelial ovarian cancer is the main cause of death among the female genital tract malignancies.[54] In patients with recurrent endometriosis, more incisive observation should be directed to a continued sampling of recurrences, once malignant transformation can take place.[56]

Endometriosis' Malignant Transformation from the Molecular Point of View

The malignization of endometriosis is considered according two main hypotheses. The first is that endometriotic lesions can directly go through cancerous transformation, maybe

Table 1 Differentially expressed genes in endometriosis (endometriotic lesions in comparison with endometrial tissue of women not affected by endometriosis) that have deregulated expression in cancer

Symbol	Locus	Type of cancer or tumor
Gene (Honda el at[36])		
RPS9	19q13.4 *	pancreatic, breast, brain
ACTN4	19q13.2 *	breast, brain, bladder, oral, pancreas, ovary, liver, renal, esophageal, colorectal, lung, leukemia
IGF2	11p15 *	adrenal, colorectal, brain, pancreas, melanoma, peripheral and central nervous systems, rhabdomyosarcoma, esophageal, renal, gastric, uterine (cervix, endometrium and myometrium), liver, breast, ovary, head and neck, meninges, bone, lung, bladder, laryngeal, synovial, leukemia
CHI3L1	1q32.1	brain, uterus (cervix and endometrium), lung, breast, pancreas, gastric, lymphoma, renal, head and neck, melanoma, liver, colorectal, multiple myeloma, leukemia
CEBPB	20q13.1 *	brain, gastric, bone, leukemia, lung, lymphoma, uterine cervix
ITGB1	10p11.2 *	brain, gastric, rectal, oral, liver, lung, kidney, esophageal, leukemia
EFEMP2	11q13.1 *	endometrium
AXL	19q13.2 *	oral, bladder, breast, melanoma, thyroid, leukemia, liver, pancreas, ovary, esophageal, brain, renal, lung, gastric, bone, synovial, colorectal, uterus (endometrium, myometrium)
DYNLRB1	20q11.22	liver
PTBP1	19p13.3 *	brain, multiple myeloma
JUND	19p13.11	breast, liposarcoma, oral, pancreas, brain, lung, lymphoma, colon, liver, melanoma, ovary
PGK1	Xq21.1	liver, gastric, lung, pancreas, colon, renal
SHC1	1q21.3	gastrointestinal, leukemia, breast, colon
NNMT	11q23.2 *	bladder, renal, brain, oral, lung, liver, pancreas, colorectal, thyroid
SMARCC2	12q13.2 *	lung
ACTG1	17q25.3 *	bone, liver
PPIE	1p32 *	brain, lung
MRLC2	18p11.31 *	ovary
HINT1	5q23.3	gastric, liver, colon
RPS14	5q33.1	leukemia
PAPSS2	10q23.2-q23.3	esophageal, gastric
B3GNT5	3q28 *	brain
ANXA2	15q22.2	pancreas, endometrium, liver, colon, breast, brain, multiple myeloma, lung, bone, leukemia
GAPDH	12p13.31	ovarian, breast, brain, colorectal, lung, liver, thyroid, pancreas, renal, uterine cervix
NUCB2	11p15.1 *	breast, gastric
CAMLG	5q23 *	breast
Gene (Dentillo et al[37])		
CRABP2	1q23.1	brain, head and neck, lung, oropharyngeal, renal, ovary, retina
TH1L	20q13 *	breast, colorectal
ATP5A1	18q21 *	colon, leukemia
UBE1	Xp11.23	gastric, lymphoma, leukemia, multiple myeloma, lung
TRIM28	19q13.4 *	breast, colorectal, gastric
SOX17	8q11.23	liver, leukemia, breast, gastrointestinal, colorectal, gastric
ENO1	1p36.2 *	gastric, thyroid, breast, lung, melanoma, brain, liver, colon, oral

Table 1 (*Continued*)

Symbol	Locus	Type of cancer or tumor
XRCC5	2q35 *	liver, lung, uterine cervical, melanoma, multiple myeloma, breast
PCBP1	2p13.3	pancreas, liver
ID2	2p25 *	multiple myeloma, lung, lymphoma, liver, leukemia, breast, brain
RNPS1	16p13.3 *	ovary
LMO4	1p22.3 *	breast, pancreas, oral
SMARCE1	17q21.2 *	breast
PABPC1	8q22.3 *	esophageal, bladder
PCBP2	12q13.13	oral
FOSB	19q13.32	pancreas, colorectal, liver, breast, melanoma, endometrium, ovary
IMPDH2	3p21.31	bone, colorectal, melanoma
SRSF3	6p21 *	ovary, lymphoma
SP1	12q13.13	breast, ovary, gastric, leukemia, pancreas, lung, melanoma, colorectal, endometrium, liver
HNRPA1	12q13.13	colorectal, leukemia
P4HB	17q25 *	endometrium
PGK1	Xq13.3	gastric, pancreas, lung, colon
PPIB	15q22.31	colorectal
LDHA	11p15.1 *	retina, colorectal, uterine cervix
PSAP	10q22.1	breast, bladder
ACSL5	10q25.2 *	brain
TCP1	6q25.3	colorectal
LCMT1	16p12.1 *	brain
TXNIP	1q21.1	head and neck, liver, gastrointestinal, breast, melanoma
ACTG1	17q25 *	bone
TP53I3	2p23.3	bladder
RTN4	2p16.1	brain, liver
HSPB1	7q11.23 *	head and neck, uterine cervix, leukemia, breast, ovary, liver, retina, gastric, brain, melanoma, pancreas, colorectal, esophageal, laryngeal
DDAH2	6p21.3 *	ovary, breast
NR2F2	15q26 *	lung, breast, lymphoma, salivary gland
EIF4G2	11p15 *	brain, bladder
TPT1	13q14 *	colon
IFITM3	11p15.5 *	colon, rectal
SERPINB6	6p25 *	colorectal
RHOC	1p13.2	lung, tongue, uterine cervix, head and neck, breast, pancreatic, melanoma, liver, renal, esophageal, gastric, colon, ovary, bladder
TRAF3	1p34.2 *	pancreas
GNB2L1	5q35.3	breast, lung, colon, oral, head and neck
GNAS	20q13.3 *	ovary
SPARC	5q33.1	lymphoma, brain, gastric, bladder, pancreas, lung, liver, ovary, melanoma, endometrium, colorectal
STC1	8p21.2	colorectal, breast, ovary
ECM1	1q21 *	breast, thyroid, esophageal, gastric, colorectal
ID1	20q11 *	thyroid, lung, head and neck, ovary, gastric, breast, multiple myeloma
CALM2	2p21 *	lymphoma

(*Continued*)

Table 1 (*Continued*)

Symbol	Locus	Type of cancer or tumor
EEF2	19p13.3 *	gastrointestinal, head and neck, lung
HBB	11p15.5 *	breast
ACTB	7p22 *	gastrointestinal, liver, lymphoma
HSD3B2	1p12 *	adrenal, endometrium
CFL1	11q13 *	breast, lung, colon, esophageal, leukemia, lymphoma
CUL3	2q36.2	breast
NGFRAP1	Xq22.2	ovary
ITGB1	10p11.2 *	ovary, brain, gastric, rectal, oral, liver, lung, kidney, esophageal, leukemia
CD81	11p15.5 *	brain, liver, multiple myeloma, lymphoma, leukemia
ILK	11p15.4	bladder, colorectal, brain, lung, breast, ovary, head and neck, gastric, pancreas, thyroid
HTRA1	10q26.13	liver, ovary, endometrium, lung, melanoma
SAT1	Xp22.1 *	bladder
LGI1	10q24 *	brain, colorectal
TMSB10	2p11.2 *	pancreas
GSN	9q33 *	breast, leukemia
PEBP1	12q24.23	pancreas, ovary, gastric, colorectal, liver, breast, melanoma, lymphoma, bladder
ATP2A2	12q24.11	colon, lung, oral, colorectal
TAGLN	11q23.2 *	colorectal, lung, bladder, esophageal, gastric
HLA-DRA	6p21.32	liver, brain, breast, lung, ovary, lymphoma, melanoma, colon, leukemia
MMP2	16q12.2 *	melanoma, brain, ovary, endometrium, liver, bladder, gastric, lung, oral, renal, head and neck, breast, colorectal, thyroid
MMP7	11q22.2	colorectal, breast, bladder, ovary, oral, pancreas, renal, lymphoma, lung, thyroid, endometrium, gastric, esophageal, colon

Source: Data provided by the National Center for Biotechnology Information (NCBI) website.
Note: *Indicates the loci (referring to breakpoints, loss or gain of the specific chromosomal region) that have been reported to be associated with every kind of cancer.

after acquiring genetic alterations; in the second, it is speculated that endometriosis and cancer have common molecular mechanisms or share similar predisposing influences (such as genetic and immune deregulations, environmental factors) that originate both diseases.[5,22,45] In any case, the genetic component is important, as it implies modifications in cellular metabolism, which can lead to the malign state. Moreover, there are molecular genetics evidences that endometriosis is a precursor of ovarian carcinoma, even though all the genes and pathways implicated in this transition are yet unidentified.[57] Then, understanding the related processes between endometriosis and cancer at a molecular level might clarify if the malignant condition can be a consequence of endometriosis or just a parallel phenomenon.

The importance of this knowledge is directly related to the early diagnostics of malignancies in endometriosis patients as well as their prognosis, as it is reported that the risk of cancer may become greater in patients with a long history of endometriosis.[48,51,53,58] Furthermore, recognizing endometriotic lesions turning malignant would require different therapeutic management to treat adequately the two disorders concomitantly.[59] In reality, comprehending the malignant transformation of endometriosis would require a long-term survey of untreated cases, which is unfeasible for obvious reasons.[28] Due to that, finding other approaches that allow a reliable characterization of the endometriosis malignization occurrence would be desirable. Thereby, molecular information can be a good tool. Previous works have shown that molecules like the inflammatory cytokine Il-1, growth factors and TNF-α are expressed in endometriosis, creating a condition comparable to the one found in malignancies.[4,17,60] Another work has detected overexpression of p53 in atypical endometriosis and cancer associated with endometriosis by immunohistochemistry. The authors concluded that the molecule may be used to identify endometriosis with premalignant potential.[50]

Additionally, genetic background obtained by observations of endometriosis patients with familial cancer history suggests the role of genes favoring the onset of cancer.[61] Studies have also provided data which show that genomic instability in endometriosis may lead to mechanisms similar to those that cause carcinogenesis.[45,57] Using polymorphic

microsatellite markers from the 22 autosomal human chromosomes, Prowse et al offer indications that endometriotic lesions carry genetic changes that can originate cells with replicative advantages, equivalent to what happens in neoplasms.[57] Another study from 2011 exposed common up and down-deregulated genes in both endometriosis and ovarian cancer.[17] All of these findings put together denote a consistent link between endometriosis and cancer. Despite that, the precise groups of genes and molecules that may contribute to endometriosis' malignant transformation are not completely elucidated.[62]

A range of studies has evidenced clearly that the endometrial tissue of women with endometriosis expresses a different repertoire of genes in relation to both ectopic endometrium and the endometrium of women not affected by the disease.[2,36,63–65] The paired comparison between eutopic endometrium versus endometriotic lesions has revealed an altered expression of some genes, such as *CTGF*, *TP53* and *MYC*, which were already described as having a deregulating expression in cancer pathways as well.[2,66–69] However, the association of differentially expressed genes in a normal endometrium (without anatomical, histological and physiological alterations) and in endometriotic implants, evidencing their participation on cancerous processes, has not been displayed until now.

The result of our search shows a list of genes that exhibit different expression in endometriotic lesions and in the endometria of women without endometriosis. Of the total 139 gene sequences analyzed, we found that 95 (68.11%) also had altered expression in diverse types of cancer; moreover, a greater part of the genetic loci where the analyzed genes are has any relation to cancer (►**Table 1**). We think that these genes may participate in molecular pathways that generate cancer-like behavior in endometriosis, and are also related to endometriosis pathogenesis. Furthermore, these genes might also contribute to the malignization of endometriotic implants, as they play a role in carcinogenesis and could be used to explain the premalignant potential of endometriosis. One example is *ITGB1*, which is involved in cell adhesion, participates in the metastasis process and contributes to the malignant enhancement in ovarian cancer cells.[70–72]

Obviously, for the description of a real involvement of these genes (presented in our work) with cancer one must do a direct comparison of cancerous and endometrial ectopic tissues. Moreover, for accurate results the use of suitable methodologies is essential, like real-time PCR, which currently is the "gold standard" confirmative technique for gene expression investigation. However, the list of genes presented here can trigger some insights regarding the pathways or group of genes that should be include in studies related to endometriosis' malignization.

We have also found genes deregulated in endometriosis and in the most frequent histotype of cancers, as well as genes that can function as tumor suppressors and oncogenes. These data expose the roles of some genes in cancerous processes in endometriosis, reinforcing its malignant transformation potential. Moreover, in our study some investigated genes play roles related to cancer onset and development, such as cell invasion, metastasis enhancement (RHOC in melanoma and GNB2L1 in breast carcinoma), angiogenesis (PEPB1) and anti-apoptosis behavior (*HSPB1* in several cancers, in which it was also referenced as a therapeutic target).[73–76] Other genes are associated with more aggressive tumor behavior and poor clinical prognosis (*ID1* in breast, cervical and endometrial carcinomas, and *ILK* in a large number of malignancies).[77–81]

The relationship of endometriosis and cancer in different types of organs does not imply that these tissues are in fact stricken directly by endometriosis. This statement aims to point to the frequency with which the genetic expression of each gene is deregulated in a variety of cancer types. At the same time, several authors have detected that having endometriosis itself may increase the risk of developing lymphoma, melanoma and breast cancer, which are not associated with pelvic or abdominal organs.[22,82] However, this is based just on empiric observations and there is no available explanation about what mechanisms cause those elevated risks in women affected by endometriosis. Perhaps a tissue could have more susceptibility to malignant transformation or correlate better with certain organs depending on the biological microenvironment where endometriotic lesions implant themselves.[45]

Conclusion

Endometriosis and cancer are complex, and heterogeneous disorders and malignization of endometrial ectopic implants must be considered particularly, as they might have more complicated provenance than each of the diseases individually.[45,83–85] Both entities can have their own proper pathogenesis associated with a particular gene or multiple genetic loci and pathways, as well as be affected by a variety of environmental factors. Identifying genomic profiles that overlap in endometriosis and cancer in distinct situations (such as stage and location) may provide clues to the understanding of the malignization of endometriotic lesions.[5,86] In our study, we've presented a list of 95 informative genes in order to understand the genetic components responsible for endometriosis' malignant transformation.

Conflict of Interest

All authors declare that there are no conflicts of interest.

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