Serican Journal of Medicine
2025, VOL. 2, NO. 3, 24036
https://doi.org/10.17161/sjm.v2i3.24036

Interactions between Pro-inflammatory Cytokines and Estrogen Receptors in Endometrial Cancer

Lin Li[1], Kana Wang[1], Kunang Liu[1], Sayed Ala Moududee[1], Dongxia Ge[2] and Zongbing You[1,2,3,4,5,6*]

[1]Department of Structural & Cellular Biology, Tulane University, New Orleans, Louisiana, USA; [2]Department of Orthopaedic Surgery, Tulane University, New Orleans, Louisiana, USA; [3]Tulane Cancer Center and Louisiana Cancer Research Consortium, Tulane University, New Orleans, Louisiana, USA; [4]Tulane Center for Stem Cell Research and Regenerative Medicine, Tulane University, New Orleans, Louisiana, USA; [5]Tulane Center for Aging, Tulane University, New Orleans, Louisiana, USA; [6]Tulane Center of Excellence in Sex-Based Biology & Medicine, Tulane University, New Orleans, Louisiana, USA.

***Correspondence**: zyou@tulane.edu; Tel.: +1-504-988-0467.

Present address: Lin Li and Kana Wang Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education & Department of Gynecology, West China Second University Hospital, Chengdu, Sichuan Province 610041, China; Kunang Liu, Institute of Biology, Hebei Academy of Sciences, Shijiazhuang, Hebei Province 050081, China.

ABSTRACT

Endometrial cancer (EC) is a hormone-driven malignancy in which estrogen receptor (ER) signaling plays a central role. Meanwhile, chronic inflammation, particularly mediated by pro-inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-17 (IL-17), has emerged as a key contributor to endometrial cancer progression. This review examines the interplay between IL-6, IL-17, and estrogen receptors (ERα and ERβ) in endometrial cancer cells, highlighting how these cytokines regulate ER expression and function through multiple signaling pathways, including the Janus kinase/signal transducer and activator of transcription (JAK/STAT), nuclear factor-κB (NF-κB), and mitogen-activated protein kinase (MAPK) pathways. IL-6 and IL-17 have been shown to upregulate ERα and suppress ERβ, thereby enhancing estrogen-mediated tumor proliferation and potentially contributing to hormonal therapy resistance. Moreover, evidence suggests a bidirectional feedback loop in which estrogen signaling further amplifies cytokine production, creating a self-sustaining inflammatory environment that promotes tumor progression. Understanding this cytokine-ER crosstalk provides novel insights into endometrial cancer pathogenesis and reveals potential therapeutic targets. Strategies that combine endocrine therapy with anti-inflammatory agents or cytokine pathway inhibitors may help overcome resistance and improve clinical outcomes in selected patients. Further mechanistic studies and clinical trials are needed to validate the prognostic and therapeutic relevance of IL-6 and IL-17 in hormone-responsive endometrial cancer.

ARTICLE HISTORY
Received: May 30, 2025
Revised: June 24, 2025
Accepted: June 25, 2025

KEYWORDS
Endometrial cancer, ERα; ERβ; Interleukin-6; Interleukin-17; Inflammation; Hormone signaling; Tumor microenvironment

Introduction

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries, with incidence rates rising globally due to increasing life expectancy, obesity, and hormonal imbalances [1, 2]. Traditionally, EC has been classified into two major molecular and clinicopathological subtypes. Type I EC, accounting for approximately 80-90% of cases, is typically estrogen-dependent, well-differentiated, and associated with a favorable prognosis [2, 3]. It often arises in the setting of unopposed estrogen exposure and is characterized by alterations in genes such as phosphatase and tensin homolog (PTEN), phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), and Kirsten rat sarcoma viral oncogene homolog (KRAS). In contrast, Type II EC is estrogen-independent and poorly differentiated; it exhibits more aggressive clinical behavior and is frequently associated with tumor protein P53 (TP53) mutations and serous or clear cell histology [3, 4].

Estrogen plays a central role in the pathogenesis of Type I EC by promoting endometrial cell proliferation and survival through the activation of estrogen receptors (ERs), primarily ERα and ERβ [5]. ERα is generally considered the dominant isoform mediating proliferative responses, whereas ERβ may exert antagonistic and tumor-suppressive effects [6, 7]. Dysregulation in the balance between ERα and ERβ expression has been implicated in the initiation and progression of endometrioid endometrial carcinoma, with increased ERα and decreased ERβ often observed in malignant tissues compared to normal endometrium [8-10].

In parallel with hormonal dysregulation, inflammation is increasingly recognized as a critical component of tumorigenesis, including in malignancies of the female reproductive tract [11, 12]. Pro-inflammatory cytokines can alter the tumor microenvironment, promote angiogenesis, and facilitate immune evasion. Among these, IL-6 and IL-17 have garnered considerable attention due to their roles in modulating cancer-related signaling pathways and influencing tumor behavior [13-15].

Emerging evidence suggests that interleukin-6 (IL-6) and interleukin-17 (IL-17) contribute to tumor-promoting inflammation and interact with hormone receptor signaling [14, 16-18]. These pro-inflammatory cytokines may influence the expression and function of ERα and ERβ through complex intracellular signaling networks, including the signal transducer and activator of transcription 3 (STAT3), nuclear factor-κB (NF-κB), and mitogen-activated protein kinase (MAPK) pathways [15, 19, 20].

This review aims to synthesize current knowledge on the regulatory effects of IL-6 and IL-17 on estrogen receptors in endometrial cancer, focusing on molecular mechanisms, biological consequences, and clinical implications. Understanding this inflammatory-hormonal interface may provide new insights into endometrial cancer pathogenesis and open avenues for targeted therapeutic strategies.

2. Pro-inflammatory Cytokines and ERs

2.1 Estrogen Receptors in Endometrial Cancer

Estrogen exerts its biological effects mainly through two nuclear receptors estrogen receptor alpha (ERα, encoded by ESR1) and estrogen receptor beta (ERβ, encoded by ESR2) as well as membrane estrogen receptors (mERs) such as G protein-coupled receptor 30 (GPR30 encoded by the GPER gene), ER-X, and Gq-coupled membrane estrogen receptor (Gq-mER). These receptors function as ligand-activated transcription factors and initiators of signaling pathways that regulate genes involved in cell proliferation, differentiation, and survival [21]. In normal endometrium, ERα and ERβ expression is temporally and spatially coordinated, contributing to cyclical growth and shedding of the uterine lining [22].

In endometrial cancer, dysregulation of estrogen receptor expression is common and correlates with tumor differentiation, histologic subtype, and clinical outcome. ERα is predominantly expressed in Type I (endometrioid) tumors, which are typically hormone-sensitive and associated with a favorable prognosis. Conversely, ERα expression is often diminished or lost in Type II (non-endometrioid) tumors, such as serous or clear cell carcinoma, which are more aggressive and less responsive to hormone therapy [5, 23].

ERβ is generally thought to counterbalance the proliferative effects of ERα, acting as a tumor suppressor in many estrogen-responsive tissues [6, 24]. However, its role in endometrial cancer remains incompletely understood. Several studies have reported reduced ERβ expression in malignant tissues compared to normal endometrial tissues, and a low ERβ/ERα ratio has been associated with more aggressive tumor features and a poorer prognosis [9, 10, 25].

The balance between ERα and ERβ expression is crucial in determining estrogen responsiveness. Changes in this ratio may result from genetic, epigenetic, or environmental factors including inflammatory cytokines that influence the transcription, translation, or degradation of estrogen receptors [26-28]. Therefore, understanding the regulation of ERα and ERβ in the context of inflammatory signaling is essential for improving hormone-based therapeutic strategies in endometrial cancer.

2.2 Inflammatory Cytokines in the Tumor Microenvironment

The tumor microenvironment (TME) is a complex and dynamic system composed of cancer cells, immune cells, stromal cells, endothelial cells, and extracellular matrix components. A hallmark feature of the TME is chronic, non-resolving inflammation, which is critical in tumor initiation, promotion, and metastasis [29, 30]. Inflammatory cytokines released by infiltrating immune cells, cancer-associated fibroblasts, and even tumor cells create a pro-tumorigenic niche.

Among the pro-inflammatory cytokines, IL-6 and IL-17 have emerged as key players in shaping the immune landscape of various solid tumors, including endometrial cancer (Figure 1). IL-6 is a pleiotropic cytokine produced by multiple cell types, including macrophages, dendritic cells, and epithelial cells. It acts through the IL-6 receptor and the gp130 co-receptor complex to activate downstream signaling pathways, including the Janus kinase/signal transducer and activator of the transcription 3 (JAK/STAT3), mitogen-activated protein kinase (MAPK) and phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT) pathways [13, 31, 32]. These pathways mediate diverse biological effects, including cell proliferation, survival, angiogenesis, and immune modulation [33, 34].

IL-17, primarily secreted by Th17 cells, has been increasingly recognized as a pro-inflammatory cytokine involved in autoimmune diseases and cancer. It exerts its effects by binding to the IL-17 receptor (IL-17R) complex, triggering the activation of NF-κB, MAPK, and C/EBP signaling pathways [14, 35, 36]. IL-17 can promote tumor growth indirectly by recruiting neutrophils, stimulating angiogenesis, and enhancing the production of other pro-tumor cytokines such as IL-6, IL-8, and TNF-α [15, 37, 38]. Significantly, IL-17 signaling may also influence the immune evasion capacity of tumors by modulating regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs) [39].

Elevated levels of IL-6 and IL-17 have been detected in tumor tissues and sera of patients with endometrial cancer, and their expression often correlates with poor differentiation, advanced stage, and unfavorable prognosis [19, 40]. While the mechanisms by which these cytokines influence tumor cell behavior are multifaceted, increasing attention is being directed toward their potential role in modulating hormone receptor signaling, particularly the expression and activity of estrogen receptors [20, 26, 41].

In addition to immune and stromal components, tumor cells themselves have also been shown to produce IL-6 and IL-17 in certain contexts, contributing to autocrine signaling loops [26]. For instance, single-cell transcriptomic studies [42, 43] suggest heterogeneous expression of IL6 and IL17 genes among epithelial tumor cells in endometrial cancer. These datasets provide further evidence that cytokine production is not confined to immune infiltrates and may originate from malignant clones with inflammatory phenotypes.

2.3 IL-6 and ER Expression in Endometrial Cancer

IL-6 is one of the most extensively studied inflammatory cytokines. Its role in endometrial cancer extends beyond immune modulation, as increasing evidence suggests that IL-6 may directly influence the expression and function of estrogen receptors (ERs), especially ERα and ERβ [13, 19, 44]. IL-6 is frequently elevated in the sera and tumor tissues of endometrial cancer patients, and its expression is associated with higher tumor grade, advanced stage, and poor prognosis [45, 46].

The effects of IL-6 on ER signaling are primarily mediated through the JAK/STAT3 pathway. Upon binding to the IL-6R/gp130 complex, IL-6 induces phosphorylation of STAT3, which translocates into the nucleus to regulate gene expression [31, 47]. Several studies have demonstrated that IL-6/STAT3 activation upregulates ERα expression in hormone-dependent cancers such as breast, endometrial, and ovarian cancer [24, 48, 49].

In vitro studies using endometrial cancer cell lines have shown that IL-6 stimulation increases ERα mRNA and protein levels, enhancing estrogen-induced cell proliferation [27, 50]. IL-6 also promotes the expression of estrogen-responsive genes, such as pS2 and progesterone receptor (PR), indicating functional amplification of ERα signaling [27, 51]. In addition, IL-6 may protect ERα from degradation by inhibiting specific ubiquitin ligases or proteasome activity [52].

In contrast, ERβ appears to be negatively regulated by IL-6. Studies indicate that IL-6 exposure leads to reduced ERβ expression, possibly through epigenetic modifications such as promoter hypermethylation or histone deacetylation at the ESR2 locus [29, 53, 54]. Since ERβ has tumor-suppressive properties in the endometrium, its downregulation may facilitate estrogen-driven carcinogenesis.

Immunohistochemical analyses of clinical specimens have revealed that high IL-6 expression often coincides with elevated ERα and diminished ERβ expression in endometrial tumors [10, 45, 55]. These findings support the hypothesis that IL-6 contributes to an altered ERα/ERβ balance, favoring a pro-proliferative phenotype. Furthermore, high IL-6 levels have been associated with resistance to progestin-based therapy, potentially due to disrupted ER signaling and reduced PR expression [56, 57].

These data suggest that IL-6 promotes a pro-inflammatory tumor environment and directly enhances ERα-mediated signaling while suppressing ERβ.

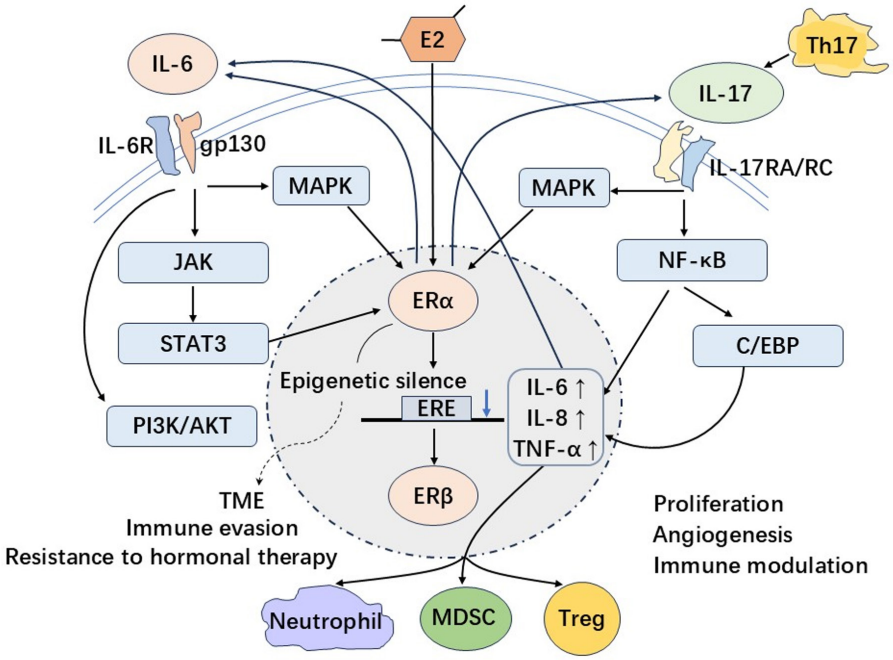

Figure 1. Interactions between cytokines and ERs. Tumor-associated macrophages, cancer cells, and stromal fibroblasts secrete IL-6. It activates the JAK/STAT3, MAPK, and PI3K/AKT pathways, promoting tumor proliferation, angiogenesis, and immune modulation. IL-17, produced mainly by Th17 cells, acts via the IL-17R complex to activate NF-κB, MAPK, and C/EBP signaling cascades, leading to enhanced secretion of IL-6, IL-8, and TNF-α. Both cytokines contribute to recruiting neutrophils, myeloid-derived suppressor cells (MDSCs), and Tregs, suppressing anti-tumor immunity. These inflammatory signals indirectly influence estrogen receptor expression, particularly increasing ERα and reducing ERβ, thereby linking inflammation with hormone responsiveness.

This dual effect may reinforce estrogen-driven tumor progression and reduce hormonal therapy efficacy in endometrial cancer.

2.4 IL-17 and ER Expression in Endometrial Cancer

IL-17, primarily secreted by Th17 cells, is a pro-inflammatory cytokine increasingly recognized for its role in tumor biology, including endometrial cancer [14, 35, 58]. Although IL-17's direct impact on estrogen receptor signaling remains less well studied than that of IL-6, emerging data suggest that IL-17 can directly and indirectly regulate ER expression [36, 59].

IL-17 signals through the IL-17 receptor complex (IL-17RA/RC), activating pathways such as NF-κB, MAPK, and C/EBP, influencing gene transcription and epigenetic regulation [36, 60, 61]. In endometrial cancer cell models, IL-17 promotes proliferation, migration, and chemoresistance by enhancing inflammatory gene expression and survival signaling [62, 63].

Indirectly, IL-17 can upregulate IL-6 and other cytokines, amplifying the IL-6/STAT3 axis and influencing ERα expression [33, 48, 64]. Some studies have also suggested that IL-17 may suppress ERβ expression through epigenetic silencing mechanisms, such as DNA methylation or histone deacetylation at the ESR2 promoter [29, 54, 65].

Limited clinical data indicate high IL-17 expression correlates with intense ERα staining and poor differentiation in endometrial tumors [40, 66]. In other hormone-sensitive cancers, IL-17 has been shown to enhance ER transcriptional activity by recruiting coactivators to estrogen response elements, supporting a similar mechanism in EC [67, 68].

Moreover, IL-17 and IL-6 may synergistically modulate ERα/ERβ balance and promote estrogen-driven tumor proliferation. Their combined signaling sustains a pro-tumor inflammatory environment, potentially driving resistance to hormonal therapies [69, 70].

In summary, IL-17 contributes to the inflammatory regulation of estrogen receptors in endometrial cancer, particularly through IL-6 dependent mechanisms and the suppression of ERβ. These actions highlight IL-17 as a critical mediator of hormone-inflammation crosstalk and a potential therapeutic target.

2.5 Crosstalk Between Inflammatory Cytokines and Estrogen Signaling Pathways

The interactions between inflammatory cytokines and estrogen receptor signaling play important roles in the pathophysiology of endometrial cancer (Figure 1). IL-6 and IL-17, two prominent pro-inflammatory cytokines enriched in the tumor microenvironment, not only drive chronic inflammation but also influence hormone receptor dynamics, particularly those of ERα and ERβ [13-15, 19, 26, 48, 58].

Mechanistically, IL-6 and IL-17 share overlapping downstream signaling pathways including STAT3, MAPK, and NF-κB, which can modulate estrogen receptor expression and transcriptional activity [31, 36, 47, 61]. IL-6, through JAK/STAT3 activation, upregulates ERα and enhances estrogen-induced gene transcription [24, 27, 49]. IL-17, by increasing IL-6 secretion and promoting a pro-inflammatory loop, indirectly strengthens the ERα-dominant profile while suppressing ERβ expression via epigenetic repression [29, 54, 64, 65].

Importantly, the interactions are bidirectional. Estrogen signaling can amplify inflammatory cytokine expression as estradiol acts via ERα to upregulate IL-6 production in stromal and epithelial cells [46, 71, 72], while estrogen exposure also influences Th17 cell differentiation and IL-17A expression [68, 73, 74]. This feed-forward loop sustains a chronic inflammatory environment that supports tumor proliferation and immune evasion [30, 34, 75].

Clinically, tumors with elevated expression of IL-6 and IL-17 as well as an altered ERα/ERβ ratio often exhibit aggressive behavior and reduced responsiveness to endocrine therapy [40, 56, 76, 77]. Cytokine-driven ERα overexpression may confer hormone hypersensitivity, while chronic inflammation may lead to PR loss and endocrine resistance[55, 57, 78]. The combined action of cytokines and estrogen also impacts the immune milieu, favoring the recruitment of immunosuppressive cell types such as Tregs and MDSCs, further promoting immune escape [33, 39, 79, 80]. These insights highlight the importance of inflammatory–hormonal crosstalk as a therapeutic target in EC. Disrupting this signaling intersection may enhance treatment efficacy and help overcome hormone therapy resistance in selected patients.

2.6 Therapeutic Implications and Future Perspectives

The emerging understanding of how IL-6 and IL-17 influence estrogen receptor signaling in endometrial cancer has opened new avenues for therapeutic intervention. Since these cytokines can upregulate ERα and suppress ERβ, thereby contributing to tumor progression and hormonal resistance, targeting the IL-6/IL-17/ER axis holds considerable potential for clinical translation [24, 27, 29, 48, 54, 64, 65, 76].

Endocrine therapeutics including progestins, aromatase inhibitors, and selective estrogen receptor modulators (SERMs) are often used in hormone-responsive endometrial cancer. Still, their effectiveness is limited in advanced or recurrent disease, particularly when cytokine-driven inflammation disrupts ER signaling [5, 56, 78, 81].

IL-6-induced STAT3 activation has been implicated in acquired hormone resistance, decreased PR expression, and immune escape [31, 46, 57]. Targeting IL-6 signaling with monoclonal antibodies such as Tocilizumab or small-molecule JAK inhibitors (e.g., Ruxolitinib) has shown efficacy in preclinical models and other inflammatory tumors [82-84]. These agents may suppress STAT3-driven ERα expression and restore sensitivity to hormone therapy [24, 49, 85]. Similarly, IL-17 inhibitors, such as Secukinumab or Ixekizumab, already approved for autoimmune conditions, may help disrupt the IL-17/IL-6/ERα loop in endometrial cancer [69, 86]. Preclinical studies suggest that combining cytokine blockade with hormone therapy may improve treatment response and delay resistance [87, 88].

In addition, epigenetic therapies, including DNA methyltransferase inhibitors (e.g., Decitabine) and histone deacetylase inhibitors (e.g., Vorinostat), may restore ERβ expression by reversing IL-6/IL-17-mediated repression of ESR2, thereby resensitizing tumors to progestins [53, 54, 89, 90].

Biomarker development is another important focus. IL-6, IL-17, ERα/ERβ ratios, and STAT3 activation status may guide patient selection and predict responsiveness to anti-inflammatory or hormonal interventions [45, 67, 91, 92].

Future clinical trials should evaluate combinatorial strategies, such as endocrine therapy plus IL-6/IL-17 inhibitors or immune checkpoint blockade with cytokine modulation in inflamed, hormone-sensitive endometrial tumors [80, 93, 94]. Integrative approaches, including transcriptomic, epigenetic, and immunologic profiling, will be essential to personalizing therapy and optimizing treatment outcomes. Disrupting the inflammatory–estrogen receptor signaling crosstalk represents a promising strategy for overcoming resistance and improving outcomes in

endometrial cancer. Translating this concept into clinically actionable treatments will require robust biomarker validation and well-designed trials.

3. Conclusion

The intricate interactions between inflammatory cytokines and estrogen receptor signaling play a pivotal role in the development and progression of endometrial cancer. IL-6 and IL-17, two central mediators of tumor-associated inflammation, have been shown to modulate estrogen receptor expression-upregulating ERα and suppressing ERβ-through signaling pathways including JAK/STAT3, NF-κB, and MAPK [13, 24, 31, 36, 47, 54, 61]. These changes enhance estrogen-driven tumor proliferation and contribute to resistance against endocrine therapies [56, 76, 78].

Moreover, evidence indicates a bidirectional feedback loop in which estrogen signaling promotes inflammatory cytokine production, creating a self-sustaining tumor-promoting microenvironment [46, 68, 72, 75]. This crosstalk also affects immune regulation, fostering the recruitment of immunosuppressive cells such as Tregs and MDSCs that may facilitate immune evasion [37, 39, 79, 80].

Targeting the IL-6/IL-17/ER axis offers promising opportunities for therapeutic intervention. Combination strategies involving cytokine inhibitors, endocrine agents, and epigenetic modulators may overcome resistance and improve clinical outcomes in selected patients [24, 48, 53, 69, 85, 90, 93, 94].

Future research should aim to clarify the spatiotemporal regulation of cytokine-ER signaling, define predictive biomarkers (e.g., IL-6/IL-17 levels, ERα/ERβ ratio, and STAT3 activation), and test rationally designed therapeutic combinations in prospective clinical trials [67, 76, 92]. As understanding deepens, targeting both inflammation and hormone signaling pathways may become a cornerstone of precision therapy in endometrial cancer.

Acknowledgement: Dr. Lin Li was supported by the Sichuan Provincial Science and Technology Department's Key R&D Project (Grant No. 2024YFFK0327) and the Chengdu Municipal Science and Technology Bureau (Grant No. 2024-YF05-00059-SN). Dr. Zongbing You was supported by an LB Grant and a COR Faculty International Travel Grant from the Office of Academic Affairs & Provost at Tulane University.

Conflict of Interest: The authors declare no conflict of interest.

References

1. Siegel RL, Giaquinto AN, Jemal A: **Cancer statistics, 2024**. *CA Cancer J Clin* 2024, **74**(1):12-49. doi: 10.3322/caac.21820.
2. Bokhman JV: **Two pathogenetic types of endometrial carcinoma**. *Gynecol Oncol* 1983, **15**(1):10-17. doi: 10.1016/0090-8258(83)90111-7.
3. Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME, Singh N: **Endometrial cancer**. *Lancet* 2022, **399**(10333):1412-1428. doi: 10.1016/S0140-6736(22)00323-3.
4. Hecht JL, Mutter GL: **Molecular and pathologic aspects of endometrial carcinogenesis**. *J Clin Oncol* 2006, **24**(29):4783-4791. doi: 10.1200/JCO.2006.06.7173.
5. Li X, Li H, Pei X, Zhou Y, Wei Z: **CCDC68 Upregulation by IL-6 Promotes Endometrial Carcinoma Progression**. *J Interferon Cytokine Res* 2021, **41**(1):12-19. doi: 10.1089/jir.2020.0193.
6. Fabre J, Giustiniani J, Garbar C, Antonicelli F, Merrouche Y, Bensussan A, Bagot M, Al-Dacak R: **Targeting the Tumor Microenvironment: The Protumor Effects of IL-17 Related to Cancer Type**. *Int J Mol Sci* 2016, **17**(9). doi: 10.3390/ijms17091433. PMC5037712.
7. Yu H, Pardoll D, Jove R: **STATs in cancer inflammation and immunity: a leading role for STAT3**. *Nat Rev Cancer* 2009, **9**(11):798-809. doi: 10.1038/nrc2734. PMC4856025.
8. Hewitt SC, Korach KS: **Estrogen receptors: structure, mechanisms and function**. *Rev Endocr Metab Disord* 2002, **3**(3):193-200. doi: 10.1023/a:1020068224909.
9. Hojnik M, Sinreih M, Anko M, Hevir-Kene N, Knific T, Pirs B, Grazio SF, Rizner TL: **The Co-Expression of Estrogen Receptors ERalpha, ERbeta, and GPER in Endometrial Cancer**. *Int J Mol Sci* 2023, **24**(3). doi: 10.3390/ijms24033009. PMC9918160.
10. Hapangama DK, Kamal AM, Bulmer JN: **Estrogen receptor beta: the guardian of the endometrium**. *Hum Reprod Update* 2015, **21**(2):174-193. doi: 10.1093/humupd/dmu053.
11. Corr BR, Erickson BK, Barber EL, Fisher CM, Slomovitz B: **Advances in the management of endometrial cancer**. *BMJ* 2025, **388**:e080978. doi: 10.1136/bmj-2024-080978.
12. Felix AS, Yang HP, Bell DW, Sherman ME: **Epidemiology of Endometrial Carcinoma: Etiologic Importance of Hormonal and Metabolic**

Influences. *Adv Exp Med Biol* 2017, **943**:3-46. doi: 10.1007/978-3-319-43139-0_1.
13. Fisher DT, Appenheimer MM, Evans SS: **The two faces of IL-6 in the tumor microenvironment**. *Semin Immunol* 2014, **26**(1):38-47. doi: 10.1016/j.smim.2014.01.008. PMC3970580.
14. Wang L, Yi T, Kortylewski M, Pardoll DM, Zeng D, Yu H: **IL-17 can promote tumor growth through an IL-6-Stat3 signaling pathway**. *J Exp Med* 2009, **206**(7):1457-1464. doi: 10.1084/jem.20090207. PMC2715087.
15. Zhong Z, Sanchez-Lopez E, Karin M: **Autophagy, Inflammation, and Immunity: A Troika Governing Cancer and Its Treatment**. *Cell* 2016, **166**(2):288-298. doi: 10.1016/j.cell.2016.05.051. PMC4947210.
16. Coffelt SB, de Visser KE: **Cancer: Inflammation lights the way to metastasis**. *Nature* 2014, **507**(7490):48-49. doi: 10.1038/nature13062.
17. He D, Li H, Yusuf N, Elmets CA, Li J, Mountz JD, Xu H: **IL-17 promotes tumor development through the induction of tumor promoting microenvironments at tumor sites and myeloid-derived suppressor cells**. *J Immunol* 2010, **184**(5):2281-2288. doi: 10.4049/jimmunol.0902574. PMC3179912.
18. Du JW, Xu KY, Fang LY, Qi XL: **Interleukin-17, produced by lymphocytes, promotes tumor growth and angiogenesis in a mouse model of breast cancer**. *Mol Med Rep* 2012, **6**(5):1099-1102. doi: 10.3892/mmr.2012.1036.
19. Bellone S, Watts K, Cane S, Palmieri M, Cannon MJ, Burnett A, Roman JJ, Pecorelli S, Santin AD: **High serum levels of interleukin-6 in endometrial carcinoma are associated with uterine serous papillary histology, a highly aggressive and chemotherapy-resistant variant of endometrial cancer**. *Gynecol Oncol* 2005, **98**(1):92-98. doi: 10.1016/j.ygyno.2005.03.016.
20. Kang YJ, Cho HJ, Lee Y, Park A, Kim MJ, Jeung IC, Jung YW, Jung H, Choi I, Lee HG *et al*: **IL-17A and Th17 Cells Contribute to Endometrial Cell Survival by Inhibiting Apoptosis and NK Cell Mediated Cytotoxicity of Endometrial Cells via ERK1/2 Pathway**. *Immune Netw* 2023, **23**(2):e14. doi: 10.4110/in.2023.23.e14. PMC10166657.
21. Heldring N, Pike A, Andersson S, Matthews J, Cheng G, Hartman J, Tujague M, Strom A, Treuter E, Warner M *et al*: **Estrogen receptors: how do they signal and what are their targets**. *Physiol Rev* 2007, **87**(3):905-931. doi: 10.1152/physrev.00026.2006.
22. Yu K, Huang ZY, Xu XL, Li J, Fu XW, Deng SL: **Estrogen Receptor Function: Impact on the Human Endometrium**. *Front Endocrinol (Lausanne)* 2022, **13**:827724. doi: 10.3389/fendo.2022.827724. PMC8920307.
23. Wik E, Raeder MB, Krakstad C, Trovik J, Birkeland E, Hoivik EA, Mjos S, Werner HM, Mannelqvist M, Stefansson IM *et al*: **Lack of estrogen receptor-alpha is associated with epithelial-mesenchymal transition and PI3K alterations in endometrial carcinoma**. *Clin Cancer Res* 2013, **19**(5):1094-1105. doi: 10.1158/1078-0432.CCR-12-3039.
24. Bardin A, Boulle N, Lazennec G, Vignon F, Pujol P: **Loss of ERbeta expression as a common step in estrogen-dependent tumor progression**. *Endocr Relat Cancer* 2004, **11**(3):537-551. doi: 10.1677/erc.1.00800. PMC2072930.
25. Hanahan D, Weinberg RA: **Hallmarks of cancer: the next generation**. *Cell* 2011, **144**(5):646-674. doi: 10.1016/j.cell.2011.02.013.
26. So KA, Min KJ, Hong JH, Lee JK: **Interleukin-6 expression by interactions between gynecologic cancer cells and human mesenchymal stem cells promotes epithelial-mesenchymal transition**. *Int J Oncol* 2015, **47**(4):1451-1459. doi: 10.3892/ijo.2015.3122.
27. Panopoulos AD, Watowich SS: **Granulocyte colony-stimulating factor: molecular mechanisms of action during steady state and 'emergency' hematopoiesis**. *Cytokine* 2008, **42**(3):277-288. doi: 10.1016/j.cyto.2008.03.002. PMC2852428.
28. Jie XL, Luo ZR, Yu J, Tong ZR, Li QQ, Wu JH, Tao Y, Feng PS, Lan JP, Wang P: **Pi-Pa-Run-Fei-Tang alleviates lung injury by modulating IL-6/JAK2/STAT3/IL-17 and PI3K/AKT/NF-kappaB signaling pathway and balancing Th17 and Treg in murine model of OVA-induced asthma**. *J Ethnopharmacol* 2023, **317**:116719. doi: 10.1016/j.jep.2023.116719.
29. Liu D, Xing S, Wang W, Huang X, Lin H, Chen Y, Lan K, Chen L, Luo F, Qin S *et al*: **Prognostic value of serum soluble interleukin-23 receptor and related T-helper 17 cell cytokines in non-small cell lung carcinoma**. *Cancer Sci* 2020, **111**(4):1093-1102. doi: 10.1111/cas.14343. PMC7156824.

30. Bai Y, Li H, Lv R: **Interleukin-17 activates JAK2/STAT3, PI3K/Akt and nuclear factor-kappaB signaling pathway to promote the tumorigenesis of cervical cancer**. *Exp Ther Med* 2021, **22**(5):1291. doi: 10.3892/etm.2021.10726. PMC8461522.
31. Zaporowska-Stachowiak I, Springer M, Stachowiak K, Oduah M, Sopata M, Wieczorowska-Tobis K, Bryl W: **Interleukin-6 Family of Cytokines in Cancers**. *J Interferon Cytokine Res* 2024, **44**(2):45-59. doi: 10.1089/jir.2023.0103.
32. Jones SA, Jenkins BJ: **Recent insights into targeting the IL-6 cytokine family in inflammatory diseases and cancer**. *Nat Rev Immunol* 2018, **18**(12):773-789. doi: 10.1038/s41577-018-0066-7.
33. Okamoto M, Suzuki T, Mizukami Y, Ikeda T: **The membrane-type estrogen receptor G-protein-coupled estrogen receptor suppresses lipopolysaccharide-induced interleukin 6 via inhibition of nuclear factor-kappa B pathway in murine macrophage cells**. *Anim Sci J* 2017, **88**(11):1870-1879. doi: 10.1111/asj.12868.
34. Sansone P, Bromberg J: **Targeting the interleukin-6/Jak/stat pathway in human malignancies**. *J Clin Oncol* 2012, **30**(9):1005-1014. doi: 10.1200/JCO.2010.31.8907. PMC3341105.
35. Bachelot T, Ray-Coquard I, Menetrier-Caux C, Rastkha M, Duc A, Blay JY: **Prognostic value of serum levels of interleukin 6 and of serum and plasma levels of vascular endothelial growth factor in hormone-refractory metastatic breast cancer patients**. *Br J Cancer* 2003, **88**(11):1721-1726. doi: 10.1038/sj.bjc.6600956. PMC2377148.
36. Douin-Echinard V, Laffont S, Seillet C, Delpy L, Krust A, Chambon P, Gourdy P, Arnal JF, Guery JC: **Estrogen receptor alpha, but not beta, is required for optimal dendritic cell differentiation and [corrected] CD40-induced cytokine production**. *J Immunol* 2008, **180**(6):3661-3669. doi: 10.4049/jimmunol.180.6.3661.
37. Berga S, Naftolin F: **Neuroendocrine control of ovulation**. *Gynecol Endocrinol* 2012, **28 Suppl 1**:9-13. doi: 10.3109/09513590.2012.651929.
38. Kura A, Saito K, Konno T, Kohno T, Shimada H, Okada T, Nishida S, Ishii D, Matsuura M, Saito T *et al*: **The roles of tight junction protein cingulin in human endometrioid endometrial cancer**. *Tissue Barriers* 2024:2361976. doi: 10.1080/21688370.2024.2361976.
39. Delbandi AA, Mahmoudi M, Shervin A, Farhangnia P, Mohammadi T, Zarnani AH: **Increased circulating T helper 17 (T(H)17) cells and endometrial tissue IL-17-producing cells in patients with endometriosis compared with non-endometriotic subjects**. *Reprod Biol* 2025, **25**(2):101019. doi: 10.1016/j.repbio.2025.101019.
40. Giangrazi F, Buffa D, Lloyd AT, Redmond AK, Glover LE, O'Farrelly C: **Evolutionary Analysis of the Mammalian IL-17 Cytokine Family Suggests Conserved Roles in Female Fertility**. *Am J Reprod Immunol* 2024, **92**(2):e13907. doi: 10.1111/aji.13907.
41. Zhao J, Chen X, Herjan T, Li X: **The role of interleukin-17 in tumor development and progression**. *J Exp Med* 2020, **217**(1). doi: 10.1084/jem.20190297. PMC7037244.
42. Jiang P, Gu S, Pan D, Fu J, Sahu A, Hu X, Li Z, Traugh N, Bu X, Li B *et al*: **Signatures of T cell dysfunction and exclusion predict cancer immunotherapy response**. *Nat Med* 2018, **24**(10):1550-1558. doi: 10.1038/s41591-018-0136-1. PMC6487502.
43. Gonzalez-Martinez S, Perez-Mies B, Cortes J, Palacios J: **Single-cell RNA sequencing in endometrial cancer: exploring the epithelial cells and the microenvironment landscape**. *Front Immunol* 2024, **15**:1425212. doi: 10.3389/fimmu.2024.1425212. PMC11368840.
44. Novitskiy SV, Pickup MW, Gorska AE, Owens P, Chytil A, Aakre M, Wu H, Shyr Y, Moses HL: **TGF-beta receptor II loss promotes mammary carcinoma progression by Th17 dependent mechanisms**. *Cancer Discov* 2011, **1**(5):430-441. doi: 10.1158/2159-8290.CD-11-0100. PMC3297196.
45. Tanaka T, Wada T, Uno K, Ogihara S, Ie H, Okekawa A, Ishikawa A, Ito T, Miyazawa Y, Sameshima A *et al*: **Oestrogen receptor alpha in T cells controls the T cell immune profile and glucose metabolism in mouse models of gestational diabetes mellitus**. *Diabetologia* 2021, **64**(7):1660-1673. doi: 10.1007/s00125-021-05447-x.
46. Chang SH, Dong C: **IL-17F: regulation, signaling and function in inflammation**. *Cytokine* 2009, **46**(1):7-11. doi: 10.1016/j.cyto.2008.12.024. PMC2663007.
47. Chen J, Huang X, Li N, Liu B, Ma Z, Ling J, Yang W, Li T: **Narasin inhibits tumor metastasis and growth of ERalpha-positive breast cancer**

cells by inactivation of the TGF-beta/SMAD3 and IL-6/STAT3 signaling pathways. *Mol Med Rep* 2020, **22**(6):5113-5124. doi: 10.3892/mmr.2020.11624. PMC7646975.

48. Kang S, Wu Q, Yang B, Wu C: **Estrogen enhanced the expression of IL-17 by tissue-resident memory gammadeltaT cells from uterus via interferon regulatory factor 4**. *FASEB J* 2022, **36**(2):e22166. doi: 10.1096/fj.202101443RR.
49. Kovats S: **Estrogen receptors regulate innate immune cells and signaling pathways**. *Cell Immunol* 2015, **294**(2):63-69. doi: 10.1016/j.cellimm.2015.01.018. PMC4380804.
50. Wang C, Dehghani B, Li Y, Kaler LJ, Vandenbark AA, Offner H: **Oestrogen modulates experimental autoimmune encephalomyelitis and interleukin-17 production via programmed death 1**. *Immunology* 2009, **126**(3):329-335. doi: 10.1111/j.1365-2567.2008.03051.x. PMC2669813.
51. Li M, Zhang J, Chen W, Liu S, Liu X, Ning Y, Cao Y, Zhao Y: **Supraphysiologic doses of 17beta-estradiol aggravate depression-like behaviors in ovariectomized mice possibly via regulating microglial responses and brain glycerophospholipid metabolism**. *J Neuroinflammation* 2023, **20**(1):204. doi: 10.1186/s12974-023-02889-5. PMC10485970.
52. Cignarella A, Boscaro C, Albiero M, Bolego C, Barton M: **Post-Transcriptional and Epigenetic Regulation of Estrogen Signaling**. *J Pharmacol Exp Ther* 2023, **386**(3):288-297. doi: 10.1124/jpet.123.001613.
53. Wei LH, Kuo ML, Chen CA, Chou CH, Lai KB, Lee CN, Hsieh CY: **Interleukin-6 promotes cervical tumor growth by VEGF-dependent angiogenesis via a STAT3 pathway**. *Oncogene* 2003, **22**(10):1517-1527. doi: 10.1038/sj.onc.1206226.
54. Hunter CA, Jones SA: **Corrigendum: IL-6 as a keystone cytokine in health and disease**. *Nat Immunol* 2017, **18**(11):1271. doi: 10.1038/ni1117-1271b.
55. Casneuf T, Axel AE, King P, Alvarez JD, Werbeck JL, Verhulst T, Verstraeten K, Hall BM, Sasser AK: **Interleukin-6 is a potential therapeutic target in interleukin-6 dependent, estrogen receptor-alpha-positive breast cancer**. *Breast Cancer (Dove Med Press)* 2016, **8**:13-27. doi: 10.2147/BCTT.S92414. PMC4745841.
56. Tanaka T, Narazaki M, Kishimoto T: **IL-6 in inflammation, immunity, and disease**. *Cold Spring Harb Perspect Biol* 2014, **6**(10):a016295. doi: 10.1101/cshperspect.a016295. PMC4176007.
57. Vitiello GA, Miller G: **Targeting the interleukin-17 immune axis for cancer immunotherapy**. *J Exp Med* 2020, **217**(1). doi: 10.1084/jem.20190456. PMC7037254.
58. Piperigkou Z, Franchi M, Gotte M, Karamanos NK: **Estrogen receptor beta as epigenetic mediator of miR-10b and miR-145 in mammary cancer**. *Matrix Biol* 2017, **64**:94-111. doi: 10.1016/j.matbio.2017.08.002.
59. Chopra V, Dinh TV, Hannigan EV: **Serum levels of interleukins, growth factors and angiogenin in patients with endometrial cancer**. *J Cancer Res Clin Oncol* 1997, **123**(3):167-172. doi: 10.1007/BF01214669.
60. Alten R: **Tocilizumab: a novel humanized anti-interleukin 6 receptor antibody for the treatment of patients with rheumatoid arthritis**. *Ther Adv Musculoskelet Dis* 2011, **3**(3):133-149. doi: 10.1177/1759720X11407540. PMC3389389.
61. Verstovsek S, Mesa RA, Gotlib J, Levy RS, Gupta V, DiPersio JF, Catalano JV, Deininger M, Miller C, Silver RT *et al*: **A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis**. *N Engl J Med* 2012, **366**(9):799-807. doi: 10.1056/NEJMoa1110557. PMC4822164.
62. Batlle E, Massague J: **Transforming Growth Factor-beta Signaling in Immunity and Cancer**. *Immunity* 2019, **50**(4):924-940. doi: 10.1016/j.immuni.2019.03.024. PMC7507121.
63. Corr B, Cosgrove C, Spinosa D, Guntupalli S: **Endometrial cancer: molecular classification and future treatments**. *BMJ Med* 2022, **1**(1):e000152. doi: 10.1136/bmjmed-2022-000152. PMC9978763.
64. Kandalaft LE, Odunsi K, Coukos G: **Immune Therapy Opportunities in Ovarian Cancer**. *Am Soc Clin Oncol Educ Book* 2020, **40**:1-13. doi: 10.1200/EDBK_280539.
65. Bogani G, Monk BJ, Powell MA, Westin SN, Slomovitz B, Moore KN, Eskander RN, Raspagliesi F, Barretina-Ginesta MP, Colombo N *et al*: **Adding immunotherapy to first-line treatment of advanced and metastatic endometrial cancer**. *Ann Oncol* 2024, **35**(5):414-428. doi: 10.1016/j.annonc.2024.02.006.
66. Nout RA, Smit VT, Putter H, Jurgenliemk-Schulz IM, Jobsen JJ, Lutgens LC, van der Steen-Banasik EM, Mens JW, Slot A, Kroese MC *et al*: **Vaginal brachytherapy versus pelvic external beam**

radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. *Lancet* 2010, **375**(9717):816-823. doi: 10.1016/S0140-6736(09)62163-2.
67. McDonald ME, Bender DP: **Endometrial Cancer: Obesity, Genetics, and Targeted Agents**. *Obstet Gynecol Clin North Am* 2019, **46**(1):89-105. doi: 10.1016/j.ogc.2018.09.006.
68. Huber D, Seitz S, Kast K, Emons G, Ortmann O: **Hormone replacement therapy in BRCA mutation carriers and risk of ovarian, endometrial, and breast cancer: a systematic review**. *J Cancer Res Clin Oncol* 2021, **147**(7):2035-2045. doi: 10.1007/s00432-021-03629-z. PMC8164576.
69. Lee F, Jure-Kunkel MN, Salvati ME: **Synergistic activity of ixabepilone plus other anticancer agents: preclinical and clinical evidence**. *Ther Adv Med Oncol* 2011, **3**(1):11-25. doi: 10.1177/1758834010386402. PMC3126033.
70. Genestie C, Leary A, Devouassoux M, Auguste A: [**Histological and molecular classification of endometrial carcinoma and therapeutical implications**]. *Bull Cancer* 2017, **104**(12):1001-1012. doi: 10.1016/j.bulcan.2017.08.004.
71. Nagle CM, O'Mara TA, Tan Y, Buchanan DD, Obermair A, Blomfield P, Quinn MA, Webb PM, Spurdle AB, Australian Endometrial Cancer Study G: **Endometrial cancer risk and survival by tumor MMR status**. *J Gynecol Oncol* 2018, **29**(3):e39. doi: 10.3802/jgo.2018.29.e39. PMC5920223.
72. Luo Y, Cheng Y, Wu C, Ye H, Chen N, Zhang F, Wei H, Xu B: **Pharmacokinetics, safety, and antitumor activity of talazoparib monotherapy in Chinese patients with advanced solid tumors**. *Invest New Drugs* 2023, **41**(3):503-511. doi: 10.1007/s10637-023-01351-w. PMC10290043.
73. Nucci MR, Castrillon DH, Bai H, Quade BJ, Ince TA, Genest DR, Lee KR, Mutter GL, Crum CP: **Biomarkers in diagnostic obstetric and gynecologic pathology: a review**. *Adv Anat Pathol* 2003, **10**(2):55-68. doi: 10.1097/00125480-200303000-00001.
74. Walsh CS, Hacker KE, Secord AA, DeLair DF, McCourt C, Urban R: **Molecular testing for endometrial cancer: An SGO clinical practice statement**. *Gynecol Oncol* 2023, **168**:48-55. doi: 10.1016/j.ygyno.2022.10.024.
75. Inoue F, Sone K, Toyohara Y, Takahashi Y, Kukita A, Hara A, Taguchi A, Tanikawa M, Tsuruga T, Osuga Y: **Targeting Epigenetic Regulators for Endometrial Cancer Therapy: Its Molecular Biology and Potential Clinical Applications**. *Int J Mol Sci* 2021, **22**(5). doi: 10.3390/ijms22052305. PMC7956745.
76. Prat J, Gallardo A, Cuatrecasas M, Catasus L: **Endometrial carcinoma: pathology and genetics**. *Pathology* 2007, **39**(1):72-87. doi: 10.1080/00313020601136153.
77. Iavarone I, Molitierno R, Fumiento P, Vastarella MG, Napolitano S, Vietri MT, De Franciscis P, Ronsini C: **MicroRNA Expression in Endometrial Cancer: Current Knowledge and Therapeutic Implications**. *Medicina (Kaunas)* 2024, **60**(3). doi: 10.3390/medicina60030486. PMC10972089.
78. Talhouk A, McConechy MK, Leung S, Li-Chang HH, Kwon JS, Melnyk N, Yang W, Senz J, Boyd N, Karnezis AN *et al*: **A clinically applicable molecular-based classification for endometrial cancers**. *Br J Cancer* 2015, **113**(2):299-310. doi: 10.1038/bjc.2015.190. PMC4506381.
79. Mylonas I, Makovitzky J, Friese K, Jeschke U: **Immunohistochemical labelling of steroid receptors in normal and malignant human endometrium**. *Acta Histochem* 2009, **111**(4):349-359. doi: 10.1016/j.acthis.2008.11.012.
80. Lightfoot M, Montemorano L, Bixel K: **PARP Inhibitors in Gynecologic Cancers: What Is the Next Big Development?** *Curr Oncol Rep* 2020, **22**(3):29. doi: 10.1007/s11912-020-0873-4.
81. Zhu X, Shen H, Yin X, Long L, Chen X, Feng F, Liu Y, Zhao P, Xu Y, Li M *et al*: **IL-6R/STAT3/miR-204 feedback loop contributes to cisplatin resistance of epithelial ovarian cancer cells**. *Oncotarget* 2017, **8**(24):39154-39166. doi: 10.18632/oncotarget.16610. PMC5503602.
82. Xu X, Ye Y, Wang X, Lu B, Guo Z, Wu S: **JMJD3-regulated expression of IL-6 is involved in the proliferation and chemosensitivity of acute myeloid leukemia cells**. *Biol Chem* 2021, **402**(7):815-824. doi: 10.1515/hsz-2020-0345.
83. Martin-Orozco N, Dong C: **The IL-17/IL-23 axis of inflammation in cancer: friend or foe?** *Curr Opin Investig Drugs* 2009, **10**(6):543-549. doi.
84. You Y, Stelzl P, Joseph DN, Aldo PB, Maxwell AJ, Dekel N, Liao A, Whirledge S, Mor G: **TNF-alpha Regulated Endometrial Stroma Secretome Promotes Trophoblast Invasion**. *Front Immunol* 2021, **12**:737401. doi: 10.3389/fimmu.2021.737401. PMC8591203.

85. Theune WC, Chen J, Theune EV, Ye X, Menoret A, Vella AT, Wang K: **Interleukin-17 directly stimulates tumor infiltrating Tregs to prevent cancer development**. *Front Immunol* 2024, **15**:1408710. doi: 10.3389/fimmu.2024.1408710. PMC11211274.
86. Parveen S, Fatma M, Mir SS, Dermime S, Uddin S: **JAK-STAT Signaling in Autoimmunity and Cancer**. *Immunotargets Ther* 2025, **14**:523-554. doi: 10.2147/ITT.S485670. PMC12080488.
87. Diep CH, Daniel AR, Mauro LJ, Knutson TP, Lange CA: **Progesterone action in breast, uterine, and ovarian cancers**. *J Mol Endocrinol* 2015, **54**(2):R31-53. doi: 10.1530/JME-14-0252. PMC4336822.
88. Jacob L, Kostev K, Kalder M: **Prescription of hormone replacement therapy prior to and after the diagnosis of gynecological cancers in German patients**. *J Cancer Res Clin Oncol* 2020, **146**(6):1567-1573. doi: 10.1007/s00432-020-03185-y.
89. Hamanishi J, Mandai M, Iwasaki M, Okazaki T, Tanaka Y, Yamaguchi K, Higuchi T, Yagi H, Takakura K, Minato N *et al*: **Programmed cell death 1 ligand 1 and tumor-infiltrating CD8+ T lymphocytes are prognostic factors of human ovarian cancer**. *Proc Natl Acad Sci U S A* 2007, **104**(9):3360-3365. doi: 10.1073/pnas.0611533104. PMC1805580.
90. Wang Y, Qu Y, Zhang XL, Xing J, Niu XL, Chen X, Li ZM: **Autocrine production of interleukin-6 confers ovarian cancer cells resistance to tamoxifen via ER isoforms and SRC-1**. *Mol Cell Endocrinol* 2014, **382**(2):791-803. doi: 10.1016/j.mce.2013.10.029.
91. Yang X, Huang M, Zhang Q, Chen J, Li J, Han Q, Zhang L, Li J, Liu S, Ma Y *et al*: **Metformin Antagonizes Ovarian Cancer Cells Malignancy Through MSLN Mediated IL-6/STAT3 Signaling**. *Cell Transplant* 2021, **30**:9636897211027819. doi: 10.1177/09636897211027819. PMC8274104.
92. Suzuki T, Hirakawa S, Shimauchi T, Ito T, Sakabe J, Detmar M, Tokura Y: **VEGF-A promotes IL-17A-producing gammadelta T cell accumulation in mouse skin and serves as a chemotactic factor for plasmacytoid dendritic cells**. *J Dermatol Sci* 2014, **74**(2):116-124. doi: 10.1016/j.jdermsci.2013.12.013.
93. Schetter AJ, Heegaard NH, Harris CC: **Inflammation and cancer: interweaving microRNA, free radical, cytokine and p53 pathways**. *Carcinogenesis* 2010, **31**(1):37-49. doi: 10.1093/carcin/bgp272. PMC2802675.
94. Bennett RL, Licht JD: **Targeting Epigenetics in Cancer**. *Annu Rev Pharmacol Toxicol* 2018, **58**:187-207. doi: 10.1146/annurev-pharmtox-010716-105106. PMC5800772.