Correction to: Adipocytokines and disease progression in endometrial cancer: a systematic review

Irene Ray^{1,2} · Lisiane B. Meira¹ · Agnieszka Michael^{1,2} · Patricia E. Ellis^{1,2}

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Correction to: Cancer and Metastasis Reviews

<https://doi.org/10.1007/s10555-021-10002-6>

The original published version of this article contained a mistake and the author would like to correct it.

The reference citations inside Table 1 are out of order as the reference citations in the article have been moved around.

The correct presentation of Table 1 is presented on the next page.

The original article has been corrected.

The original article can be found online at <https://doi.org/10.1007/s10555-021-10002-6>.

✉ Irene Ray
i.ray@surrey.ac.uk; dr.ireneray@gmail.com

¹ University of Surrey, Daphne Jackson Road, Guildford GU2 7WG, UK

² Royal Surrey NHS Foundation Trust, Egerton Road, Guildford GU2 7XX, UK

Table 1 Characteristics of review articles

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[33]	Zhang (2015) China	Human sample: 88 endometrial cancer 90 without cancer (controls) Cell lines: Human endometrial cancer cell lines: AN3CA, RL95-2, Ishikawa3-H-12	Design: Experimental and observational Lab methods: 1. Proliferation assay—MTT assay 2. Apoptosis assay—Annexin V-FITC/PI	Adiponectin	1. Decreased serum adiponectin levels (< 8 mg/L) associated with higher grade 2/3 or lymph nodal involvement lower adiponectin < 8 mg/L 2. Adiponectin was reported to suppress cell proliferation and induce apoptosis in Ishiwa cells 3. Adiponectin reduced cell proliferation, colony formation, adhesion and invasion of endometrial cancer cell lines in vitro in the endometrial cancer cell lines
[34]	Moon (2011) USA, Greece	Cell lines: Human endometrial cancer cell lines: RL95-2 and KLE	Design: Experimental and observational Lab methods: 1. MTT assay 2. Clonogenic assay 3. Adhesion assay 4. Matrigel invasion assay	Adiponectin	1. Adiponectin inhibited cell cycle proliferation as shown by an increase in cells in G0/G1 phase and a decrease in cells in S-phase 2. Significant increase in the percentage of apoptotic cells
[35]	Cong (2007) USA, China	Cell lines: Human endometrial cancer cell lines: HEC-1-A and RL95-2	Design: Experimental Lab methods: 1. Flow cytometry 2. Cell cycle study 3. Apoptotic cells detection—Annexin-V-FITC kit and PI staining	Adiponectin	1. Leptin treatment stimulated cell proliferation 2. Acrp30 treatment inhibited endometrial cancer cell proliferation 3. Higher apoptotic rate was noted with adiponectin and lower with leptin 4. Acrp30 increased cells in G0/G1 phase and decreased cells in S phase. Opposite effect noted with leptin 5. Lowered invasion rate with adiponectin (66%), and increased (65%) with leptin 6. Acrp30 was able to inhibit leptin-induced SPEC-2 cell proliferation and partly suppressed the invasion stimulated by leptin
[36]	Wu (2006) China	Cell lines: Human endometrial cancer cell lines: Ishikawa cell line SPEC2 cell line	Design: Experimental Lab methods: 1. Flow cytometry 2. Proliferation assay 3. Matrigel transwell assay—cell invasion 4. Immunoblot 5. Cell immunofluorescence	Adiponectin (Acrp30) Leptin	1. Leptin significantly increased S-phase progression 2. Higher rate of S-phase progression noted in type 2 endometrial cancer (two-fold increase) rather than type 1 (1.5-fold increase) 3. Higher rate of leptin induced endometrial cancer cell proliferation noted in type 2 endometrial cancer (3–3.5-fold increase) rather than type 1 (2–2.5-fold increase) 4. Leptin also significantly induced endometrial cancer cell migration (more in type 2 endometrial cancer cells)
[41]	Daley-Brown (2019) USA	Cell lines: Human endometrial cancer cell lines: HEC-1A, Ishiwa (type 1 endometrial cancer) KLE, An3Ca (type 2 endometrial cancer)	Design: Experimental Lab methods: 1. MTT assay 2. Cell cycle assay 3. Cell invasion assay 4. Annexin V—FITC/PI assay	Leptin	1. Leptin significantly increased S-phase progression 2. Higher rate of S-phase progression noted in type 2 endometrial cancer (two-fold increase) rather than type 1 (1.5-fold increase) 3. Higher rate of leptin induced endometrial cancer cell proliferation noted in type 2 endometrial cancer (3–3.5-fold increase) rather than type 1 (2–2.5-fold increase) 4. Leptin also significantly induced endometrial cancer cell migration (more in type 2 endometrial cancer cells)

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[71]	Zhang (2014) China	Human sample: 50 normal endometrium samples 60 early endometrial cancer (stages 1 and 2) 20 late endometrial cancer (stages 3 and 4) samples	Design: Observational Lab method: 1. Immunohistochemistry	Leptin	1. Significantly higher levels of leptin and leptin receptor (ObR) in endometrial cancer tissue (72.5% and 65%) compared to normal endometrial tissue (54% and 44%) 2. Leptin concentration positively correlated with depth of myometrial invasion ($p=0.001$), and lymph node metastasis (not significant, $p=0.156$) 3. 3-year survival of leptin positive patients was significantly lower than leptin negative endometrial cancer patients (74.14 vs 95.45%, $p<0.05$)
[66]	Zhou (2015) China	Cell lines: Human endometrial cancer cell lines: Ishikawa and HEC-1A	Design: Experimental Lab methods: 1. ELISA 2. Flow cytometry 3. Apoptosis assay- annexin V/PI	Leptin	1. Leptin protected endometrial cancer cells from apoptosis 2. High serum leptin concentration was correlated with degree of endometrial cancer differentiation ($p=0.035$)
[70]	Cymbaluk-Ploska (2018) Poland	Human sample: 168 samples, endometrial cancer 92 and benign endometrium 76	Design: Observational Lab methods: 1. Multiplex immunoassay	Leptin Omentin-1 Vaspin Galectin-3	1. Higher leptin level correlated with lymph vessel involvement and poorly differentiated endometrial cancer 2. Lower concentration of Vaspin was noted in presence of LN involvement ($p=0.022$), lymphatic vessel invasion ($p=0.03$) and deep myometrial invasion ($p=0.04$) 3. Significantly lower concentration of Omentin-1 was noted in presence of lymphatic vessel invasion ($p=0.002$) and deep myometrial invasion ($p=0.01$) 4. Galectin -3 although found to be significantly higher in endometrial cancer patients ($p=0.03$), had no significant correlations with clinico-pathological features
[42]	Liu (2011) China	Cell lines: Human endometrial cancer cell line: Ishiwaka	Design: Experimental Lab methods: 1. Colorimetric MTT assay for cell proliferation study 2. Matrigel assay for cell invasion study	Leptin	1. Leptin stimulated the growth of Ishiwaka cells in a time- and dose-dependent fashion (100 ng/ml leptin) $p<0.01$ 2. Leptin treatment (100 ng/ml) also demonstrated significant endometrial cancer cell invasion $p<0.01$

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[65]	Catalano (2009) Italy	Cell lines: Human endometrial cancer cell line: Ishiwaka	Design: Experimental Lab methods: 1. Flow cytometry 2. Transient transfection assay 3. Electrophoretic mobility shift assay	Leptin	1. Leptin stimulates cell cycle progression-reduced the numbers of cells in G0/G1-phase while increased cell population in S-phase ($p < 0.01$) 2. There is also up-regulation of cyclin D1 (critical modulator of G1/S transition) together with a down-regulation of major cyclin-dependent kinase inhibitor p21 ^{WAF1/Cip1}
[43]	Gao (2009) China	Cell lines: The human endometrial cancer cell lines used were Ishikawa (36) and ECC-1, (37) both derived from well-differentiated endometrial adenocarcinoma; HEC-1A and a substrain HEC-1B derived from moderately differentiated endometrial adenocarcinoma; (38,39) RL95-2 derived from moderately differentiated adenosquamous carcinoma of the endometrium; (40) and AN3CA derived from undifferentiated endometrial adenocarcinoma (41) Of six cell lines, Ishikawa and AN3CA were gifts from Dr Teruhiko Tamaya (Gifu University School of Medicine, Japan); others were purchased from the America Type Culture Collection (Manassas, VA, USA) Human endometrial cancer cell lines: Ishikawa and ECC-1, HEC-1A and HEC-1B, RL95-2 AN3CA (undifferentiated endometrial adenocarcinoma)	Design: Experimental Lab methods: 1. Thymidine incorporation assay	Leptin	1. Leptin stimulated endometrial cancer cell proliferation in all 6 endometrial cancer cell lines

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[72]	Koda (2007) Poland	Human sample: 60 endometrial cancer undergoing hysterectomy (different grades and stages), 25 benign, having hysterectomy for leiomyoma	Design: Observational Lab methods: 1. Immunohistochemistry	Leptin	1. No statistically significant relation between the expression of leptin (Ob), ObR and HIF-1 α with extent of tumour growth (pT), or histological grade
[44]	Sharma (2006) USA	Cell lines: Human endometrial cancer cell lines: ECC1, Ishiwaka	Design: Experimental Lab methods: 1. XTT cell proliferation assay 2. Matrigel invasion assay	Leptin	1. Leptin stimulated the growth of both cell lines in a time and dose-dependent manner and the effect was maximum for 100 ng/ml leptin for 24 h of treatment ($p < 0.01$) 2. ECC1 cells exhibited remarkable invasion ($p < 0.01$) in response to 100 ng/mL leptin treatment
[73]	Cymbaluk-Ploska (2018) Poland	Human samples: 64 endometrial cancer 14 non-endometrial cancer 63 normal endometrium (all had hysterectomy)	Design: Observational Lab methods: 1. Multiplex immunoassay	Visfatin	1. Significantly higher visfatin level also found in patients with invasion of blood vessels ($p = 0.02$), lymph node metastasis ($p = 0.01$), deeper infiltration of the endometrium ($p = 0.0004$) (no difference in lymphatic vessel invasion) 2. The higher the visfatin level above 20.7 ng/mL, the shorter the overall survival of patients ($p = 0.03$)
[45]	Wang (2016) China	Cell lines: Human endometrial cancer cell lines: Ishiwaka, KLE cell lines	Design: Experimental Lab methods: 1. Cell proliferation assay- Cell Counting Kit (CCK)-8 2. Cell cycle analysis 3. Annexin V-fluorescein isothiocyanate (FITC) apoptosis assay	Visfatin	1. CCK 8 assay demonstrated time-dependant increased endometrial cancer cell proliferation compared with untreated control cells on exposure to visfatin ($p < 0.05$) 2. Cell cycle analysis- reduced G1 fraction and increase in S-phase fraction 3. Visfatin-treated endometrial cancer cells demonstrated decreased rate of apoptosis ($p < 0.05$)
[74]	Ilhan (2015) Turkey	Human samples: 42 endometrial cancer patients and 42 controls	Design: Observational Lab methods: 1. ELISA	Visfatin Resistin	1. Visfatin had significant association with deep myometrial invasion ($p = 0.01$) 2. Resistin was associated with increased lymph node metastasis ($p = 0.046$)
[75]	Tian (2013) China	Human samples: 234 samples from endometrial cancer patients (serum-120, tissue-164, both serum and tissue- 50) Non-cancer endometrial tissues: 24 hyperplastic endometrium, 25 atypical hyperplastic endometrium, 86 normal endometrium	Design: Observational Lab methods: 1. ELISA 2. Tissue micro-array 3. Immunohistochemistry	Visfatin	1. High visfatin expression in endometrial cancer tissues was associated with advanced disease stage ($p = 0.023$) and deep myometrial invasion (myometrial invasion $\geq 1/2$; $p = 0.016$) 2. Overall survival (OS) rate of endometrial cancer patients was significantly higher in the group with negative visfatin expression than with positive visfatin expression ($p = 0.035$)

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[46]	Che (2014) China	Cell lines: Human endometrial cancer cell lines: Ishikawa and RL95	Design: Experimental Lab methods: 1. Cell proliferation assay	IL -6	1. IL-6 increased cell growth in Ishikawa and RL95-2 cells after IL-6 treatment and the effect continued even after withdrawal of IL-6 from the medium (autocrine IL-6 signalling) 2. The concentration of IL-6 in the culture media doubled after 7 days of culture
[47]	Che (2019) China	Cell lines: Human endometrial cancer cell lines: Ishikawa and RL95-2 cells	Design: Experimental Lab methods: 1. Cell proliferation assay (MTT) 2. Wound healing assay 3. Cell invasion assay (Matrigel)	IL -6 17- β estradiol	1. Administration of estradiol was found to significantly increase cells growth of endometrial cancer cells. However, treatment with IL-6-neutralizing antibody reduced the increased proliferation ability more than 60% 2. Estradiol incubation group demonstrated faster wound healing and migration—1.68-fold for Ishikawa and 2.37-fold for RL95-2, which was partially attenuated, 58 and 85%, respectively, by addition of IL-6 antibody
[48]	Wang (2019) China	Human samples: 7 paired tumour tissues and adjacent normal tissues Cell lines: Human endometrial cancer cell lines: Ishikawa, RL95-2, HEC1A, AN3CA, KLE cells endometrial stromal cell (ESC)	Design: Experimental + Observational Lab methods: 1. qRT-PCR 2. Immunoblot 3. Cell proliferation assay 4. ELISA	Yes-associated protein (YAP) IL-6 IL-11	1. YAP was upregulated in endometrial cancer cells and tissues more than ESC/benign tissue 2. Knockdown of YAP suppressed the endometrial cancer cell proliferation 3. Targeted inhibition of YAP can decrease the expression of IL-6 and IL-11 in endometrial cancer cells; i.e., YAP can regulate expression of IL-6 and IL-11 in endometrial cancer cells 4. Recombinant IL-6 or IL-11 can attenuate si-YAP-suppressed proliferation of endometrial cancer cells
[49]	Chu (2018) China	Human samples: Human ADSC from omentum tissues from healthy adult female donors who underwent abdominal surgery for benign gynaecologic disease	Design: Experimental Lab methods: 1. 5-Ethynyl-2'-deoxyuridine (EdU) cell proliferation kit 2. ELISA 3. qRT-PCR 4. Immunoblotting 5. IHC 6. Cell invasion assay 7. Multiplex analysis- Bio-Plex Pro Human Cytokine 17-plex Assay	IL -6 Human adipose derived stem cells (ADSC)	1. IL-6 levels were significantly increased in the supernatants of conditioned media (CM) of Ishikawa and KLE cells treated with ADSC supernatants 2. ADSC and IL-6 promoted the proliferation of endometrial cancer cells—threefold and twofold, respectively 3. ADSC and IL-6 promoted endometrial cancer cells invasion 3- to 5-fold

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[38]	Subramaniam (2013) Malaysia	Human samples: Endometrial cancer tissue -4, endometrial hyperplasia- 1 Cell lines: 1. Human endometrial cancer cell lines: ECC-1 and HEC-1A 2. Human normal endometrial fibroblast cell line- T-HESC	Design: Experimental Lab methods: 1. Human cytokine array	IL-6, MCP-1, RANTES Cancer associated fibroblasts (CAF)	1. CAF secrete higher levels of inflammatory cytokines compared to control fibroblasts -macrophage chemoattractant protein (MCP)-1, IL-6, IL-8, RANTES
[39]	Subramaniam (2016) Malaysia	Human samples: Endometrium formalin-fixed paraffin blocks for both benign and cancer conditions Cell lines: 1. Human endometrial cancer cell lines: ECC-1 and HEC-1A 2. Immortalized human normal endometrial fibroblast cell line, T-HESC	Design: Experimental Lab methods: 1. Methyl thiazolyl tetrazolium (MTT) assay- cell proliferation 2. ELISA 3. Human cytokine array	IL-6 CAF	1. CAF secrete higher levels of inflammatory cytokines compared to control fibroblasts – IL-6 (tenfold), MCP-1(5.6-fold), RANTES (threefold) 2. Endometrial cancer cell lines treated with increasing concentrations of IL-6 neutralizing antibody led to a remarkable inhibitory effect on proliferation of almost 50% in CAF conditioned media and only 5% in CAF unconditioned media. This indicates that IL-6 was present in CAF secretion and had directly induced endometrial cancer cell proliferation 3. Endometrial cancer cells treated with IL-6 recombinant protein without the presence of CAF conditioned media also demonstrated dose-response increase in cell proliferation
[37]	So (2015) Korea	Cell lines: 1. Human endometrial cancer cell line: Ishiwaka 2. human mesenchymal stem cells (hMSCs)	Design: Experimental Lab methods: 1. Matrix metalloproteinases (MMP-2 and MMP-9) assay 2. Matrigel invasion assay 3. Wound healing assay 4. RT-PCR 5. Immunoblot 6. Human cytokine array 7. Immunofluorescence	IL-6, TGF- β 1 human mesenchymal stem cells (hMSCs)	1. In the human cytokine array, only IL-6 was found to increase in all endometrial cancer and hMSC co-culture assay 2. IL-6 and TGF- β 1 treatment significantly enhance cell migration and invasion ability compared to untreated cells ($p < 0.05$) 3. After IL-6 and TGF- β 1 treatment of cancer cell lines, there was decrease in an epithelial marker (E-cadherin) and an increase in mesenchymal markers (Snail, N-cadherin) 4. IL-6 and TGF- β 1 treatment causes over-expression of MMP-2 and MMP-9
[50]	Che (2019)	Cell lines: Human endometrial cancer cell lines: Ishikawa and RL95-2	Design: Experimental Lab methods: 1. Immunofluorescence 2. Wound healing assay 3. Transwell migration assay 4. Immunoblot 5. Rt-PCR 6. ELISA	IL-6	1. IL-6 increased endometrial cancer cell migration and invasion abilities 2. IL-6 induced MMP 2 expression (EMT marker)

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[76]	Kotowicz (2017) Poland	Human samples: 118 endometrial cancer—hysterectomy	Design: Observational Lab methods: 1. ELISA	IL-8	<p>1. Endometrial cancer cases were found to have elevated IL-8 (65%) both in early and late stages of the disease, no correlation with stage noted</p> <p>2. Higher levels of IL-8 were associated with higher rate of relapse ($p < 0.011$) and shorter disease-free survival ($p < 0.048$)</p> <p>3. Elevated IL-8 was found to be associated with shorter OS and it is an independent prognostic factor for OS in patients with type I endometrial cancer</p> <p>4. Levels of IL-8 were significantly higher ($p < 0.002$) in patients who died during follow-up compared to the group of surviving patients</p>
[77]	Smith (2012) USA	<p>Human samples: 50 endometrial cancer hysterectomy samples. Among them, 26 tissue cultures were evaluated</p> <p>Cell lines: Human endometrial cancer cell lines: KLE and RL 95-2</p>	<p>Design: Observational Lab methods: 1. ELISA 2. Cytokine arrays</p>	IL-8 IL-6 TNF- α	<p>1. The highest production rates were for IL-8, which were significantly higher than rates for IL-6 which were significantly higher production rates for TNF-α</p> <p>2. Rate of cytokines production was higher from primary tumour than from metastatic sites or from cell lines</p> <p>3. Raised TNF-α was observed more frequently in samples from women with advanced disease (stage III/IV)</p> <p>4. Marginally lower survival rates were also observed in patients with high epithelial cell IL-6 ($p = 0.052$) and IL-8 ($p = 0.078$). Paradoxically higher survival was noted in case of high stromal TNF-α (not statistically significant)</p> <p>5. Combining tumour grade and cytokine levels, OS declined from 100% in patients with low-grade tumours where cytokine production rates were low to 0% and 25%, respectively, in patients with high-grade tumours and high IL-6 production rates. Similarly, combining histology and TNF-α, the impact on survival was greater for type 2 tumours and approached statistical significance</p>

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[51]	Lay (2012) Australia	Cell lines: Human endometrial cancer cell lines: Ishikawa, HEC-1A and AN3CA (derived from endometrial cancers grade I, II and III, respectively)	Design: Experimental Lab methods: 1. Cell proliferation and viability -Bromodeoxyuridine assay and WST-1 assays 2. Cell adhesion assay 3. Modified boyden chamber assay—cell migration and invasion 4. SDS PAGE 5. Immunoblot	IL-11	1. IL-11 had no effect on cell proliferation and viability 2. IL-11 increased adhesion of AN3CA cells to fibronectin, while having no effect on the other extracellular matrix proteins (co-treatment with the specific IL-11 inhibitor abolished the effect), no effect on adhesion properties of Ishiwaka and HEC1-A 3. In the AN3CA cells, IL-11 treatment resulted in a 50% increase in migration and co-treatment with the specific IL-11 inhibitor abolished the effect
[63]	Choi (2009) USA, South Korea	Human samples: Endometrial stromal cells derived from endometrial tissue from patient who had hysterectomy without any sign of endometrial diseases Cell lines: Human endometrial cancer cell lines: HEC-1A cells (well differentiated) and KLE cells (poorly differentiated)	Design: Experimental Lab methods: 1. Matrigel invasion assay 2. Immunoblot 3. Rt-PCR 4. Immuno-precipitation 5. Wound healing assay 6. ELISA	TNF- α Hepatocyte growth factor (HGF)	1. Estrogen enhanced endometrial cancer cell invasion and progesterone inhibited it. However, addition of human recombinant TNF- α to progesterone enhanced cancer invasion ($p < 0.05$) 2. HGF treatment increased estradiol-induced invasiveness of endometrial cancer cells 3. IL-6 and TNF- α are HGF inducers. Co-culture of endometrial cancer with stromal cells resulted in increasing HGF secretion dependent on increasing concentration of TNF- α . Addition of neutralising TNF- α antibody reduced estradiol-mediated endometrial cancer cell invasion in both HEC 1A and KLE cell lines ($p < 0.05$)

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[58]	Zhu (2015) China	Human samples: Paraffin embedded tissue blocks 73 endometrial cancer 26 normal, 20 atypical hyperplasia Cell lines: Human Endometrial cancer cell lines: Ishikawa and HEC-1B	Design: Experimental and observational Lab methods: 1. IHC 2. ELISA 3. Immunoblot 4. RT-PCR 5. Cell migration and invasion assay – Transwell and Matrigel assay 6. Cell proliferation assay – CCK8 assay	Oncostatin M (OSM)	1. OSM expression higher in endometrial cancers when compared with normal endometrial tissues 2. Increased OSM expression significantly related to depth of myometrial invasion, lymph node metastasis, advanced disease stage (stages III or IV) and poor histological differentiation (grade 3) (all $p < 0.05$). No significant difference in OSM expression between endometrioid and non-endometrioid endometrial cancer 3. Recombinant OSM (rhOSM) promoted cell migration and invasion in Ishikawa and HEC-1B cells; however, no direct effect was found on HEC-1B or Ishikawa cell growth
[55]	Wang (2017) China	Human samples: Endometrial cancer tissue and adjacent normal tissue	Design: Experimental Lab methods: 1. Immunofluorescence 2. Immunoblot 3. RT-PCR 4. ELISA 5. Matrigel invasion assay 6. Wound healing assay 7. Immunohistochemistry	Cytokines Cancer-associated fibroblasts (CAF)	1. CM of CAF had decreased levels of E-cadherin and increased the levels of N-cadherin and vimentin and showed increased invasion and metastasis in endometrial cancer cells 2. CAF induce secretion of TGF- β 3. On addition of TGF- β , compared with the CM of CAF, the number of invading HEC-1A and RL-952 cells was markedly increased in the CM of the normal fibroblast group, but the difference was not significant ($p > 0.05$)
[54]	Gu (2017) China	Human samples: 30 endometrial cancer Cell lines: Human endometrial cancer cell lines: Ishikawa and AN3CA (Estrogen receptor is expressed in Ishikawa, but not in AN3CA)	Design: Experimental Lab methods: 1. IHC 2. RT-PCR 3. Immunoblot 4. Cell proliferation assay 5. Cell migration assay	SDF-1 CXCR7	1. CXCR7 and its ligand SDF-1 were highly expressed in Ishikawa, AN3CA and endometrial cancer tissue 2. 17 β -estradiol pre-treatment significantly increased the levels of CXCR7 and SDF-1 3. SDF-1 significantly promoted the growth and migration Ishikawa and AN3CA 4. Knockdown of CXCR7 inhibited the proliferation of Ishikawa and AN3CA cells 5. Knockdown of CXCR7 inhibited 17 β -estradiol and SDF-1 induced invasion in endometrial cancer cells

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[78]	Walentowicz-Sadlecka(2014) Poland	Human samples: 92 patients with endometrial cancer had hysterectomy + archived samples	Design: Observational Lab methods: 1. IHC	SDF-1	<ol style="list-style-type: none"> 1. SDF-1 was expressed in 90% endometrial cancer and CXCR4 and CXCR7 were found in 100% endometrial cancer compared with adjacent normal endometrial tissue 2. Significant correlations ($p < 0.01$) between SDF-1 and the higher clinical stage of disease, lymph node metastases, distant metastases, deep myometrial invasion ($\geq 50\%$), cervical involvement and involvement of adnexa. No such correlation was found with CXCR4 and CXCR7 expression 3. Significant correlation was found between SDF-1 expression and the risk of the recurrence of endometrial cancer ($p = 0.0001$) 4. Kaplan–Meier analyses demonstrated a stepwise reduction of OS with increasing SDF-1 expression
[40]	Teng (2016) China	Human samples: 202 endometrial cancer patients 348 endometrial samples- normal endometrium, hyperplastic endometrium, atypical hyperplasia, endometrial cancer Cell lines: Human endometrial cancer cell lines: HEC-1B and ECC-1 cells CAF were isolated from endometrial tissues	Design: Experimental Lab methods: 1. ELISA 2. MTT assay 3. Transwell assay	<p>SDF-1α, CXCR4</p> <p>Macrophage chemoattractant protein-1 (MCP-1)</p> <p>Migration inhibitory factor (MIF)</p> <p>Interleukin-1 (IL-1)</p>	<ol style="list-style-type: none"> 1. CAF promoted proliferation, migration and invasion of endometrial cancer cells by secreting SDF-1α. This was blocked by AMD3100, a chemokine receptor 4 (CXCR4) antagonist 2. CAF secreted greater amount of SDF-1α, MCP-1 and MIF when compared to normal fibroblasts and endometrial cancer cells (SDF-1α being of the highest amount) 3. High SDF-1α expression levels were associated with deep myometrial invasion ($p = 0.018$) and lymph node metastasis ($p = 0.038$), but not with grade or stage of endometrial cancer. Lower expression was associated with lower rate of recurrence. No such clinico-pathological connection with CXCR4

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[59]	Liu (2016) China	Human samples: Endometrial cancer tissue of different stages I-III) Cell lines: Human endometrial cancer cell lines: HEC-1A and Ishiwaka cells	Design: Experimental Lab methods: 1. Wound healing migration assay 2. Immunohistochemistry 3. Transwell assay 4. ELISA 5. Immunofluorescence	Receptor activator of nuclear factor (RANK)/ Receptor activator of nuclear factor κ B ligand (RANKL) Chemokine ligand 20 (CCL20)	1. RANK/RANKL expression was significantly elevated in higher stages of endometrial cancer 2. RANK level positively connected with N-cadherin ($p=0.029$) and vimentin ($p=0.0398$), but negatively with E-cadherin ($p=0.0118$) (i.e. RANK initiates EMT in endometrial cancer cells) 3. Migration and invasion of endometrial cancer cells were significantly promoted by RANK/RANKL 4. RANK promoted expression and secretion of CCL20 5. CCL20 facilitated invasion and EMT in RANK over-expressed endometrial cancer cells
[68]	Wang (2015) China	Human samples: Endometrial cancer tissue of different stages I-III)- 70 samples Cell lines: Human endometrial cancer cell lines: HEC-1A and Ishiwaka cells	Design: Experimental Lab methods: 1. Wound healing migration assay 2. Immunohistochemistry 3. Transwell assay 4. ELISA 5. Immunoblot	RANK/RANKL	1. High expression of RANK demonstrated decreased overall survival ($p=0.01$) and progression-free survival and fivefold higher risk of death 2. RANK/RANKL significantly promoted endometrial cancer cell migration and invasion
[52]	Winship (2016) Australia	Human samples: Endometrial cancer tissue -10 hysterectomy Benign endometrium -4 hysterectomy Cell Lines: Human endometrial cancer cell lines: HEC-1A, Ishiwaka	Design: Experimental Lab methods: 1. Immunohistochemistry 2. Rt-PCR 3. PCR 4. xCELLigence real time cell proliferation assay 5. Wound healing assay	IL-11 Chondroitin sulphate proteoglycan protein (CSPG4)	1. threefold increase in CSPG4 gene expression after treatment with IL-11 (100 ng/ml) 2. CSPG4 protein levels are elevated in type I endometrioid cancer with increasing tumour grade G2 and G3 ($p<0.05$) 3. G2-derived HEC1A cells expressed CSPG4, although G1-derived Ishikawa cells did not in response to IL-11 treatment 4. CSPG4 siRNA knockdown decreases HEC1A cell proliferation and migration 5. CSPG4 knockdown reduces SNAIL mRNA expression in HEC1A cells
[79]	Zeng (2016) China	Human samples: Serum samples of 160 benign, 160 endometrial cancer patients	Design: Observational Lab methods: 1. ELISA	IL-31 IL-33	1. Serum levels of IL-31 and IL-33 in patients were significantly elevated compared to those of healthy controls ($p<0.0001$) 2. IL-31 related to clinical characteristics, including tumor stages ($p=0.024$) and IL-33 related to tumour stages ($p=0.035$), depth of invasion ($p=0.008$), existence of node metastases ($p=0.029$) and distant metastases ($p=0.036$)

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[88]	Zeng (2020) China	Human samples: Endometrial tissue sample 150 benign, 260 endometrial cancer	Design: Observational Lab methods: 1. ELISA 2. Immunohistochemistry	IL-31 IL-33	1. IL-31, IL-33 and their receptors (IL31R and ST2) were significantly accumulated within endometrial cancer, in comparison to the controls ($p < 0.001$) 2. Expression of IL-31 and IL-33 in endometrial adenocarcinoma tumour tissues increased with the degree of differentiation and correlated with clinical characteristics, including tumour stage, differentiation and disease-free survival
[60]	Wang (2014) China	Human samples: 70 endometrial cancer tissue samples, 30 normal endometrium, 20 endometrial hyperplasia samples Cell lines: Human endometrial cancer cell lines: Ishiwaika and KLE	Design: Experimental Lab methods: 1. Cell proliferation assay 2. Migration and invasion assay 3. Apoptosis analysis 4. RNA extraction 5. RT-PCR 6. Immunoblot 7. ELISA	RANKL	1. RANK/RANKL is upregulated in endometrial cancer tissues 2. Higher RANK/RANKL expression levels were observed in carcinomas with myometrial invasion ($p = 0.006$), lymph node metastasis ($p = 0.045$) and lymphovascular space involvement ($p = 0.025$) 3. RANK/RANKL promoted endometrial cancer cell proliferation, migration and invasion
[57]	Huang (2018) China	Human samples: 32 paired endometrial cancer tissue and normal endometrium next to them Cell lines: Human endometrial stromal cell (ESC) and human endometrial cancer cell lines: HEC1A, HEC1B, ECC1, AN3CA, KLE and RL95-2	Design: Experimental Lab methods: 1. qRT-PCR 2. Immunoblot 3. Wound healing and cell invasion assay 4. ELISA 5. Chromatin immunoprecipitation (ChIP)	TGF- β 1	1. Expression of TGF- β 1 in endometrial cancer tissues was significantly greater than that in the adjacent non-neoplastic normal tissues 2. Targeted inhibition of estrogen receptor (ERR α) by si-ERR α -1 suppressed migration and invasion of endometrial cancer cells and reduced expression of MMP2 and MMP-9 as well 3. si-ERR α -1 and XCT (specific inverse agonist of ERR α) can significantly decrease the expression of TGF- β 1 in HEC1A cells and ECC cells 4. TGF- β 1 can attenuate the XCT-790 suppressed invasion of HEC1A and ECC cells. This confirmed that ERR α regulated the motility of endometrial cancer cells via modulating TGF- β 1 5. ERR α can trigger the cell migration via upregulating the expression of TGF- β 1. TGF- β 1 neutralization antibody can suppress the invasion of HEC1A cells
[56]	Xiong (2016) Canada	Cell lines: Human endometrial cancer cell lines: KLE and HEC-50	Design: Experimental Lab methods: 1. ELISA 2. Immunoblot 3. Cell migration assay	TGF- β 1	1. TGF- β 1 increases the migration of type II endometrial cancer cells KLE and HEC-50

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[53]	Bokhari (2015) Maryland	Cell lines: Human endometrial cancer cell lines: Ishikawa and HEC-1B	Design: Experimental Lab methods: 1. Cell viability assay 2. Cell invasion assay 3. Immunoblot	Chinese herbs <i>Scutellaria baicalensis</i> (SB) and <i>Fritillaria cirrhosa</i> (FC) TGF- β 1	1. SB and FC treatment of cancer cells resulted in a significant decrease in expression of TGF- β isoforms 2. TGF- β 1-induced cell viability and cell invasion in HEC-1B and Ishikawa cells, SB and FC inhibited this effect
[62]	Chang (2016) Taiwan	Cell lines: Human endometrial cancer cell lines: HEC-1A and RL95-2 cells	Design: Experimental Lab methods: 1. Cell proliferation assay 2. Cell migration assay 3. Immunoblot	Chinese herb <i>Siegesbeckia orientalis</i> (SOE) TGF- β 1	1. TGF- β 1-induced cell proliferation, cell migration and cell invasion. SOE inhibits proliferation, migration and invasion of endometrial cancer cells even under induction by TGF- β 1 2. TGF- β 1-induces an invasive mesenchymal phenotype in endometrial cancer cells, including loss of the cell–cell junction and the formation of a lamellipodia-like structure. SOE inhibits this
[80]	Engerud (2018) Norway	Human sample: Endometrial cancer (235 + 466) patients Endometrial hyperplasia—78	Design: Observational Lab methods: 1. ELISA	Plasma growth differentiation factor-15 (GDF-15)	1. High GDF levels correlated with reduced disease-free survival ($p=0.001$), reduced recurrence-free survival ($p<0.001$), advanced FIGO stage non-endometrioid histology, high-grade tumour and deep myometrial infiltration (all $p<0.003$), recurrent disease, lymph node metastasis and associated with the following findings on MRI—larger tumour volume ($p=0.008$), deep myometrial infiltration ($p=0.05$) and cervical stromal invasion ($=0.03$)
[69]	Jing (2018) China	Human sample: Endometrial cancer specimen – 86 Normal endometrial tissue—85 Cell lines: Human endometrial cancer cell line: Ishikawa	Design: Experimental Lab methods: 1. IHC	ER- α Chemokine Ligand 18 (CCL18)	1. M2 macrophages treated with ER- α agonist induced EMT and promoted migration of Ishikawa cells via CCL18 and this effect was reversed by anti-CCL18 neutralising antibody
[67]	Wang (2019) China	Cell lines: Human endometrial cancer cell line: Ishikawa	Design: Experimental Lab methods: 1. Immunoblot 2. Cell counting kit - 8 – cell viability and proliferation assay 3. Cell scratch test – cell migration assay 4. Transwell assay	Fluorene-9-bisphenol (BHPF) TGF- β	1. BHPF significantly inhibited the EMT process of Ishikawa cells by blocking transforming growth factor- β (TGF- β) signalling pathway, more specifically by reducing the downstream proteins of TGF- β pathway, p-Smad2/3 and slug proteins 2. By the same mechanism, BHPF significantly attenuated cell viability in terms of proliferation, migration and invasion, and eventually retarded the malignant progression of Ishikawa cells

Table 1 (continued)

Ref No	First author, year and country	Study population	Study design and laboratory methods	Exposure	Results
[61]	Schmidt (2013) Germany	Cell lines: Human endometrial cancer cell line: HEC-1A and Ishiwaka Osteoblast-like osteosarcoma cell line (MG63)	Design: Experimental Lab methods: 1. Microinvasion assay 2. Immunoblot	Kisspeptin 10 (KP-10) SDF-1	1. Co-culture of endometrial cancer cell with MG63 increased SDF-1 expression by MG63 2. SDF-1 induced endometrial cancer cell invasion ($p < 0.001$)—dose-dependent 3. This increased invasion rate was inhibited by co-treatment with KP-10 ($p < 0.001$) or addition of SDF-1 antibody ($p < 0.05$) 1. Promotes endometrial cancer metastasis by EMT and cellular invasion
[64]	Billaud (2016) Abstract only		Design: Experimental Lab methods: 1. RNA sequence analysis	GDF15	

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