Supplemental information

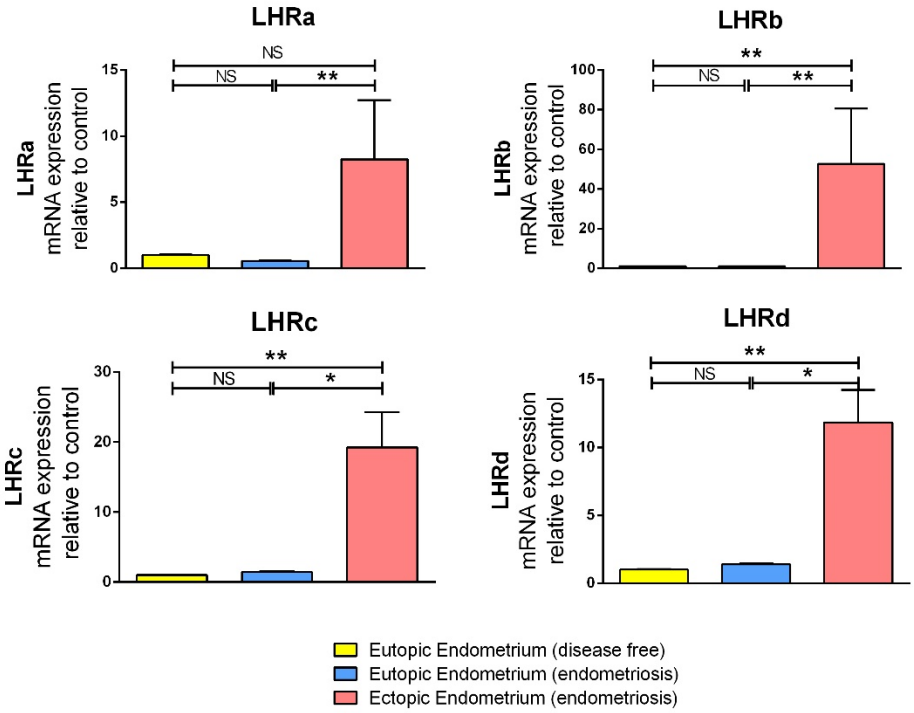
S1. Patients' characteristics for q-RT-PCR analysis

	Controls (n=11)	Endometriosis (n=13)	p
Age (years)	30.4 ± 1.7	29.9 ± 1.4	ns[a]
Body Mass Index (kg/m²)	23.4 ± 1.0	25.2 ± 3.8	ns[a]
On going treatment (n, %)			ns[b]
- none	8 (72.7)	9 (69.2)	
- estroprogestative	1 (9.1)	1 (7.7)	
- progestative	2 (18.2)	1 (7.7)	
- LHRH agonists	0 (0)	2 (15.4)	
- unknown status	0 (0)	2 (15,4)	
Age of first menstruation (years)	13.6 ± 0.5	13.1 ± 0.5	ns[a]
Parity	0.1 ± 0.1	0.1 ± 0.1	ns[a]
Gravidity	0.5 ± 0.3	0.6 ± 0.3	ns[a]
Infertility (n, %)	6 (54.5)	3 (23.1)	ns[c]
since (months)	31.0 ± 13.5	80.0 ± 41.8	ns[a]
Painful symptoms scores[d]			
- Dysmenorrhea	4.8 ± 0.8	6.8 ± 0.8	ns[a]
- Dyspareunia	3.9 ± 1.0	5.8 ± 1.0	ns[a]
- Pelvic pain	2.3 ± 1.0	4.2 ± 0.9	ns[a]
- Gastrointestinal symptoms	0.8 ± 0.6	4.4 ± 0.8	0.003[a]
- Lower urinary symptoms	0.5 ± 0.5	0.9 ± 0.7	ns[a]
DIE lesions (n, %)	*n.a.*	4 (30.8)	*n.a.*
OMA lesions (n, %)	*n.a.*	13 (100)	*n.a.*
SUP lesions (n, %)	*n.a.*	5 (38.5)	*n.a.*
Total rAFS score	*n.a.*	35.8 ± 6.4	*n.a.*
rAFS stage	*n.a.*	3.2 ± 0.2	*n.a.*

Note: Data are presented as means ± SEM unless otherwise specified.
a Mann Whitney's test.
b Pearson's Chi-2 -test.
c Fisher's test.
d Pain intensity was evaluated preoperatively using a 10-cm VAS.
n.a. : not applicable
ns : not significant

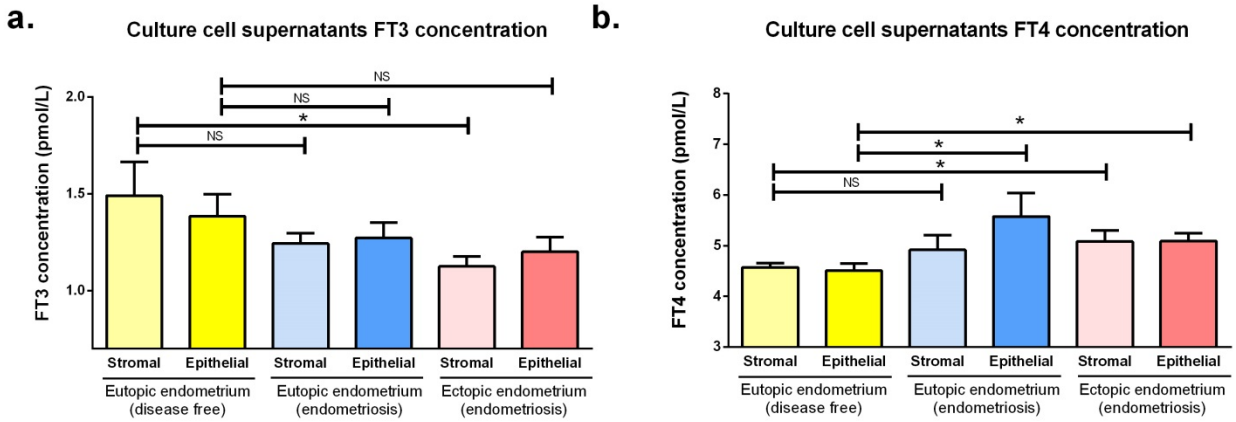
The 13 endometriotic patients provided biopsies from their ectopic and/or their eutopic lesions, resulting in 11 ectopic and 11 eutopic biopsies for the study.

S2. Increased expression of LH receptors mRNA in ectopic endometrium of endometriotic patients



Relative levels of transcrips for LHRa, LHRb, LHRc and LHRd were quantified by real-time RT-PCR for eutopic endometrium from endometriosis free patients, eutopic endometrium and ectopic endometrium from endometriosis patients. The graphs show mean expression levels in arbitrary units ± SEM. P-values are indicated (Kruskal-Wallis and Dunn's post-oc test ; NS : non significant)

S3. Concentrations of T3 and T4 measured in the supernatants of cell cultures.



Concentrations of T3 and T4 were assessed by Automated Biological Diagnosis Service of Cochin Hospital. Free T3 (FT3) and free T4 (FT4) were measured on Cobas automate (Roche®) using an electrochemiluminescence assay.

FT3 concentration (a) and FT4 concentration (b) measured in the supernatant of epithelial and stromal endometrial cells from disease-free women and of stromal and epithelial eutopic and ectopic endometriotic cells from patients with endometriosis. Cells were

cultured in complete media with 2.5% FCS and supernatant collected after 24 hrs for free T3 and free T4 assays.

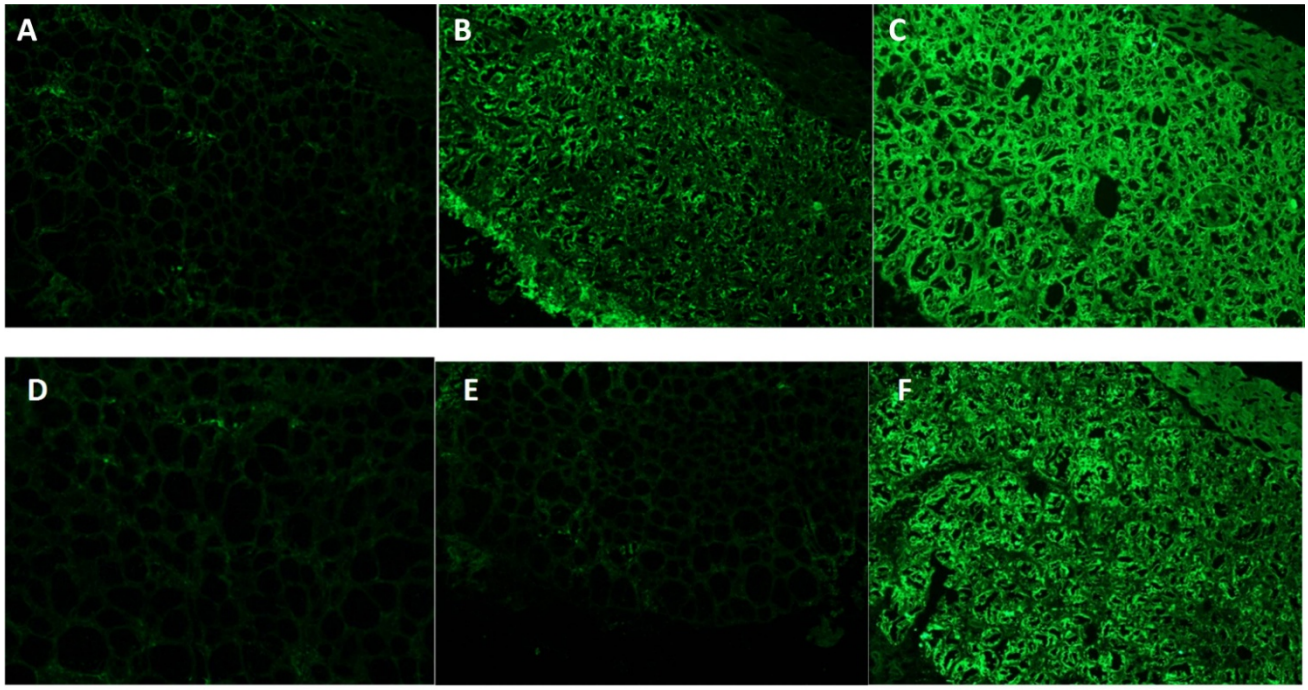
Results are expressed mean ± SEM. P-values are indicated (Mann Whitney's test). We showed here a decreased production of free T3 in vitro by stromal endometriotic cells compared to controls (p=0.0417) and an increased in vitro production of free T4 by eutopic endometriotic epithelial (p=0.0291) cells and by ectopic endometriotic stromal (p=0.0379) and epithelial (p=0.0262) cells compared to control endometrial cells from disease free women.

S4. Patients' characteristics for *in vitro* analysis

	Controls (n=8)	Endometriosis (n=15)	p
Age (years)	29.0 ± 1.5	35.7 ± 1.4	0.01 [a]
Body Mass Index (kg/m²)	23.1 ± 2.0	24.9 ± 1.0	ns [a]
On going treatment (n, %) [d]			
- none	6 (85.7%)	7 (87.5 %)	
- estroprogestative	0 (0%)	0 (0%)	*n.a.*
- progestative	0 (0%)	0 (0%)	
- LHRH agonists	1 (14.3%)	1 (12.5 %)	
Age of first menstruation (years)	13.6 ± 0.7	11.7 ± 0.4	ns [a]
Parity	0.2 ± 0.2	0.3 ± 0.2	ns [a]
Gravidity	0.7 ± 0.3	0.9 ± 0.5	ns [a]
Infertility (n, %) [d]	5 (100 %)	4 (57.1 %)	ns [b]
since (months)	18.6 ± 5.1	51.0 ± 13.3	ns [a]
Painful symptoms scores [c]			
- Dysmenorrhea	4.3 ± 1.0	7.5 ± 0.7	0.04 [a]
- Dyspareunia	4.4 ± 1.7	3.4 ± 1.4	ns [a]
- Pelvic pain	1.2 ± 0.8	2.1 ± 1.2	ns [a]
- Gastrointestinal symptoms	1.7 ± 1.2	1.3 ± 0.8	ns [a]
- Lower urinary symptoms	0.0 ± 0.0	0.6 ± 0.6	ns [a]
DIE lesions (n, %)	*n.a.*	11 (73.3 %)	*n.a.*
OMA lesions (n, %)	*n.a.*	5 (33.3 %)	*n.a.*
SUP lesions (n, %)	*n.a.*	1 (6.7 %)	*n.a.*
Total rAFS score	*n.a.*	15.8 ± 5.2	*n.a.*
rAFS stage	*n.a.*	2.2 ± 0.5	*n.a.*

Note: Data are presented as means ± SEM unless otherwise specified.
a Mann Whitney's test.
b Fisher's test.
c Pain intensity was evaluated preoperatively using a 10-cm VAS.
d Missing values
n.a. : not applicable
ns : not significant

S5. Detection of porcine and human TG-antibodies towards mouse thyroid by Indirect immunofluorescence (IIF)



Observation with a fluorescence microscope Nikon Eclipse 80i (objective 10X). Murine IgG1 are visualized in green through an FITC-labelled anti-murine IgG1 antibody.

At the top(A-B-C): a frozen section of normal murine thyroid (Balb/c) incubated with sera obtained at different times after mice immunization with porcine thyroglobulin. A : Day 0 (negative control). B : Day 21 after immunization. C : Day 35 after immunization.

At the bottom (D, E, F): a frozen section of normal murine thyroid (Balb/c) incubated with sera obtained at different times after mice immunization with human thyroglobulin. D : Day 0 (negative control), E : Day 21 after immunization, F : Day 35 after immunization.

Cross-reactivity of porcin and human TG-antibodies towards mouse thyroid has been evaluated with IFI assay. Sera of mice before or after immunizations with porcine or human TG were incubated with frozen section of mouse thyroids and the fixation of autoantibodies revealed using an FITC-labeled anti-murin IgG1. As observed, the fixation of autoantibodies on mouse thyroid was observed after immunization with porcine and human thyroglobuline at day 35 after immunization. This result suggest that sera from mice immunized either with porcine or human thyroglobuline contain similar amounts of anti-thyroid autoantibodies..

S6. Clinical characteristics of endometriosis patients with or without thyroid disorders

	ART Department			Gyneacology Department			Both departments		
	EndoOnly (225)	EndoThyro (18)	P value	EndoOnly (314)	EndoThyro (14)	P value	EndoOnly (539)	EndoThyro (32)	P value
Age (years)	35,9 ± 0,3	36,2 ± 1,1	0.38	37.5 ± 0.3	41.6 ± 1.1	**0.005**	36.8 ± 0.2	38.6 ± 0.9	**0.034**
Weight (kg)	61,6 ± 0,7	67,2 ± 2,9	**0.02**	59.8 ± 0.6	69.5 ± 4.1	**0.00037**	60.5 ± 0.5	68.2 ± 2.4	**5E-5**
Height (cm)	167 ± 1,4	165,1 ± 1,4	0.349	165.3 ± 0.4	165.8 ± 1.1	0.386	166 ± 0.6	165.4 ± 0.9	0.41
Body Mass Index (m2/kg)	22,3 ± 0,3	24,7 ± 1,1	**0.006**	21.9 ± 0.2	25.2 ± 1.4	**0.001**	22.1 ± 0.2	24.9 ± 0.8	**3E-5**
Family history of endometriosis (n,%)	51 (23)	4 (22)	0.942	33 (11)	1 (7)	0.671	84 (16)	5 (16)	0.973
Previous endometriosis surgery (n,%)	87 (39)	5 (28)	0.359	77 (25)	7 (50)	**0.035**	164 (31)	12 (38)	0.412
Gravidity >=1 (n,%)	53 (27)	1 (7)	0.078	87 (28)	6 (60)	**0.028**	140 (28)	11 (38)	0.235
Parity >= 1 (n,%)	23 (12)	0 (0)	0.226	45 (14)	5 (38)	**0.019**	68 (14)	6 (21)	0.291
Painful symptoms (VAS score)									
Dysmenorrhea	6,9 ± 0,2	6,8 ± 0,5	0.427	7.2 ± 0.1	7.3 ± 0.8	0.428	7.1 ± 0.1	7 ± 0.4	0.469
Deep dyspareunia	3,9 ± 0,2	4,7 ± 0,6	0.127	4.5 ± 0.2	3.7 ± 1	0.254	4.2 ± 0.2	4.3 ± 0.6	0.464
Non-cyclic chronic pelvic pain	2,4 ± 0,2	4 ± 0,7	**0.01**	3.3 ± 0.2	4.8 ± 1	**0.047**	2.9 ± 0.1	4.3 ± 0.6	**0.006**
Gastrointestinal symptoms	3,7 ± 0,2	4,8 ± 0,9	0.112	3.9 ± 0.2	3.4 ± 1.1	0.29	3.8 ± 0.2	4.2 ± 0.7	0.289
Lower urinary tract symptoms	1,2 ± 0,2	0,2 ± 0,2	0.054	1.5 ± 0.2	1.6 ± 0.8	0.427	1.4 ± 0.1	0.9 ± 0.4	0.161
ASRM total score*				26 ± 1.5	44.1 ± 11.8	**0.008**			
ASRM stage III/IV n, (%)				159 (53)	10 (71)	0.172			
Endometriosis Phenotype n (%)			0.85			0.846			0.946
SUP	57 (25)	4 (22)		61 (27)	5 (33)		118 (26)	9 (27)	
OMA	19 (9)	1 (6)		45 (20)	3 (20)		64 (14)	4 (12)	
DIE	149 (66)	13 (72)		121 (53)	7 (47)		270 (60)	20 (61)	
Mean Total number of DIE lesions	3,2 ± 0,1	3,6 ± 0,4	0.166	2.7 ± 0.1	3.3 ± 1.1	0.212	2.9 ± 0.1	3.5 ± 0.5	0.078

VAS: Visual analogue scale ; ART : Assisted Reproductive Technology
*: Score according to the American Society for Reproductive Medicine classification (rAFS, 1997)
EndoOnly: endometriosis patient without thyroid dysfunction, EndoThyro: endometriosis patient with thyroid dysfunction
Statistical test: t-test for quantitative variable, Chi-square test for qualitative variable or proportion comparison with >=1 case per category, Fisher exact test otherwise

S7. Inclusion criteria

Patients were recruited on the base of a prospective observational study evaluating symptomatic women younger than 42 years of age who were undergoing surgery for benign gynecological pathologies. This study was approved by the local institutional review board (approval number 05-2006 provided by the 'Comité de Protection des Personnes et des Biens dans la Recherche Biomédicale' of Paris Cochin) and all participants gave written informed consent.

Indications for surgery (possibly more than one per patient) included:

1) infertility: defined as at least 12 months of unprotected intercourse that did not result in pregnancy (1).
2) chronic pelvic pain: defined as the presence, for at least 6 months, of dysmenorrhea and/or intermenstrual pelvic pain and/or dyspareunia of moderate to severe intensity
3) presence of a pelvic mass (e.g. uterine myomas, benign ovarian cysts, etc.)
4) miscellaneous: e.g. infection, uterine bleeding, request for tubal ligation…

Excluded from this population were the following:

1) pregnant patients
2) patients who had undergone surgery for cancer
3) endometriotic patients for whom surgical exeresis was considered as being incomplete by the surgeon
4) patients who refused to give their consent for the participation in the study.

Patients were divided into two groups: the endometriosis group (included women with histologically proven endometriosis) and the endometriosis free group (included patients without any visual endometriotic lesions as determined during the surgical procedure).

Patients who were visually diagnosed as having endometriosis but lacking histological confirmation were excluded from the study. Histologically proven endometriotic lesions were classified into three phenotypes: SUP, OMA and DIE, as previously described by our team (2-4).

For each patient, data were recorded during face-to-face interviews conducted by the surgeon in the month preceding the surgery, using a structured previously published questionnaire (2, 3). For each painful symptom, the intensity was assessed using a 10-cm visual analog scale (VAS) (5). When present during surgery, the extent of the endometriosis (e.g. stages and mean scores: total, implants and adhesions) were assessed according to the revised American Fertility Society (rAFS) classification of endometriosis (6).

S8. Real time RT-PCR.

For this assay, 11 endometrioma and 11 control biopsies were used. After surgical resection, the samples were immediately frozen in liquid nitrogen. Total RNA was extracted in TRIzol® (Invitrogen, Carlsbad, CA), according to the manufacturer's instructions. Total RNA concentration was quantified using spectrophotometry by measuring absorbance at 260 nm. RNA was treated with DNAse (Invitrogen) to remove any contaminating DNA. Four micrograms of total RNA were reverse transcribed using Maxima First Strand cDNA Synthesis Kit (ThermoScientific, Waltham, Massachusetts, USA) according to the manufacturer's instructions. A negative control without RNA was included in each series of reverse transcription reactions. Each sample was resuspended in presence of RNAseOut (Invitrogen).

A set of 12 genes, including 11 target genes (luteinizing hormone receptors A, B, C and D (LHRa, LHRb, LHRc, LHRd), thyroid stimulating hormone receptor (TSHR), thyroid hormone receptor alpha 1 and 2 (THRA-1 and THRA-2), type 2 and 3 iodothyronine deiodinase (DIO-2 and DIO-3), thyroglobulin (TG) and monocarboxylate transporter 8 (MCT-8)), and 1 reference genes (internal controls : SDHA) was analyzed by real-time RT-PCR. Primers for real-time RT-PCR were chosen using PRIMER3PLUS software (http://www.bioinformatics.nl/cgi-bin/primer3plus/primer3plus.cgi) or designed elsewhere (7) (SI Appendix Table 9). All primers were aligned with BLAST to avoid non-specific annealing and cross-amplifications (https://blast.ncbi.nlm.nih.gov/Blast.cgi). Primers were synthetized by Eurofins Genomics (Luxembourg, Luxembourg). Quantitative PCR was carried out on a LightCycler480, 96-wells apparatus (Rocher Diagnostics, Manheim, Germany) using the amplification kit SensiFAST®

SYBR No-ROX Kit (Bioline, London, UK) according to the manufacturer's instructions. The relative abundance fold changes of each target gene compared with a set of internat controls was determined by the -2ΔΔCt formula. Results were analyzed with the LightCycler software using a second derivate max method.

S9. Primers for real time RT-PCR using SYBR Green

Gene	Forward primer 5'-3'	Reverse primer 5'-3'	Primer locations (exons)	Product size (pb)
TSHR	AGATGTCTATGAACTGATTGA	CTACACTACTCACAATGGT	3'UTR	114
THRA1	CGCTTCCTCCACATGAAAGT	TGTGTGTGTGGGAGCTGAAT	9 and 3'UTR	226
THRA2	CAAACACAACATTCCGCACTTC	GCCCCCTTGTACAGAATCGA	9 and 10	81
THRB	GACAAAGTCACGCGAAATCA	GTCTTTTCTCCCGGTTCTCC	6 and 7	139
THRB-1	GGCACTGGTAATTTGGCTAGA	GTAATCATTCTGGATCCCTTTTT	1 and 3	150
DIO2	ACTCGGTCATTCTGCTCAAG	ATTGCCACTGTTGTCACCTC	3 and 4	215
DIO3	TGAGACTCCTGGGGAATGAC	ACACTCACCAAATGGCCTTC	3'UTR	158
TG	ACTGGCTGAGACAGGTTTGG	GCTGTAAACCGCTCCACTTC	6-7 and 8	192
MCT8 (SLC16A2)	TGCCCTTGGCTACTTTGTTC	CCTGAGGTAGCCCCAATACA	3 and 4	111
LHCGRa	ATTTGTCAATCTCCTGGAGGC	CACTCAGTTCACTCTCAGCA	9 and 11	191
LHCGRb	AGGGCCGAAAACCTTACAGAA	CACTCAGTTCACTCTCAGCA	8-10 and 11	131
LHCGRc	ATTTGTCAATCTCCTGGAGGC	CCCCATGCAAAAAGTGTTTTG	9 and 10-11	167
LHCGRd	AGGGCCGAAAACCTTACAGAA	CCCCATGCAAAAAGTGTTTTG	8-10 and 10-11	107
SDHA	TACAAGGTGCGGATTGATGA	CAAAGGGCTTCTTCTGTTGC	13-14 and 14	67

S10. Western blot assays.

Briefly, cells were washed twice with PBS then lysed with RIPA lysis buffer (Thermofisher ref 89900) in the presence of protease inhibitor cocktail (HaltProtease Phosphatase Inhibitor cocktail, Thermofisher ref 78445).

Cells were freezed at -20°C before use. After defreezing and centrifugation, the protein content was determined with the Colorimetric protein assay Coomassie Blue G-250 dye-binding. 40µg of each sample was separated by migration on gel (BIORAD Mini Protean TGX Gels 10%, Cat #456-1033) on a migration machine (BIORAD Power Pac 300). The migrated proteins were then transferred on nitrocellulose membrane and then blocked and incubated with the primary antibodies (mouse monoclonal anti-TSHR antibody Santa Cruz ref sc-53542 at 1/500 overnight 4°C, strip at 115kD ; polyclonal rabbit IgG anti-DIO2 antibody Abcam ref ab77779 at 1/1000 overnight at 4°C strip at 31 kD ; polyclonal rabbit IgG anti-DIO3 antibody Novusbio ref NBP1-05767 at 1/2000 1h at 20°C, strip at 31 kD ; monoclonal mouse IgG1 anti-THRβ1 antibody clone J52 ThermoFisher scientific ref MA1-216 at 1/1000 overnight at 4°C, strip at 55kD ; polyclonal rabbit IgG anti-THRα1 antibody ThermoFisher Scientific PA1-211A at 1/1000 2h at 37°C, strip at 48 kD ; polyclonal rabbit IgG anti-THRα2 antibody ThermoFisher Scientific PA1-216 at 1/500 2h at 37°C, strip at 58 kD). Monoclonal anti-β-actin

HRP clone AC-15 Sigma Aldrich ref A3854 at 1/25000 was used as an intern control. After incubation of appropriate secondary horseradish peroxidase-conjugated antibodies including goat anti mouse IgG HRP Thermofisher scientific ref A28177 at 1/5000 and rabbit anti-Goat IgG HRP ThermoFisher Scientific ref A27014 at 1/5000, blots were revealed with peroxydase and visualized on LAS-3000 Imaging System, Fujifilm. Band intensities were measured with Multi-Gauge 3.0 software. Variations in protein levels were expressed after normalization to β-actin.

S11. ROS production by endometrial and endometriotic cells in vitro.

Cells (10^4 per well) were seeded in 96-well plates and incubated for 24 hours in triplicate with culture medium. Culture media were then removed and replaced by 100 µl per well of 5 µmol/L 2',7'-dichlorodihydrofluorescein diacetate (H2DCFDA) in PBS for hydrogen peroxide (H_2O_2) assay. Immediately, cells were treated with either 0 ; 0,5 ; 1 ; 2 or 4 µg/mL of recombinant human TSH (Thyrogen® 0,9mg, Genzyme, Naarden, Netherlands) or thyroxine 0, 10, 50, 100nM (Sigma Aldrich, Saint Louis, Missouri, USA) or tri-iodothyronine 0, 10, 50, 100nM (Sigma Aldrich, Saint Louis, Missouri, USA). Cellular levels of H_2O_2 were assessed by spectrofluorimetry using a Fusion spectrofluorimeter (Packard Bell, Paris, France). Fluorescence intensity was recorded on T0 and T6h. Fluorescence excitation/emission maxima were for 2',7'-dichlorodihydrofluorescein diacetate, 488/515 nm. The levels of H_2O_2 were calculated in each sample as follows: H_2O_2 rate (arbitrary units/min/10^6 cells) = (fluorescence intensity [arbitrary units] at T6h − fluorescence intensity [arbitrary units] at T0)/number of adherent cells determined by the crystal violet assay as a measure for membrane integrity. In brief, cells were stained with 0.5% crystal violet and 30% ethanol in PBS for 30 minutes at room temperature. After two washes in PBS, the stained cells were resuspended in 50% methanol, and absorbance was measured at 560 nm on an enzyme-linked immunosorbent assay multiwell reader. Production of H_2O_2 was explored in all of the cell lines extracted from the 8 controls and from the 11 endometriotic patients.

S12. Endometrial and endometriotic cells *in vitro* proliferation assay.

Cells (10^4 per well) were seeded in 96-well plates and incubated in triplicate for 48 hours. Cell proliferation was determined using the Uptiblue proliferation test. The proliferation of the cells induces a reduction of Uptiblue from its blue oxidized form to its reduced red

fluorescent form. After 24 hours of incubation in the culture medium, two washes in PBS were carried out, and then various amounts of thyrogen, thyroxine and tri-iodothyronine as indicated in the previous section were added in DMEM with 2.5% FCS. After 24h incubation, Uptiblue reagent was added and the fluorescence read on a Fusion spectrofluorimeter (Packard Bell, Paris, France) 24h after. Viable cells were detected using Crystal violet assay as mentioned above. The proliferation rate and the viability of the cells were determined in all of the cell lines extracted from the 8 controls and from the 11 endometriotic patients.

S13. Animal model of thyroiditis and endometriosis

Six week old C57BL/6, CBA/J and BALB/c female mice were purchased from Janvier Laboratory (Le Genest Saint Isle, France). All experimental procedures and animal care were approved by the institutional board: the present study was reviewed and approved by the Ethics Committee "Comité d'Ethique en matière d'Expérimentation Animale", Paris Descartes University (CEEA 34), Paris, (permit number #2016040716219897). Three mice models have been developed: toxic thyroiditis, EAT and thyroid immunization with euthyroidism. Each model of thyroid disorder was coupled with the endometriosis model.

Toxic thyroiditis. Toxic hypothyroiditis was induced in mice (n=10) by 0.05% methimazole (MMI) and 1% potassium perchlorate ($KClO_4$) in distilled water for 8 weeks, as previously describe (8). Control mice (n=7) received distilled water only. Blood samples were collected after 8 weeks and at the time of sacrifice to screen thyroid function. After 8 weeks of treatment, all mice underwent surgery to induce endometriosis. Mice were sacrificed 21 days after the surgery.

EAT. CBA/J mice (n=25) were immunized s.c. just above the tail with 100µg Porcine thyroglobulin (pTg) (Ref T1126, Sigma Aldrich) emulsified in complete Freund's adjuvant (CFA) on day 0 and in incomplete Freund's adjuvant (IFA) for challenge on day 14 as already describe (9). Control mice (n=18) were only injected with the adjuvant. All mice underwent surgery to induce endometriosis on day 15 and were sacrificed at day 35 after immunization.

Thyroid immunization with euthyroidism. BALB/c mice (n=10) were immunized s.c. just above the tail with 10µg Human Tg (hTg) (ref T6830, Sigma Aldrich) emulsified in CFA on day 0 and in IFA on day 14 (10). Control mice (n=10) were only injected with the adjuvant. Blood samples were drawn at day 35 to check for antibodies production and thyroid function tests.

All mice underwent surgery to induce endometriosis on day 15 and were sacrificed on day 35 after immunization.

Endometriosis induction in the mouse and histology. The model of endometriosis performed for the study has already been described elsewhere (11). This model is a syngenic graft of uterine horns to generate endometriosis like lesions.

Donor C57BL/6, CBA/J and BALB/c provided uterine horns to generate syngenic endometriosis like lesions. Donor mice were sacrificed by cervical dislocation and uterine horns were surgically extracted and transferred into a Petri dish containing 37°C warm Dulbecco's modified Eagle's medium (DMEM; 10% fetal calf serum, 100 1 U/mL penicillin, 0.1 mg/mL streptomycin; PAA, Paris, France). The uterine horns were opened longitudinally with microscissors under a stereo-microscope (M651; Leica Microsystems, Paris, France) and 5-mm-length samples were prepared for grafting in the peritoneal cavity of recipient mice. A preoperative gavage of all recipient mice with 56 µg/kg/day 17β-estradiol (Provames®, Sanofi-Aventis, France) was performed for 3 days before implantation. Recipient mice were anesthetized with isoflurane, intubated and mechanically ventilated. An incision was made on the ventral midline, and one 5-mm donor horn fragment was sutured onto the parietal peritoneum with two 7/0 polypropylene stitches (Prolen®, Ethicon, Somerville, NJ). In all mice, tissue samples were sutured at identical positions of the abdominal wall to ensure that host tissue sites exhibited a comparable vascularization. The cutis was sutured with a 6/0 nylon thread.

Seven, 14 and 20 days after implantation, the mice underwent ultrasonography to confirm the viability of the implant and to measure its size as previously described (12). See details in SI Appendix 14 just below. Three weeks after implantation, animals were sacrificed by cervical dislocation. Endometriotic implants were surgically removed, weighed and measured using a rule caliper and thyroids were also removed using a stereo-microscope (M651; Leica Microsystems, Paris, France). All tissus were then fixed with 10% formaldehyde, set in paraffin sliced into sections thick of 5µm and stained with H&E. The presence of glandular and stromal cells validated the endometriosis model. The histological grade of EAT was assessed by blind evaluation of the infiltration indexes by two observers as previously described (13). Thyrocyte hypertrophy was assessed as follows: from each slide of mice thyroid, 10 randomly selected thyroid follicles were analyzed for colloid containing

area, whole follicle area and thyrocyte area. Then, we calculated the ratio thyrocyte area/follicle area for 10 follicles.

S14. Monitoring of implant size.

Monitoring of implant size was performed as previously described (12). Briefly, serial ultrasound imaging with the Vevo 2100 high-frequency ultrasound imaging system (VisualSonics; Toronto, CA) was used to measure the endometriotic implants after surgery. During imaging, the mouse was kept under anesthesia with 1.5% isoflurane and restrained on a heated stage. Ultrasound contact gel was applied to the abdomen, and an image sequence with two-dimensional axial views of the endometriotic implant was acquired, as the probe was manually swept from the upper to the lower abdominal wall of the mouse. The implant volume was calculated as follows: IV (mm3) = $\pi/6$ x L × W x H (14), where L is the length, W is the width and H the height of the implant in millimeters. The same blinded operator performed all of the image acquisitions.

S15. Screening of mice sera for anti-thyroglobulin auto-antibodies and thyroid function tests

After retro-orbital blood collection, sera were obtained after centrifugation at 1500g at 4°C for 10 min. Autoantibodies to pTg and to hTg were detected using an ELISA as previously described (15) (10). See details in SI Appendix 16. Reactivity towards mouse thyroid was assessed by indirect immunofluorescence assay as explained in SI Appendix 17. T3 and T4 levels in the sera were performed using a Cobas 8000 electrochemiluminescent analyser (Roche Diagnostics, Indianapolis, IN, USA). Mouse TSH levels were assessed using the ELISA kit (ref abx575817, Abbexa, Cambridge, UK) following the manufacturer's instructions.

S16. Screening of mice sera for autoantibodies to pTg and hTg.

ELISA anti-pTg

Briefly, flat bottom microtiter plates (Costar™, Thermofisher, Waltham, Massachusetts, USA) were coated with 100µL of 100µg/mL of pTg. After washing with PBS-0,1% Tween 20, the plates were blocked by adding PBS-1,5% BSA and sera from individual mice, diluted $1/10^3$, $1/10^4$, $1/10^5$ and $1/10^6$ in PBS-BSA were incubated for 2h at 37°C and washed out extensively. Alkaline phosphatase-conjugated goat anti-mouse IgG (Novex™ Life

Technologies, Thermofisher, Waltham, Massachusetts, USA), diluted 1/2000 in PBS-BSA was added as second antibody.

ELISA anti-hTG

ELISA plated were coated with 100 µL of 10 µg/mL of hTg and blocked with PBS-5% BSA. Following extensive washing out, mice sera (diluted 1/200 in tris-buffered saline (TBS) were added to the wells. Alkaline phosphatase-conjugated goat anti-mouse IgG (Novex™ Life Technologies, Thermofisher, Waltham, Massachusetts, USA) diluted 1/2000 in TBS was added as second antibody.

For both ELISA the colorimetric reaction was revealed by substrate addition. The plates were read at 405 nm with Fusion spectrofluorimeter (Packard Bell, Paris, France).

S17. Indirect immunofluorescence (IIF) for detection of TG-antibodies.

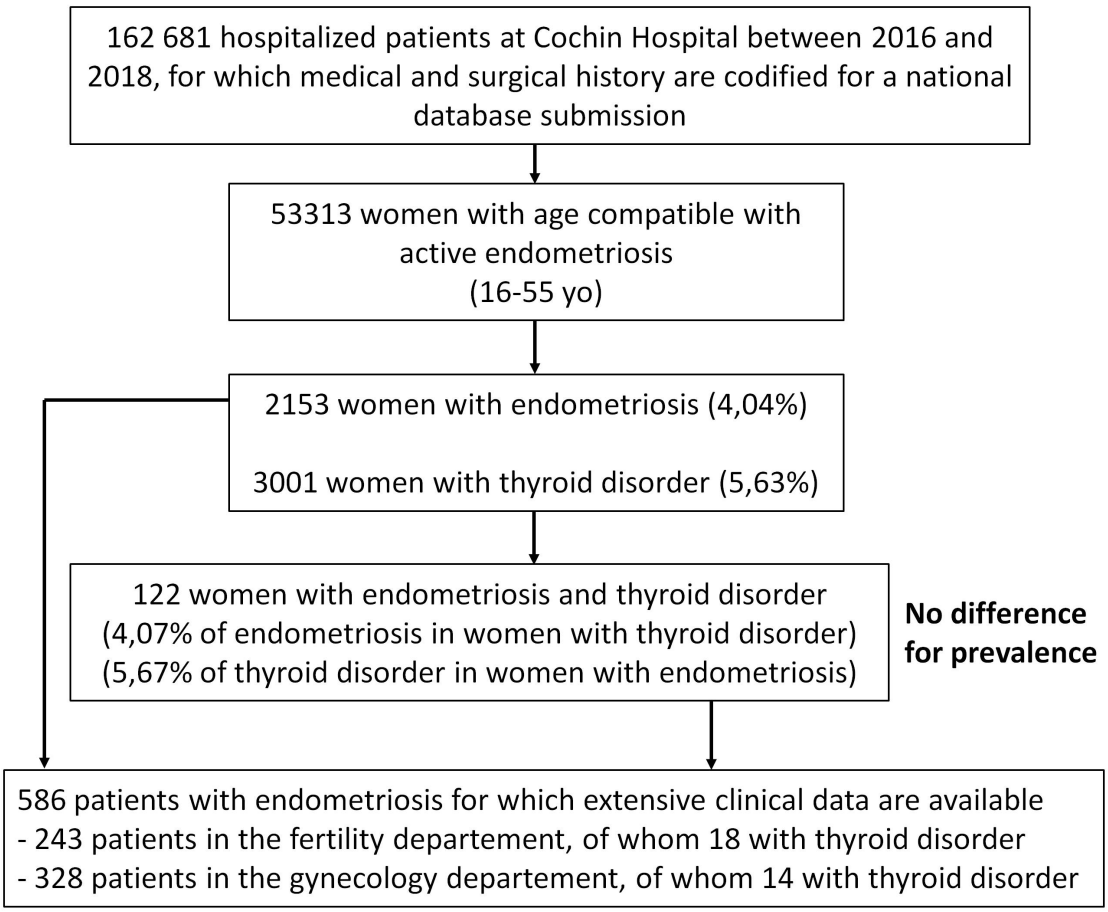
For the detection of antibodies to thyroglobulin, frozen section (7µM) of normal murin thyroid (HistIM platform Institut Cochin, Paris) were incubated with sera obtained at different times (Day 0, Day 21 and Day 35 after immunization) from 2 mice immunized with human thyroglobulin and 2 mice immunized with porcin thyroglobulin. Sera were diluted at 1/10 in PBS 1X and incubated 30 minutes in a humidity chamber. After gentle washing in PBS-Tween 0.05%, thyroid sections were incubated with an anti-murin IgG1 antibody labeled with FITC diluted in 1/20 in PBS 1X during 30 minutes in an humidity chamber and obscurity (16). Sections fluorescence was observed with a fluorescence microscope (Nikon Intensilight C-HGFI) at objective 10X. Background staining was assessed by using normal murin sera and PBS 1X.

S18. Clinical study of relationship between thyroid disorder and endometriosis.

Data related to hospitalizations were corresponding to information that each French hospital have to submit to a national database called Programme de Médicalisation des Systèmes d'Information (literally Medicalization of Information System Program), intended to collect and gather standardized data measuring hospital activities so as to eventually regulate resource allocation. Data notably include information on patient demographics (gender and age), the main and associated diagnosis codes (based on WHO International Classification of Diseases, 10th edition), and procedure codes [in French Classification Commune des Actes Médicaux (CCAM)]. For each hospitalization case between 2016 and 2018 at Cochin Hospital

in Paris, we retrieved these data (gender, codified medical and surgical history) as well as the first, last name and date of birth of the patient, in order to only consider individual patients (a patient hospitalized several times was only counted once). By this way, we obtained 3 lists of patients: all the hospitalized patients, patients hospitalized with a code for endometriosis and patients hospitalized patients with codes for hypothyroidism. The number of patients in each list and common to several lists were counted as depicted in the flow chart (SI Appendix 19). As Cochin hospital is a national reference center for endometriosis, we were able to get extensive clinical data for endometriosis patients hospitalized either in the Gynaecology or in the Assisted Reproductive Technology department. The medical file of each endometriosis patient with a thyroid disorder was then retrieved to get more details on the thyroid disorder. In all cases, patients had hypothyroidism (Hashimoto thyroiditis), and for most of them a treatment with levothyroxine was indicated (without any indication on the dosage).

S19. Flow chart of inclusion strategy for the clinical study



Data have been supplied by the medical information department of Groupe Hospitalier Paris Centre.

S20. Statistical analysis. All statistics and graphics were made on the GraphPad Prism 6 and appears in more details in Appendix 20. For quantitative variables, ANOVA was performed when more than two datasets were compared, with Tukey's post-hoc test. In the case of non-parametric data, the Mann-Whitney test (two groups) and the Kruskal Wallis test (> two groups) were used, with Dunn post-hoc test. For qualitative variables, the Fisher (two-group) and Chi² (> two groups) test were used. In all figures, error bars represent the standard error of the mean (SEM). A value of $p<0.05$ was recognized as significant (* $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$).

Supplemental information references

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