Table 1: Summary of Study Characteristics and Key Findings on the Use of Liquid Biopsy Analysis in Patients with Endocrine Neoplasia

Reference	Site	Biomarker Type(s)	Genes or Molecular Target (Diagnostic Assay Used)	Cases (Controls)	Sampling Time	Aim(s)	Results (prevalence of detection and/or estimate of diagnostic accuracy)
Creemers et al. 2017[22]	Adrenal	cfDNA	19 (multigene panel developed using Ampliseq™, Thermo Fisher Inc., Waltham, MA, US)	6	Before and after surgery	Examined detection of ctDNA in the plasma of patients with ACC by identifying specific mutations present in both the primary tumor and cfDNA.	Mutations were found in the primary tumor of half (3/6) of the patients with ACC. Of these patients, one patient had matching mutations detected in both the primary tumor and the cfDNA samples. No cfDNA was examined in patients without mutations detected in the tumor. Calculated sensitivity based on the patients with mutations detected in plasma is 33.0% (1/3).
Garinet et al. 2018[23]	Adrenal	ctDNA	20 (multigene panel developed using Ampliseq™, Thermo Fisher Scientific Inc., Waltham, MA, US)	11	Before and after surgery	Compared deep NGS and ddPCR analytical methods for detection of ctDNA in patients with ACC. The evolution of ctDNA during the course of the disease was also assessed.	*TP53*, *CTNNB1, NF1, TERT*, *RPL22*, *ATRX*, *MED12* and/or *MEN1* mutations were detected in the primary tumor of 72.7% (8/11) of patients. Plasma samples were obtained for these eight patients with varying tumor burden and DNA concentration. ctDNA concentrations paralleled tumor evolution. Of the eight patients with tumor mutations detected, two had ctDNA with the same mutations (25.0% sensitivity).
Perge et al. 2018[24]	Adrenal	hsa-miR-22-3p, hsa-miR-27a-3p, hsamiR-210-3p, hsa-miR-320b and hsa-miR-375	--	35	Before surgery	Evaluated the expression of EV-associated miRNAs in patients with NFA (n=13), CPA (n=13) and CP-ACC (n=9).	A significant difference in overrepresentation of miRNAs were observed in CPA and CP-ACC relative to NFAs. A sensitivity of 88.9% (specificity: 76.9%) for the differentiation of CP-ACC and CPA by hsa-miR-320b was determined.

Salvianti et al. 2017[25]	Adrenal	*miR483* and *miR483-5p*; CTC	--	27 ACC and 13 ACA (10)	Before and after surgery	Measured levels of *miR483* and *miR483-5p* and evaluated the levels with disease stage. Some ACC samples (n=13), were isolated for comparison between CTC number and *miR483* and *miR483-5p* levels.	Overall, *miR483* and *miR483-5p* plasma levels were significantly different in high-risk patients (stages III/IV) and low-risk patients (stages I/II) before and after surgery. A significant positive correlation was found between CTC count in both *miR483* and miR-483-5p levels. A sensitivity of 83.0% and a specificity of 100.0% was determined using a cut-off value of 0.221 ng/mL for *miR483-5p* levels. A sensitivity of 87.5% and specificity of 63.6% was determined for a cut-off value of 0.101 ng/ml for *miR483* levels.
Banys-Paluchowski et al. 2017[26] (Abstract)	Ovarian, pathology not specified	CTC	EpCAM (CellSearch®, Menarini Silicon Biosystems, Inc., Huntington Valley, PA, US)	OC (n=50); fallopian tube (n=5); peritoneal (n=5)	Serial sampling	Evaluated CTCs during chemotherapy to assess clinical relevance of CTC changes.	At baseline, 43.3% (26/60) patients had ≥1 CTC/7.5 mL blood. Patients with CTC detection at baseline had significantly shorter overall survival compared with CTC negative patients. The presence of CTCs was not statistically correlated with FIGO stage, nodal status or grading.
Färkkilä et al. 2017[27]	Ovarian	ctDNA	*FOXL2* 402C>G (C134W) mutation (Taqman®, Thermo Fisher Scientific Inc., Waltham, MA, US)	33	Serial sampling	(1) Determined whether ctDNA *FOXL2* mutation is detectable in patients with primary and recurrent AGCTs of the ovary (2) Monitored disease recurrence.	All 33 patients had measurable tumor at the time of sample collection, and 36.4% (12/33) harbored a detectable ctDNA *FOXL2* mutation. Median tumor size was significantly larger in ctDNA *FOXL2* mutation positive samples compared with mutation-negative samples. Four patients without clinical disease had the mutation detected, and one of these patients relapsed during follow-up.

Iwahashi et al. 2018[28] (Abstract)	Ovarian, pathology not specified	ctDNA	197 (AVENIO ctDNA Surveillance Kit, Roche Diagnostics, San Jose, CA, US)	5	Not specified	Examined ctDNA mutation profiles of plasma samples and compared liquid biopsy results to match tumor tissue samples.	ctDNA mutations were detected in 100.0% of OC patients (n=5). Tumor tissue samples detected matching gene mutations in 80.0% (4/5) of OC patients.
Londono et al. 2017[29] (Abstract)	Ovarian, pathology not specified	ctDNA	50 (Circulogene Theranostics, Birmingham, AL, US)	30	Time of recurrence	Investigated molecular profiling using NGS of tumor and ctDNA in patients diagnosed with recurrent OC.	An average of 3.7 mutations per patient from the tumor sample were detected by tumor NGS panels. An average of 1.7 mutations per patient were detected in ctDNA. In total, 23.3% (7/30) patients were found to have a *TP53* genomic alteration in both the tumor and ctDNA. There was no concordance between tumor and ctDNA genomic alterations in the other patients.
Lou et al. 2018[30]	Ovarian	CTC	EpCAM (CellSearch®, Menarini Silicon Biosystems, Inc. Huntington Valley, PA, US)	2	Before treatment	Compared presence of CTCs with histopathologic diagnosis in women with newly diagnosed pelvic masses (n=49).	Neither of the patients with stromal ovarian tumors (n=2) had CTCs present, whereas 18.5% (5/27) of epithelial OC patients had CTCs present.

McConechy et al. 2014[31] (Abstract)	Ovarian	ctDNA	*FOXL2* 402C>G mutation (Taqman®, Thermo Fisher Scientific Inc., Waltham, MA, US)	2	Time of recurrence	Described detection of *FOXL2* 402C>G mutation in two patients with AGCT.	Patient one: No mutation was detected in the sample taken at the time of recurrence (12 years from diagnosis). Six months later, in a second plasma sample, taken after chemotherapy and surgery for extensive tumor burden, 16.0% allelic frequency of the *FOXL2* mutation was detected in ctDNA. Patient two: No mutation was detected in the sample taken at primary diagnosis. *FOXL2* ctDNA mutation was present at 6% in the recurrent plasma sample taken at relapse, two years after primary surgery.
Nakabayashi et al. 2018[32]	Ovarian	cfDNA	CNAs (NIPT WGS)	1	Before surgery	Determined whether the use of a NIPT platform for CNA in plasma from patients with gynecological cancer (n=100) could serve as a predictive marker of patient outcome.	One patient with dysgerminoma, stage IA showed alterations (detected CNA > 10 Mb).
Obermayr et al. 2016[33] (Abstract)	Ovarian, pathology not specified	CTC	*EpCAM, PPIC, TUSC3, EMP2, LAMB1, MAL2, FN1*	Not specified	At primary diagnosis or time of recurrence	Measured CTCs using developed gradient enriched cells immune-fluorescently stained targeting CK8/18/19, *PPIC*, *TP53* and CD45.	Concordance between immunofluorescent staining and RT–qPCR was obtained in 30.0% of OC samples. By adding further 22 RT–qPCR markers, 92.0% of all cancer patients (n=13) and 100.0% of the OC patients (n=7) were classified as being CTC–positive by RT–qPCR.

Phallen et al. 2017[34]	Ovarian	cfDNA, ctDNA	58 (TEC-Seq method)	5 (44)	Before treatment	Evaluated novel assay for analysis of sequence alterations in driver genes in cfDNA that are commonly mutated in colorectal, lung, ovarian, breast and other cancers.	Of the patients with OC, four were diagnosed with germ cell tumors and one patient had a granulosa cell tumor. None of these patients had metastases at diagnosis. One patient with a germ cell tumor had a germline mutation detected and two other patients (one with a germ cell tumor and one with a granulosa cell tumor) each had a somatic mutation detected (supplemental material).
Ratajka et al. 2017[35]	Ovarian, pathology not specified	ctDNA	*BRCA1/2*	121	Before treatment	Assessed ctDNA for frequency of germline and somatic *BRCA1/2* mutational analysis using NGS from unselected OC patients.	In total, 72.0% of the patients had a histological diagnosis of stage III or IV serous ovarian cancer. ctDNA detected pathogenic germline in 19.0% of patients (23/121) and somatic variants in 6.6% of patients (8/121).
Vanderstichele et al. 2017[36]	Ovarian	cfDNA	WGS	2 (44)	Before surgery	Examined plasma DNA samples from patients presenting with an adnexal mass (n=68) prior to surgery.	Two patients with a histological diagnosis of teratoma had calculated z-scores similar to the healthy control group.
Wang et al. 2018[37]	Ovarian	ctDNA	18 (PapSEEK)	2 (1002)	Before treatment	Assessed whether testing for mutations in both the plasma and Pap test fluid would increase sensitivity for ovarian cancers (n=656).	In 83 OC patients, ctDNA was present in 43.0%. When plasma and Pap brush samples were both tested, the sensitivity for OC increased to 63.0%. Two had ovarian endocrine tumors with histopathologic diagnosis of papillary thyroid carcinoma (right)/mature cystic teratoma (left), stage I and endometrioid (60.0%) and sex cord-like (40.0%), stage I. Plasma samples were not taken in either of these samples. Both patients

							had negative Pap and Tao brush results and were negative for somatic and aneuploidy using PapSEEK. The patient with a sex cord like tumor had *KRAS* and *PIK3CA* mutations identified in the primary tumor (supplemental material).
Widschwendter et al. 2017[38]	Ovarian	ctDNA	Three-marker DNA methylation panel	5 (21)	At time of diagnosis, before treatment	Examined tissue and serum samples using a novel DNA methylation assay among females with various benign and malignant conditions.	Pattern frequencies for the three different regions analyzed did not show a significant difference between granulosa cell tumor patients and healthy controls. CA125 levels were significant different in patients with in granulosa cell tumors compared to healthy controls.
Cwikla et al. 2015[39]	GEP-NET	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	63	Before and during treatment	Evaluated NETest score in prediction of response to SSA treatment in patients with known stable or progressive GEP-NETs during an 11-month follow-up.	In a set of patients with known disease status (n=35), a cut-off of at least 80.0% had sensitivities and specificities of >80% and >95%, respectively as an indicator of PD. Of patients enrolled in the prospective group (n=28), using a NETest score of 80.0%, the sensitivity was 100.0% and specificity was 57.0%.
Filosso et al. 2017[40]	BP-NET	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	BP-NET (n=118); other lung NET (13); lung cancers (n=49); COPD (n=18); controls (n=90)	Not specified in diagnostic cohort Before surgery and 30 days post-surgery in surgical cohort (n=28)	(1) Evaluated the NETest score to diagnose BP-NETs compared to CgA levels. (2) Correlated NETest results with clinical status and other lung pathologies. (3) Examined whether the	The NETest was positive in all BP-NETs and the AUROC for differentiating carcinoids from controls was 0.98 (95% CI: 0.96–1.00) compared to the CgA AUROC of 0.68 (95% CI: 0.61–0.76). The sensitivity was 93.0% and specificity was 89.0%. The AUROC for differentiating benign or neoplastic from disease-free patients was 0.99 (95% CI: 0.97–1.00, p<0.001) and 0.91 (95% CI: 0.87–0.96, p<0.001) for differentiating PD from SD.

						completeness of surgical resection correlated with a decrease in blood transcript values detected by NETest.	The NETest was significantly reduced at post-operative Day 30 ($p<0.001$) in NET patients and surgery had no effect on NETest scores in non-NET lung cancers.
Genç et al. 2018[41]	pNET	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	35 (11)	After surgery or during treatment	(1) Examined cancer recurrence using the NETest score after surgery. (2) CgA levels were compared with the NETest score.	Using a NETest score cut-off value of 40% for differentiating recurrence from no recurrence yielded an AUROC of 0.82 ± 0.08 (95% CI: 0.65–0.93) for NETest compared to an AUROC of 0.51 ± 0.09 (95% CI:0.34–0.69) for CgA. Six patients (18.0%) were incorrectly identified by the test using a 40% cut-off. The combination of size, grade, and lymph node metastases and the NETest exhibited the greatest association with disease recurrence (91.0%).
Kidd et al. 2015[42]	GEP-NET	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	Nine matched tumor and blood samples; and 159 prospective clinical blood samples	At surgery	(1) Evaluated whether blood transcript levels directly correlated with tumor tissue levels collected at the same time point (2) Examined if expression differed between SD (n=111) or PD (n=48).	In the matched tumor and blood samples, comparison analysis identified that the blood NET scores significantly correlated with tumor tissue samples. The NET score correctly classified samples as either ‘normal’ or ‘tumor’ with 100.0% accuracy. Identified clusters differentiated SD from PD (AUC=0.81) and integration with blood-algorithm increased the AUC to 0.92 for differentiating PD and SD.
Kidd et al. 2017[43]	BP-NET	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	Surgical cohort: n=7; pilot study: NETs (n=50), other cancers	Surgical cohort: at surgery; pilot study: at regular follow-up	(1) Evaluated the concordance of matched tissue and blood samples	All matched tissue-blood sample in the surgical cohort (n=7) had detectable mRNA of all 51 marker genes irrespective of the histological subtype (typical carcinoids: n=2 or atypical

				(n=65), COPD (n=14), controls (n=65); validation study: carcinoids (n=25), controls (n=25)		(2) Compared the NETest score of tumor and control groups and determined if NETest distinguished between PD from SD.	carcinoids: n=5) or tissue or blood source. There was a significant correlation between tissue and blood ($p<0.001$). The concordance between gene expression was significant between small bowel and BP-NET patient samples. There was poor correlation between BP-NETs and other lung diseases. In the validation group, NETest levels in BP-NET patients were significantly elevated compared to age- and gender-matched controls, and levels were increased in those with PD compared to SD $p<0.001$).
Liu et al. 2018[44] (Abstract)	NETs	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	100	Before and after surgery or treatment	Evaluated the NETest assay for diagnostic accuracy and prediction of clinical disease status among patients with NETs in two cohorts: treated and watch-and-wait during a 6-month follow-up period.	NET type included 68.0% GEP-NET, 20.0% lung, 12.0%, and unknown origin. The diagnostic accuracy was 96% and there was 95% concordance between with image demonstrable disease. In the watch-and-wait cohort, the NETest result (low score) was 100.0% concordant with stable disease, and a high score NETest result resulted in a management change among 83.0% of these patients. In the treatment cohort, 100.0% of the patients with a low NETest remained stable and 100.0% of patients with a high NETest result had intervention and treatment stabilization.
Modlin et al. 2014[45]	NETs	mRNA	51 NET marker genes (NETest®,	125 (79)	Before surgery or treatment	Compared plasma CgA levels with the NETest assay for detection of NETs	Using a cut-off NETest score of ≥2, 98.4% (123/125) of prospectively collected NETs had a positive test. The two patients who did not have a positive

			Wren Laboratories, Branford, CT, US)			in patients with GEP-NETs (n=91, of which 41 were), and CUP (n=18).	score had a 13 mm pNET with cystic features, and the second was pancreatic metastasis from an ovarian NET. The sensitivity of the test for the detection of NETs was 98.4% (95% CI: 94.3–99.8%) compared to a sensitivity of 40.0% (95% CI: 31.2–49.4%) for CgA. No patients treated with PPI (n=29) or the control group (n=50) had a positive NETest of ≥2.
Modlin et al. 2015[46]	NETs	mRNA	51 NET marker genes (NETest®, Wren Laboratories, Branford, CT, US)	179	Before surgery or treatment	Evaluated plasma CgA levels and NETest assay for diagnostic accuracy among patients pNETs and small intestinal NETs.	Using a cut-off NETest score of ≥2, 93.3% (42/45) pNETs had a positive test compared with 34.0% (15/45) with elevated CgA. For pNET cases, the sensitivity was 94.0% and specificity was 96.0%. Using a cut-off NETest score of ≥2, 100.0% (41/41) small intestinal NETs had a positive test compared with 56.1% (23/41) with elevated CgA. For gastrointestinal neoplasia cases, the sensitivity was 100.0% and specificity was 93.0%.
Rizzo et al. 2018[47] (Abstract)	pNET	CTC	CXCR4, (CellSearch®, Menarini Silicon Biosystems, Inc., Huntington Valley, PA, US)	128	Not specified	Investigated the role of CTCs as a marker of bone metastases and evaluate the expression of CXCR4 on CTCs as a potential predictor for skeleton involvement in patients with NETs (n=251).	Of the 128 pNET patients, 38.0% had detectable CTCs (mean CTC count = 11). Bone metastases were found in 23.0% of pNET patients and were significantly associated with CTC presence. There was no association between lung, peritoneal or lymph node metastases and CTC presence. CXCR4-positive CTCs were found in patients with bone metastases compared with those without in a subset of 40

							patients, but the association was not significant.
Sikora et al. 2015[48]	pNET	cfDNA	Alu83 and Alu244 amplicons	23 (43)	Serial sampling	Evaluated the specificity of cfDNA as a biomarker for pancreatic tumors (23 pNET and 50 PDAC patients) versus non-neoplastic disease (20 chronic pancreatitis patients and 23 healthy controls).	Alu83 levels were found to be significantly higher in PDAC patients compared to the other patient groups. Substantial overlap between cfDNA levels in patients with pNET, chronic pancreatitis and healthy controls was noted. No significant association between tumor size or other pathological variables and Alu83 and Alu244 levels were observed in pNET or PDAC patients. Age was a confounding factor for the association between Alu83 and Alu244 levels and tumor status (subjects with the highest Alu244 values included those >65 years).

Wolff et al. 2018[49]	PDAC with develop-ment of NET features	cfDNA and exoDNA	*KRAS* MAFs	1	Serial sampling	Case report detailing the molecular and cellular alterations and responses to treatments during a five-year period of a 50-year old male initially diagnosed with PDAC which subsequently developed neuroendocrine tumor features.	Of 15 liquid biopsy measurements, detected exoDNA and cfDNA *KRAS* MAFs rose from non-detectable to detectable levels when therapy was changed from FOLFIRINOX to Gemcitabine/Abraxane and thereafter. Levels sharply spiked after the patient received adoptive T-cell therapy, and regressed once the patient resumed cytotoxic chemotherapy “cocktail”.
Xin et al. 2016[50] (Abstract)	pNET	CTC	EpCAM (CellSearch®, Menarini Silicon Biosystems, Inc., Huntington Valley, PA, US)	10	After tumor resection	Evaluate EpCAM-positive CTCs in NENs.	There were 10 patients with pNETs (30.0% grade I; 70.0% grade II) and four had liver metastases. The median size of the primary tumor was 3 cm and the median Ki-67 index was 5.0. CTCs were detected in 54.5% of patients (mean CTC count = 2).
Gupta et al. 2018[51] (Abstract)	Testicular	CTC	(TargetSelector™ Biocept Inc., San Diego, CA, US)	1	Serial sampling	Evaluated the prognostic and predictive significance of CTCs in a single patient with refractory GCT cancer during treatment with brentuximab, vedotin and bevacizumab.	Two CTCs were detected at baseline; during treatment detection of one CTC corresponded to tumor marker response and CT scan showing stable disease; and after treatment four CTCs were detected, corresponding with disease progression in tumor markers and CT scan.

Lu et al. 2016[52] (Abstract only, full article not in English)	Testicular	CTC	Not specified	1	Serial sampling	Analyzed the clinicopathological data in a 47-year old patient with TMLCT and detected the CTCs in venous blood, and reviewed the related literature.	Immunohistochemistry showed the tumor cells to be positive for α-inhibin, Ki-67, CD30, vimentin, EMA, and PLAP, but negative for CK, CK7, S100, CD10, SMA, desmin, AFP, hCG, CEA, CK19, CD117, OCT4, LCA, CD20, Pax-5, CD3, and CD43. Two CTCs were detected in the peripheral venous blood.
Majewski et al. 2018[53]	Testicular	microarray analysis	--	5	Before and 5–7 days after surgery	Determined which candidate gene mRNA decreased >5 fold after surgery.	In total, 20 genes in the seminoma patients had a significant decrease in copy number after surgery.
Nastaly et al. 2014[54]	Testicular	CTC	Ficoll density gradient centrifugation and staining of keratins 8, 18, 19, EpCAM, SALL4 and OCT3/4 (CellSearch®, Menarini Silicon Biosystems, Inc., Huntington Valley, PA, US)	143	At time of initial therapy	(1) Determined the incidence of CTCs in patients with GCTs using two assays. (2) Correlated the findings to clinical parameters.	In total, CTCs were detected in 17.5% (25/143) GCT patients. In three patients (2.5%; 3/122), CTCs were found in parallel with both detection methods. About 10% (14/143) of patients were positive for CTCs using keratins 8, 18, 19, EpCAM, SALL4 and OCT3/4 markers. Using CellSearch, 11.5% (14/122) of the patients were classified as CTC positive. No controls were found positive in either assay. The presence of CTCs in peripheral blood was significantly correlated with tumor histology, stage of disease, and tumor marker levels in blood serum.

Abbreviations for adrenal neoplasia articles: ACA = adrenocortical adenoma; ACC = adrenocortical carcinoma; cfDNA = cell-free DNA; CPA = cortisol-producing adrenocortical adenoma; CTC = circulating tumor cells; CP-ACC = cortisol-producing adrenocortical carcinoma; ctDNA = circulating tumor deoxyribonucleic acid; ddPCR = droplet digital polymerase chain reaction; EV = extracellular vesicle; miR = microRNA; NGS = next generation sequencing; NFA = non-functioning adrenocortical adenoma.

Abbreviations for ovarian neoplasia articles: AGCTs = adult granulosa cell tumors; CA125 = cancer antigen 125; CD45=cluster of differentiation 45; cfDNA = cell-free DNA; CK8/18/19=cytokeratin 8,18,19; CTC = circulating tumor cells; ctDNA = circulating tumor DNA; *EMP2*=epithelial membrane protein 2; EpCAM = epithelial cell adhesion

molecule; *FN1* = fibronectin 1; LAMB1 = laminin beta 1; LDFWAR = low-dose fractionated whole abdominal radiation; *MAL2* = mal T-cell differentiation protein 2 (gene/pseudogene);NAC = neoadjuvant chemotherapy; NGS = next-generation sequencing; NIPT = non-invasive prenatal testing; Pap = Papanicolaou; PFS = progression-free survival; PPIC=peptidyl-prolyl cis-trans isomerase C; OC = ovarian cancer; RT–qPCR = quantitative reverse transcription polymerase chain reaction; TEC-Seq = targeted error correction sequencing; TUSC3 = tumor suppressor candidate 3; WGS = whole-genome sequencing.

Abbreviations for neuroendocrine neoplasia articles: AUROC = area under the receiver operator characteristic; BP-NETs = bronchopulmonary neuroendocrine tumors; CUP = carcinoid of unknown primary; cfDNA cell free DNA; CgA = Chromogranin A; COPD = chronic obstructive pulmonary disease; CTC = circulating tumor cells; CXCR4 = X-C chemokine receptor 4; exoDNA = exosomes-derived DNA; GEP-NET = gastroenteropancreatic neuroendocrine tumors; NENs = neuroendocrine neoplasms; MAFs = mutation allele frequencies; mRNA = messenger ribonucleic acid; PD = progressive disease; PDAC = pancreatic ductal adenocarcinoma; pNET = pancreatic neuroendocrine tumors; PPI = proton pump inhibitor; SD = stable disease; SSA = somatostatin analog.

Abbreviations for testicular neoplasia articles: Abbreviations: AFP = alpha-fetoprotein; CD = cluster of differentiation; CEA = carcinoembryonic antigen; CK = cytokeratin; CT = computerized tomography; CTC = circulating tumor cells; EMA = epithelial membrane antigen; EpCAM = epithelial cell adhesion molecule; GCTs = germ cell tumors; hCG = human chorionic gonadotropin; LCA = leukocyte common antigen; Pax-5 = paired box protein; miR = microRNA; mRNA = messenger ribonucleic acid; OCT4/ OCT3/4 = octamer-binding transcription factor 4; PALP = placental alkaline phosphatase; SALL4 = sal-like protein 4; TMLCT = testicular malignant Leydig cell tumor; TVB = testicular vein blood.