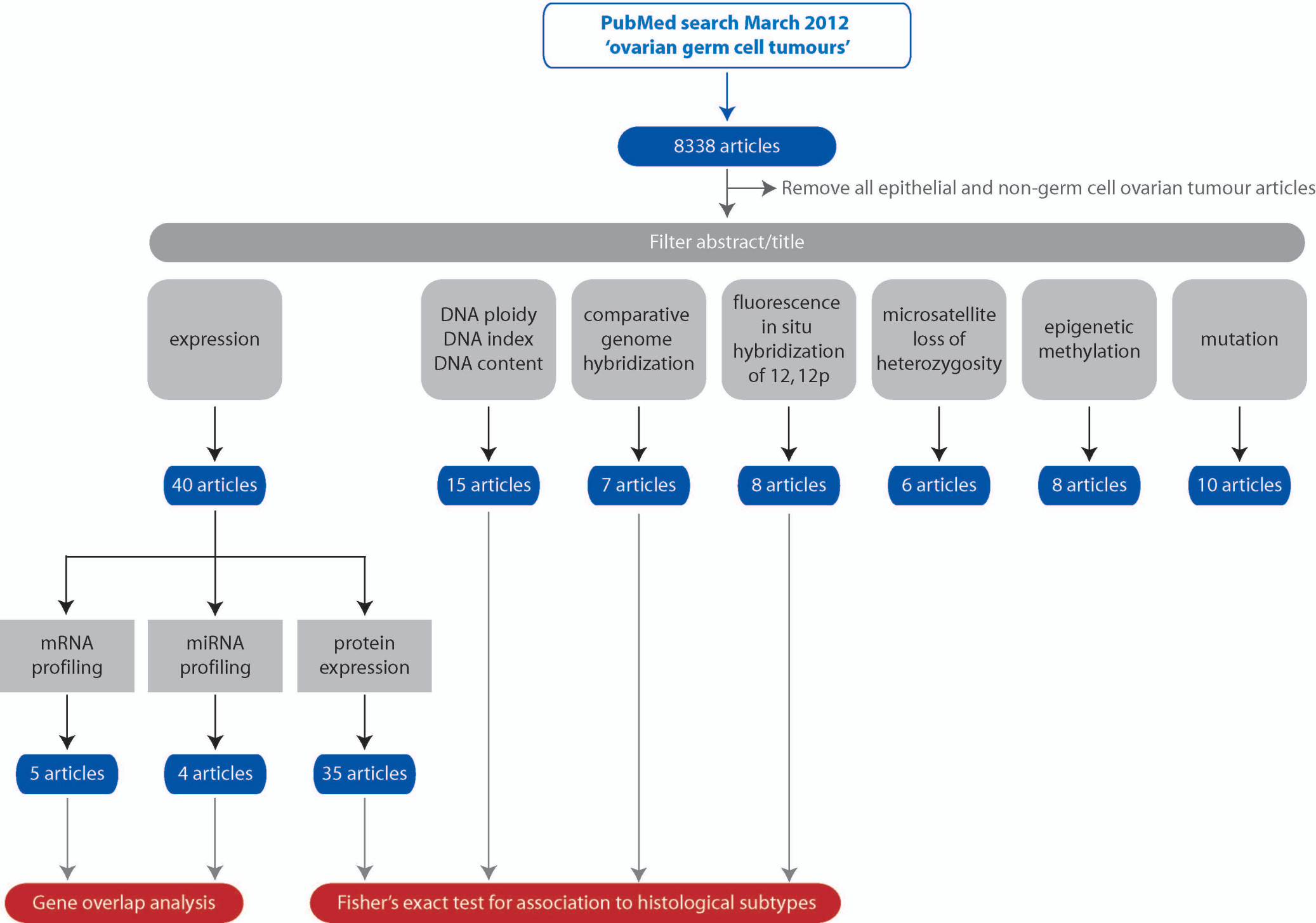
Supplementary Fig. 1 Kraggerud - Hoei Hansen



Supplemental figures

Supplemental Fig. 1. Flowchart of the article searches and filtering applied for this review.

Supplemental Tables

Supplemental Table 1. Ploidy status among mOGCT histological subtypes as determined by image cytometry or flow cytometry. Abbreviations: D, diploid, DG, dysgerminoma; CC, choriocarcinoma EC, embryonal carcinoma; IT, immature teratoma; NonD; non-diploid; YST, yolk sac tumour. If reported, further number of tumours and ploidy classification is given by T, tetraploid, A, aneuploid, and P, polyploid. *, 4/4 metastasing teratoma, no further specification; IT¤, IT with YST components detected on second review.

n patients (*n* samples)	DG		YST		IT		EC		Mixed or components of mixed mOGCT		Ref
	D	NonD	D	NonD	D	NonD	D	NonD	D	NonD	
44(45)	0/16	16/16 (9T, 7A)	0/9	9/9 (5T, 3A, 1P)	13/13	0/13			2/7 (2 IT)	5/7 (4A, 1P) (3DG, 1CC, 1YST)	(135)
1(2)	0/2	2/2 (1T, 1A)									(132)
22 (26)	1/6	5/6 (3T, 2A)	1/4	3/4 (2T, 1A)	5/5	0/5			4/11 (3IT, 1IT¤)	7/11 (1T, 6A) (1mixed, 2IT¤, 3YST, 1EC)	(139)
9 (11)			0/3	3/3 (2T, 1A)	2/4	2/4 (2A)			1/4 (1DG)	3/4 (2A, 1T) (2YST, 1IT)	(136)
4 (5)	0/2	2/2							1/3 (1MT)	2/3 (1CC/YCT, 1YST)	(148)
4 (4)	0/2	2/2 (2A)							0/2	2/2 (2A) (1DG/YST, 1DG/YST/EC)	(137)
22 (24)	5/24	19/24 (16T, 3A)									(138)
5 (5)			1/3	2/3 (2A)					1/2 (mixed/YST)	1/2 (1A) (mixed/YST)	(141)
2(2)			0/2	2/2 (2A)							(146)
20 (22)			1/14	13/14					2/8 (2DG)	6/8 (2YST/MT, 1YST/EC, 1YST/CC, 2 YST/DG)	(142)
3 (3)	0/1	1/1	2/2	0/2	*						(147)
25 (25)	0/25	25/25 (14A, 11P)									(140)
2 (2)	0/1	1/1			1/1	0/1					(145)
1 (1)							0/1	1/1			(143)
4(4)	1/2	1/2 (1A)			2/2	0/2					(144)
168 (181)	7/81	74/81	5/37	32/37	23/25	2/25	0/1	1/1	11/37	26/37	**Total**
	9%	**91%**	**14%**	**86%**	**92%**	**8%**	**0%**	**100%**	**30%**	**70%**	**(%)**

Supplemental Table 2. DNA copy number alterations in 81 primary mOGCT detected by chromosomal/metaphase or array CGH, sorted by histology and retaining original case number as in references (131;132;149-152). Abbreviations: Bil. DG, bilateral DG; DG, dysgerminoma; GB, gonadoblastoma; IT, immature teratoma; MT, mature teratoma; TER, teratoma (unspecified); YST, yolk sac tumour. For ref. 152, specific regions for gains and losses were not reported explicitly; as such these were extracted from the graphical illustrations to the resolution of chromosome arms.

Tumour type	Case no.	Gains	Losses	Age (yrs)	Ref.
DG	04T	None	X	18	(131)
DG	09T	1p31-ter, 1q22-24, 3p14-21, 3q21-23, 6, 7, 12pter-q12, 12q22-ter, 15q, 17, 19, 20, 22q	4, 5, 9p21-ter, 13q21-ter	59	(131)
DG	14T	1p33-ter, 6p21.1-21.3, 9q33-ter, 11q12-13, 12q24.1-ter, 14q31-ter, 16p12-ter, 16q23-ter, 17, 19, 20q, 21q22, 22q	3q25-26.2, 4p13-q32, 5q14-22, 6q12-23, 9p21-22, 13q21-31, Xq13-23	14	(131)
DG	15T	1q21-23, 7, 8q23-ter, 12pter-q14, 12q23-ter, 17, 21q, 22q12-ter	13q21-22	17	(131)
DG	16T	12pter-q13, 12q23-ter, 16p12-ter, 21q21-ter	11q21-ter	20	(131)
DG	19T	8, 12p	None	32	(131)
DG	27T	1p33-ter, 6p21.3, 9q33-ter, 17pter-q21, 17q24-ter, 20q12-ter, 21q22	None	36	(131)
DG	35T	1q21-24, 1q32-ter, 7, 8, 12q23-ter, 15q, 17, 19, 21q, 22q13	13q14-ter	18	(131)
DG	40T	3p21, 3q24-26.3, 6p11.2-21.3, 7, 8, 12, 15q, 19, 20, 21q22	4p, 5p, 13q13-ter, X	21	(131)
DG	48T	1p33-ter, 8, 12pter-q13, 12q23-ter, 15q, 17, 19, 21q, 22q	None	41	(131)
DG	49T	4q12-13, 7, 8, 12, 15q, 19, 20q, 22q	4q23-ter, 11p, 11q14-ter, 13q21-22, Xp21-ter, Xq21-ter	28	(131)
DG	52T	2q12-13, 4p15.1-15.3, 8p, 12p, 12q23-ter, 19q, 20, 21q22, 22q13	13q21-ter	32	(131)
DG	1	2q,12q	None	12	(152)
DG	2	1q, 10q, 12p, 12q, 21	1p, 11q, 13	13	(152)
DG	3	2p, 2q, 6p, 6q, 7p, 8p, 8q, 11p, 12p, 12q, 15, 20p, 20q	1p, 11q, 17p, 19p, 19q	14	(152)
DG	4	1q, 2q, 12q, 18q, 21	4q, 13	10	(152)
DG	5	1q, 7q, 12p, 17q, 19p, 19q	None	6	(152)
DG	6	1q, 8q, 12p, 12q, 19p	3p, 13	12	(152)
DG	7	2q, 7q, 12p, 12q	5p, 9p, 11q, 14	12	(152)
DG	8	12p, 19p,19q, 21	13	13	(152)
DG	1	12q	None	18	(149)
DG	2	3, 12p	13q21	10	(149)
DG	3	8, 12p, 15, 21	None	16	(149)
DG	4	1q, 8, 21	None	22	(149)
DG	5	1q, 7, 8, 12, 15, 19, 20, 21	5, 13	28	(149)
DG	6	1q, 4q11, 7, 8, 12, 15, 21	1p, 3, 13	14	(149)
DG	7	1q, 12	4, 7p	14	(149)
DG	8	20q	None	9	(149)
DG	9	8, 12p, Y	4	17	(149)
DG	10a	6p, 12p, 21	None	12	(149)
DG	10b	7, 12p, 21	None	12	(149)

DG	29	1q, 7, 8, 10, 12p13-pter, 12p11, 19, 21	18q	11	(151)
DG	19	12p	1p35-pter, 4q, 13, 21	12	(150)
DG (left ovary)	Bil. DG	1q22-qter, 8, 12, 15q15-qter, 19, 21q22	X	16	(132)
DG (right ovary)	Bil. DG	2q14-qter, 19, 22q	X	16	(132)
DG+CC	17	None	None	10	(150)
DG+TER	11	19p, 21	13	12	(152)
EC+YST+TER	26	7, 8, 12p, 19	18q	7	(151)
GB	Bil. DG	1q21-qter, 21q21-qter	13q32-qter, X	16	(132)
IT	06T	22q13	None	20	(131)
IT	12T	None	None	16	(131)
IT	18T	1p35-ter, 16p, 19	13q21-31	37	(131)
IT	22T	None	None	20	(131)
IT	34T	1p35-ter, 9q34, 22q12-ter	None	34	(131)
IT from mixed IT/YST	36T	11q12-13, 14q21-24	None	23	(131)
IT	44T	None	None	11	(131)
IT	46T	None	None	15	(131)
IT	51T	16p12-ter, 17q24-ter, 19	None	25	(131)
IT	20	None	None	21	(149)
IT	21	None	None	2	(149)
IT	22	None	None	4	(149)
IT	23	None	None	11	(149)
IT	24	14	None	21	(149)
IT	25	None	None	25	(149)
IT	30	7, 8, 12p, 21	None	12	(151)
IT	3	None	None	1	(150)
mixed mOGCT	17	8, 12p	None	4	(149)
mixed mOGCT	18	12p, 21	None	8	(149)
mixed mOGCT	19	7, 8, 12p	4, 10, 18	15	(149)
MT	27	None	None	8	(151)
MT	28	12p	None	11	(151)
YST	33T	1p32-36.1, 1p13-q22, 6p21.2-21.3, 8, 12pter-q13, 12q24.1-ter, 15q13-ter, 17, Xp11.2-q13	10p14-ter, 13q21-32, 18q21-22	11	(131)
YST	43T	1q41-ter, 11q14-ter, 12p, 20q	1p34.1-ter, 18q21-ter	12	(131)
YST from mixed IT/YST	45T	3, 11, Xp	None	70	(131)
YST	55T	1q21-23, 1q32-42, 3p21, 12p	None	22	(131)
YST	20	3p, 3q, 8q, 11p	1p, 4q, 5q	14	(152)
YST	21	3p, 3q, 4q, 5q, 8q, 12p, 12q, 20p, 20q, 21	1p, 6q, 15	13	(152)
YST	22	1q, 14	1p, 4p, 4q, 16p, 16q	12	(152)
YST	23	3q, 5q, 6p, 7p, 9p	1p, 15, 16p,19p	12	(152)
YST	24	1q, 2q, 3p, 3q, 6q, 11p,11q, 21	16p, 19p,19q, 22	9	(152)
YST	25	1q, 10p, 10q, 12p, 20p, 20q	1p, 6q, 8p	14	(152)
YST	26	1q, 11q, 19p	6q	13	(152)
YST	33	10q, 14, 20q	1p, 4q, 20p	0	(152)

YST	11	1q, 12p, 20	1p, 5, 13, 18q	12	(149)
YST	13	None	None	20	(149)
YST	16	None	None	17	(149)
YST+DG+IT	16	None	None	10	(150)
YST+IT	12	7p, 8, 12p, 21	1p, 9, 11, 13, 15, 20, 22	24	(149)
YST+IT	14	12p, 21	None	24	(149)
YST+IT	15	1q, 10, 12	None	17	(149)
YST+IT	18	3	None	12	(150)

Supplemental Table 3. Overview of gains of whole or parts of chromosome arm 12p among mOGCT histological subtypes as evaluated by FISH, CGH and aCGH. Abbreviations: DG, dysgerminoma; IT, immature teratoma; MT, mature teratoma; YST, yolk sac tumour. *, only the EC components were analyzed.¤ gain of chromosome 12 detected by G-banding.

	DG	YST	IT	MT	Mixed or component of mixed mOGCT	Technique	Ref
	1/1		1/1	1/2	1/1	aCGH	(151)
	1/1					aCGH	(134)
	7/10	1/3	0/6		6/6	CGH	(149)
	8/12	3/3	0/8		0/2	CGH	(131)
	1/2					CGH	(132)
	1/1		0/1		0/3	CGH	(150)
	6/8	2/8			0/1	CGH	(152)
	2/2				2/2	FISH	(137)
	1/1					FISH	(157)
		1/2				FISH	(146)
	1/2	0/1¤	0/3	0/4	0/1	FISH	(158)
	17/21					FISH	(154)
			0/3	0/5	5/6	FISH	(155)
	18/22					FISH	(156)
					5/6*	FISH	(153)
Total	64/83	7/17	1/22	1/11	19/28		
%	77%	41%	5%	9%	68%		

Supplemental Table 4. An overview of genome-wide gene expression profiling studies that include mOGCT. The number of samples profiled, the type of analyses performed and the number of significant differentially expressed genes identified are listed. Abbreviations: *cf.,* compared to; DG, dysgerminoma; ex.gd., extragonadal; Germ, germinoma; IT, immature teratoma; MT, mature teratoma; ova, ovarian; Sem, seminoma; SS, spermatocytic seminoma; tes., testicular; YST, yolk sac tumour. *, includes one sample from a female patient with extragonadal germinoma. ¤, includes both gonadal and extragonadal samples of both histological subtypes, both male and female.

Study	Samples	Genes with higher expression in	# mRNAs in gene list	# miRNAs in gene list	Ref
Looijenga *et al.*, 2006	3 DG, 4 Sem, 5 SS	DG/Sem *cf.* SS	80		(165)
Fritsch *et al.*, 2006	4 DG, 4 ova. YST	DG *cf.* YST	22		(164)
		YST *cf.* DG	11		
Palmer *et al.*, 2008	8 DG, 1 Sem, 8 ova. YST, 7 tes. YST	DG/Sem *cf.* YST	11		(167)
		YST *cf.* DG/Sem	11		
Palmer *et al.*, 2010	9 female Germ (7 ova. DG) 4 male Germ (2 Sem) 8 female YST (5 ova. YST) 4 male YST (3 tes. YST) 3 male EC (1 ex.gd.)	DG/Sem/YST/EC *cf.* IT/MT/normal gonads/foetal tissue	44	10	(168)
	2 female, 1 male IT (ex.gd.) 3 female MT (1 ex.gd.) 2 normal testis, 2 normal ovaries, 2 foetal yolk sacs, 2 foetal ovaries	IT/MT/normal gonads/foetal tissue *cf.* DG/Sem/YST/EC	126		
Gillis *et al*,. 2007	10 DG, 15 Sem, 1 ova. YST, 7 tes. YST, 1 ova EC, 13 tes. EC, 10 teratomas, 4 SS, 3 normal testis, 5 EC cell lines	SEM *cf.* EC *cf.* teratoma		11	(169)
Murray *et al.*, 2010¤	9 female Germ (7 ova. DG), 4 male Germ (2 Sem)	DG/Sem/Germ *cf.* YST		37	(170)
	8 female YST (5 ova. YST), 4 male YST (3 tes. YST)	YST *cf.* DG/Sem/Germ		29	
Fustino *et al.*, 2011	4 DG*, 2 ova. YST, 5 tes. YST	DG *cf.* YST	5	14	(166)
		YST *cf.* DG	29	20	

Supplemental Table 5. Overview of mRNA/miRNA studies of mOGCT.

mRNA studies

Ref	Platform name	# probes/genes
(164)	Clontech Atlas Human Cancer array	588 cancer genes
(165)	Affymetrix HG-U133A plus 2.0	54k
(166)	RT-PCR	84 TGF-β/BMP pathway genes
(167)	Affymetrix HG-U133A	22k
(168)	Affymetrix HG-U133A	22k

miRNA studies

Ref	Platform name	# miRNAs profiled
(166)	µParaflo	782
(168)	miRCURY LNA array v9.2	615
(169)	TaqMan MicroRNA Assays Human Panel	156
(170)	miRCURY LNA array v9.2	615

Supplemental Table 6. Case studies reporting mRNA/protein expression and/or gene mutations among mOGCT patients. Abbreviations: DG, dysgerminoma; GB, gonadoblastoma; YST, yolk sac tumour; *g*, mRNA study; p, IHC study.

Gene/protein expression in OGCT, single patient reports

Gene/protein	Associated syndrome	Histology	mRNA	IHC	Ref
TRC8	translocation t(8;22)	DG	*g*	p	(134)
KIT	D816V *KIT* mutation	DG		p	(270)
POU5F1, TSPY	Swyer syndrome	GB, DG, YST		p	(341)
AFP, TP53	endometrioid	YST		p	
	adenocarcinoma				(342)
	-	YST	*g*		(343)
HOX8					
ALPP		DG		p	(344)

[a]Northern blotting

Gene mutations in OGCT, single patient reports

Gene	Mutation origin	Tumour alteration	Histology	Patient syndrome	Ref
SOX9	germline	Nonsense mutation	DG	campomelic dysplasia, 46,XY sex-reversal	(345)
PTEN	germline	Nonsense mutation, tumour LOH	DG	Cowden syndrome	(346)
BRCA2	germline	No tumour LOH	mixed mOGCT	-	(347)
FGFR2	germline	Gain of function mutation	DG	Apert syndrome	(348)
KIT	germline	Activating mutation	IT	Systemic mastocytosis	(349)
KIT	somatic	Activating mutation	DG	-	(270)
WT1	germline	Disturbed splicing	GB	Frasier syndrome	(350)
BRCA1	germline	-	DG	-	(351)