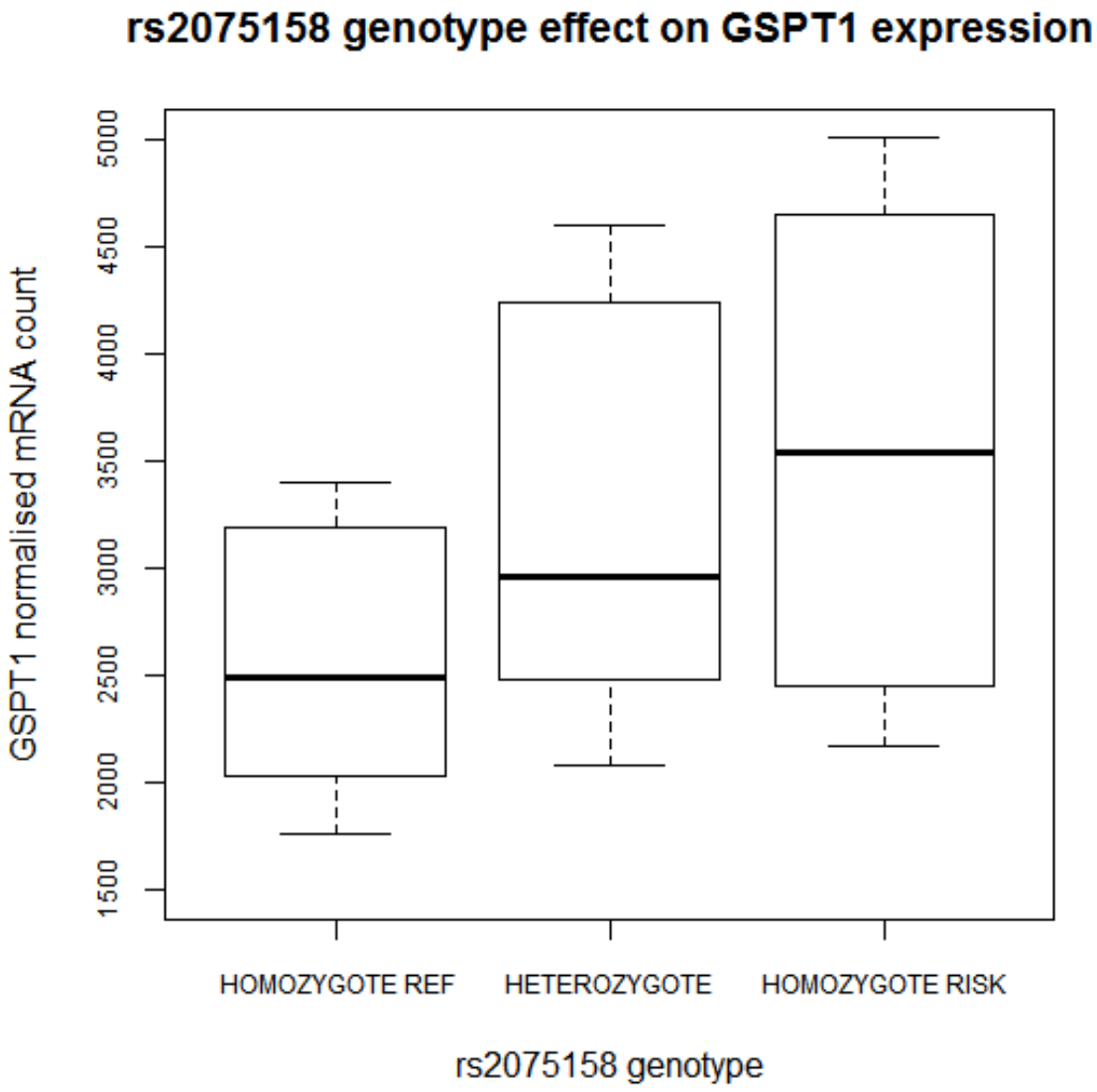
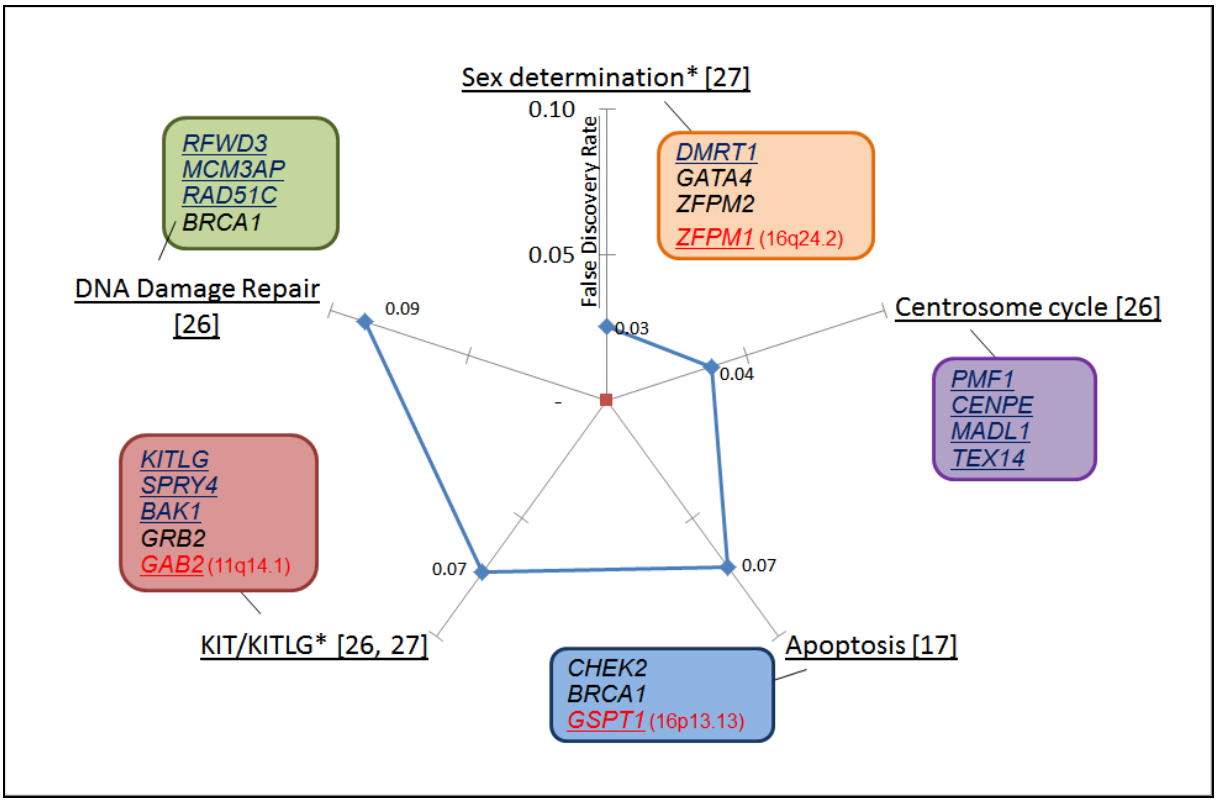
Supplementary Figures

Supplementary figure 1 – Boxplot of eQTL at 16p13.13. The dark black line represents the median expression value for each genotype and the box represents the upper and lower quartiles of data above/below the median. The whiskers extend out to 0.2 times the interquartile range.



Supplementary figure 2 - Significantly enriched TGCT Pathways, implicated in this paper and at least one other study (references in brackets). Gene set names are in underlined black text, ordered with the most significant pathway first (Sex Determination) and then subsequent pathways presented in clockwise order with decreasing significance. The values on the blue line represent the false discovery rate for each pathway as calculated by the iGSEA4GWAS algorithm. In the text boxes are selected genes related to each pathway, colour-coded as follows: dark blue underlined text = genes in LD with risk SNPs identified in previous TGCT GWAS, red underlined text = genes in LD with the four new loci identified in this study, black plain text = genes not yet in LD with any TGCT risk SNPs but highlighted as significant by the iGSEA4GWAS algorithm. Pathways marked with an asterisk are custom gene sets, with "Sex determination" pathway defined as per [1] and the "KIT/KITLG" pathway defined based on known interacting partners of KIT/KITLG using the STRING database[2].



Supplementary Tables

Supplementary table 1 – *P*-values from eQTL tests performed. *P*-value threshold 0.0028 considered significant, corrected for 18 multiple tests.

	11q14.1		3q23	16q24.2		16p13.13	
	rs2450140	**rs11237477**	**rs11705932**	**rs3859027**	**rs12597021**	**rs2018199**	**rs2075158**
GAB2	0.909	0.7395					
USP35	0.1896	0.04572					
TFDP2			0.3403				
ATP1B3			0.7273				
ZFPM1				0.2993	0.1304		
BCAR4						0.2793	0.1407
GSPT1						0.00059	0.00051
TNFRSF17						0.5626	0.4104
RSL1D1						0.05329	0.0431

Supplementary table 2 - TGCT predisposition loci identified to date, presented in chronological order with functional grouping based on previous review paper[3]. For loci with multiple reported SNPs the marker listed is taken from first study in the reference column.

SNP	Locus	Candidate Gene(s)	Functional Grouping	Reference(s)
rs995030	12q21	*KITLG*	1) *KIT/KITLG* signalling	[4,5]
rs210138	6p21	*BAK1*	1) *KIT/KITLG* signalling 2) Apoptosis	[4,5]
rs4624820	5q31	*SPRY4*	1) *KIT/KITLG* signalling	[4]
rs4635969	5p15	*TERT*	3) Telomerase function	[6]
		CLPTM1L	2) Apoptosis	
rs755383	9p24	*DMRT1*	7) Sex determination	[6]
rs2900333	12p13	*ATF7IP*	3) Telomerase function	[6,7]
rs8046148	16q12.1	*HEATR3*	unknown/other	[8]
rs2839243	21q22.3	*non-coding*	unknown/other	[8]
rs3805663	5q31.1	*CATSPER3*	unknown/other	[8]
		PITX1	3) Telomerase function	
rs10510452	3p24.3	*DAZL*	4) Male germ cell development	[8]
rs2720460	4q24	*CENPE*	5) Centrosome cycle	[8]

rs7010162	8q13.3	*PRDM14*	4) Male germ cell development	8
rs9905704	17q22	*RAD51C*	6) DNA Repair	9
		PPM1E	unknown/other	
		TEX14	5) Centrosome cycle	
rs3790672	1q24.1	non-coding	unknown/other	8,10
rs2072499	1q22	*PMF1*	5) Centrosome cycle	8,9
rs4888262[c]	16q22.3	*RFWD3*	6) DNA Repair	9
rs12699477	7p22.3	*MAD1L1*	5) Centrosome cycle	9
rs17021463	4q22.2	*HPGDS*	4) Male germ cell development	9
rs1510272	3q25	*SSR3*	unknown/other	11
		TIPARP	unknown/other	
rs7501939	17q12	*HNF1B*	unknown/other	12
rs2195987	19p12	non-coding	unknown/other	12
rs11705932	3q24	*TFDP2*	unknown/other	new
		ATP1B3	unknown/other	
rs7107174	11q14	*GAB2*	1) *KIT/KITLG* signalling	new
		USP35	unknown/other	
rs4561483	16p13	*BCAR4*	unknown/other	new
		RSL1D1	unknown/other	
		GSPT1	2) Apoptosis	
		TNFRSF17	unknown/other	
rs55637647	16q24	*ZFPM1*	7) Sex determination	new

Supplementary table 3 – Pathway associations with FDR < 0.1

Pathway/Gene set name	***P*-value**	**False Discovery Rate**
CELLULAR COMPONENT DISASSEMBLY	< 0.001	0.0210
Sex determination gene set (Custom Set)	< 0.001	0.0252
CENTROSOME CYCLE	< 0.001	0.0375
INDUCTION OF APOPTOSIS BY INTRACELLULAR SIGNALS	< 0.001	0.0706
KIT/KITLG Signalling (Custom Set)	< 0.001	0.0729
PROTEIN COMPLEX DISASSEMBLY	< 0.001	0.0738
MACROMOLECULAR COMPLEX DISASSEMBLY	< 0.001	0.0738
CONDENSED CHROMOSOME	0.001	0.0784
SINGLE STRANDED RNA BINDING	< 0.001	0.0796
TRANSCRIPTION FROM RNA POLYMERASE III PROMOTER	0.001	

		0.0798
CHROMOSOME	0.003	0.0806
TRANSITION METAL ION BINDING	0.004	0.0806
INTRA GOLGI VESICLE MEDIATED TRANSPORT	0.001	0.0806
ZINC ION BINDING	0.001	0.0808
CELLULAR PROTEIN COMPLEX DISASSEMBLY	< 0.001	0.0812
NKCELLSPATHWAY	< 0.001	0.0823
DNA DAMAGE RESPONSE SIGNAL TRANSDUCTION BY P53 CLASS MEDIATOR	< 0.001	0.0826
HSA04120 UBIQUITIN MEDIATED PROTEOLYSIS	< 0.001	0.0826
IL17PATHWAY	0.001	0.0837
RESPONSE TO ABIOTIC STIMULUS	0.001	0.0840
RESPONSE TO IONIZING RADIATION	0.001	0.0855
SMALL PROTEIN CONJUGATING ENZYME ACTIVITY	< 0.001	0.0871
DNA DAMAGE RESPONSE SIGNAL TRANSDUCTION RESULTING IN INDUCTION OF APOPTOSIS	< 0.001	0.0873
HYPERTROPHY MODEL	0.001	0.0878
MANNOSYLTRANSFERASE ACTIVITY	< 0.001	0.0891
CELLULAR PROTEIN METABOLIC PROCESS	< 0.001	0.0901
CELLULAR MACROMOLECULE METABOLIC PROCESS	< 0.001	0.0921
G2PATHWAY	0.002	0.0928
DNA DAMAGE RESPONSE SIGNAL TRANSDUCTION	0.002	0.0935
IGF1PATHWAY	0.001	0.0991
RESPONSE TO RADIATION	< 0.001	0.0997

Supplementary Note

Supplementary note 1: The UK Testicular Cancer Collaboration (UKTCC)

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Supplementary References

1. Koster, R. *et al.* Pathway-based analysis of GWAs data identifies association of sex determination genes with susceptibility to testicular germ cell tumors. *Hum Mol Genet* (2014).
2. Szklarczyk, D. *et al.* STRING v10: protein-protein interaction networks, integrated over the tree of life. *Nucleic Acids Res* **43**, D447-52 (2015).
3. Litchfield, K., Shipley, J. & Turnbull, C. Common variants identified in genome-wide association studies of testicular germ cell tumour: an update, biological insights and clinical application. *Andrology* **3**, 34-46 (2015).
4. Rapley, E.A. *et al.* A genome-wide association study of testicular germ cell tumor. *Nat Genet* **41**, 807-10 (2009).
5. Kanetsky, P.A. *et al.* Common variation in KITLG and at 5q31.3 predisposes to testicular germ cell cancer. *Nat Genet* **41**, 811-5 (2009).
6. Turnbull, C. *et al.* Variants near DMRT1, TERT and ATF7IP are associated with testicular germ cell cancer. *Nat Genet* **42**, 604-7 (2010).
7. Kanetsky, P.A. *et al.* A second independent locus within DMRT1 is associated with testicular germ cell tumor susceptibility. *Hum Mol Genet* **20**, 3109-17 (2011).
8. Ruark, E. *et al.* Identification of nine new susceptibility loci for testicular cancer, including variants near DAZL and PRDM14. *Nat Genet* **45**, 686-9 (2013).
9. Chung, C.C. *et al.* Meta-analysis identifies four new loci associated with testicular germ cell tumor. *Nat Genet* **45**, 680-5 (2013).
10. Schumacher, F.R. *et al.* Testicular germ cell tumor susceptibility associated with the UCK2 locus on chromosome 1q23. *Hum Mol Genet* **22**, 2748-53 (2013).
11. Litchfield, K. *et al.* Multi-stage genome wide association study identifies new susceptibility locus for testicular germ cell tumour on chromosome 3q25. *Hum Mol Genet* (2014).
12. Kristiansen, W. Two new loci and gene sets related to sex determination and cancer progression are associated with susceptibility to testicular germ cell tumour. *Human Molecular Genetics (In press)* (2015).