Molecular comparison of pure ovarian fibroma with serous benign ovarian tumours

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Abstract

Objective: Ovarian fibromas and adenofibromas are rare ovarian tumours. They are benign tumours composed of spindle-like stromal cells (pure fibroma) or a mixture of fibroblast and epithelial components (adenofibroma). We have previously shown that 40% of benign serous ovarian tumours are likely primary fibromas due to the neoplastic alterations being restricted to the stromal compartment of these tumours. We further explore this finding by comparing benign serous tumours to pure fibromas.

Results: Performing copy number aberration (CNA) analysis on the stromal component of 45 benign serous tumours and 8 pure fibromas, we have again shown that trisomy of chromosome 12 is the most common aberration in ovarian fibromas. CNAs were more frequent in the pure fibromas than the benign serous tumours (88% vs 33%), however pure fibromas more frequently harboured more than one CNA event compared with benign serous tumours. As these extra CNA events observed in the pure fibromas were unique to this subset our data indicates a unique tumour evolution. Gene expression analysis on the two cohorts was unable to show gene expression changes that differed based on tumour subtype. Exome analysis did not reveal any recurrently mutated genes.

Keywords: Ovarian fibroma, Adenofibroma, Cystadenomas, Cystadenofibroma, Copy number aberrations, Gene expression, Exome sequencing, Microarrays

Introduction

Ovarian fibromas and adenofibromas form part of the sex-cord stromal family of tumours and are relatively uncommon, accounting for approximately 8% of all diagnosed ovarian tumours [1]. These tumours are benign entities composed in significant part of fibroblasts (pure fibroma), or as compound tumours composed of a mix of fibroblast and epithelial (adenofibroma) or sex-cord (granulosa-stromal tumours) components. Tumours with a cystic epithelial component are termed cystadenomas or cystadenofibromas.

Due to their relative rarity and benign nature these tumours have not been well molecularly characterised, with the majority of studies focussing on immunohistochemistry and cytogenetics. Ovarian fibromas differ from fibromas arising in other organs in that they frequently express hormone receptors (e.g. ER-β, PR, AR) and are typically negative for the characteristic markers of other cells derived from a fibroblast/myofibroblastic origin (e.g. SMA, CD34, CD117, S-100) [1, 2].

Genomic aberrations involving trisomy and tetrasomy of chromosome 12 appear to be particularly prevalent in tumours arising in the female genitourinary tract, including uterine leiomyomas [3, 4], thecomas [5–7], fibromas [7–10] and granulosa cell tumours [11, 12]. The underlying biological driver for this recurrent event has yet to be established. Other genomic aberrations that arise less frequently may be more cell type-specific. Imbalances...
involving chromosomes 4 and 9 are also common in the fibroma-thecoma subgroup, with chromosome 9 aberrations potentially being associated with cellular fibromas [13].

We previously reported that around 40% of benign serous cystadenomas and cystadenofibromas show copy number aberrations (CNA) exclusively in the stroma [14] and are thus likely misdiagnosed primary fibromas with epithelial inclusion. To investigate this further we undertook molecular characterisation of these epithelial-stromal tumours in comparison to pure fibromas.

**Main text**

**Materials and methods**

**Tissue samples**

Fresh frozen tissue samples were used for copy number, exome and expression analyses. All samples were collected with the patient’s informed consent and the study was approved by the Human Research Ethics Committees at the Peter MacCallum Cancer Centre. Patients with ovarian tumors were identified through hospitals in the Wessex Region, UK (n = 25) [15] and the Australian Ovarian Cancer Study (AOCS) (n = 31) [16, 17]. Pathology review was conducted on cryosections adjacent to the tissue from which DNA was extracted (PA). Microdissections and DNA/RNA extractions were performed as previously described [18]. Samples were selected for inclusion based on availability of tissue for DNA and RNA extraction.

**Copy number data**

The Affymetrix SNP6.0 Human Mapping (1.8 M probe set) array was utilised for ultra-high resolution allele-specific copy number analysis. Arrays were performed as recommended by the manufacturer with the exception that the input was reduced from the recommended 500 ng to 250 ng by reducing reaction volumes by half for all processes prior to the SNP6.0 PCR step. Reduction in DNA input does not result in any loss in the quality of the data. Copy number analysis was performed as previously described [18], using Partek Genomics Suite v 6.5. Copy number and allele-specific copy number was generated paired (when matching normal available) or unpaired and circular binary segmentation was performed to identify regions of copy number and loss of heterozygosity. Thresholds were >2.3 for gains, <1.7 for losses and <0.75 for homozygous deletions. All SNP data has been made publicly available through Gene Expression Omnibus (http://www.ncbi.nlm.nih.gov/geo/ - GSE67189).

**Exome sequencing**

For each case 500 ng–1 µg of microdissected tumour DNA and matched lymphocyte DNA when available was sheared to <1000 bp using a Covaris® ultra-sonicator (Covaris®), libraries prepared using the Illumina TruSeq DNA Sample Preparation procedure (Illumina), and enriched for exome sequencing using the SeqCap EZ Human Exome Library v2.0 (Roche NimbleGen). Exomes were sequenced with 100 bp PE reads in pools of three per lane on a HiSeq 2000 (Illumina).

Sequence reads were aligned to the human genome (GRCh37/hg19) using BWA-MEM (v0.7.7-r441) [19, 20]; duplicates marked using Picard (v1.77); local indel realignment and base quality recalibration performed using GATK (v2.7-2-g6bda569) [21, 22]; indel detection performed using GATK Unified Genotyper (v2.7-2-g6bda569), Indel Genotyper, Pindel (v0.2.5a3) [23], and VarScan2 (v2.2.4) [24]; SNV prediction performed using GATK Unified Genotyper, MuTect (v2.7-1-g42d771f) [25], SomaticSniper [26], JointSNVMix2 (v0.8-b2) [27], and VarScan2 (v2.2.4); and variants annotated using Ensembl variant effect predictor v73. Exome bam files are available from the Sequence Read Archive Accession number PRJNA631561 (https://www.ncbi.nlm.nih.gov/sra/PRJNA631561).

Variants were enriched for genuine somatic events by filtering for those called by >=2 variant callers, with the exception of MuTect, which is capable of detecting variants at lower frequencies and therefore all MuTect variants were included; germline allele frequency <=0.01 and tumour allele frequency >=0.05, with >=0.1 difference in allele frequency between tumour and germline; variant observed in <=3 of 250 in-house germ-line exomes. All variants with a tumour allele frequency >=0.1 were taken forward for Sanger sequencing validation.

**Expression data**

Expression data was generated using the Affymetrix Human Gene 1.0 ST array according to the manufacturer’s recommendations. An input of 300 ng of total RNA was used, as quantified by Nanodrop spectrophotometer. RIN values were determined using the Agilent Bioanalyzer RNA 6000 Nano assay, the average RIN value for the 25 samples was 4.7 (range 1–7.9). Analysis of the data was performed using the Partek Gene Expression workflow. CEL files were processed using RMA normalisation and batch correction. All Gene 1.0 ST data has been made publicly available through Gene Expression Omnibus (http://www.ncbi.nlm.nih.gov/geo/ - GSE67223).

**Results**

The clinical features of the ovarian cohort are presented in Table 1. Women with ovarian fibromas compared to benign serous ovarian tumours had very similar median ages and ranges (64, range 35–80 and 61, range 27–80 respectively). Interestingly, there appeared to be a strong
preponderance for both fibromas and benign serous tumours to be bilateral or detected on the right ovary (Binomial test for left vs right P = 0.02).

### Copy number aberrations

Genome-wide copy number analysis was performed for eight unselected pure fibromas, and compared to copy number data from the stroma of 27 serous cystadenofibromas and 18 serous cystadenomas (collectively referred to as benign serous tumours). CNAs were detectable in 7/8 (88%) of the pure fibromas, with gain of chromosome 12 being the most recurrently observed aberration in five of eight (63%) cases (Additional file 1: Table S1). Other recurrent CNAs in the fibromas were gain of chromosomes 9 or 9q (50% cases), 18 and 21 (20% cases each). CNAs were detected in the stroma of 33% of benign serous tumours. Recurrent gain of chromosome 12 was also observed in 31% of serous cystadenofibromas (8/27) and 17% of serous cystadenomas (3/18), gain of 9q was only observed in single serous cystadenofibroma case, while loss of chromosome 22 was detected in 11% of cystadenofibromas (3/27). No CNAs were detected in the stroma of the normal ovaries.

### Expression analysis

Gene expression arrays were used to compare the stromal RNA of three normal ovaries against eight pure fibromas (seven with CNAs), seven cystadenomas (two with CNAs), and seven cystadenofibromas (four with CNAs). Comparing normal ovary to benign serous tumours or fibromas did not identify any differentially expressed genes following multiple testing correction. Comparison of benign serous tumours to fibromas also did not

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**Table 1 Clinical features of cohort**

| Sample ID | Age | Laterality       | CN | Gene expression | Exome |
|-----------|-----|------------------|----|-----------------|-------|
| Pure Fibromas |     |                  |    |                 |       |
| IC33      | 80  | Bilateral (same) | Y  | Y               |       |
| IC4       | n/a | Bilateral (same) | Y  | Y               |       |
| IC269     | 59  | Right            | Y  | Y               |       |
| IC425     | 49  | Left             | Y  | Y               |       |
| IC458     | 35  | Right            | Y  | Y               |       |
| IC494     | 53  | Bilateral (same) | Y  | Y               |       |
| IC181     | 65  | Right            | Y  | Y               |       |
| IC137     | 64  | Bilateral (other)| Y  | Y               |       |
| Cystadenofibroma |     |                  |    |                 |       |
| IC149     | 66  | Bilateral (same) | Y  | Y               |       |
| IC10      | 59  | Right            | Y  | Y               |       |
| IC164     | 72  | Left             | Ya | Y               |       |
| IC158     | 82  | Bilateral (same) | Ya | Y               |       |
| IC5       | 81  | Left             | Ya | Y               |       |
| IC103     | 56  | Bilateral (same) | Ya | Y               |       |
| IC467     | 52  | Right            | Ya | Y               |       |
| IC120     | 74  | Right            | Y  | Y               |       |
| A4        | 74  | Right            | Ya | Y               |       |
| A3        | 61  | Bilateral (same) | Ya | Y               |       |
| A2        | 63  | Bilateral (same) | Ya | Y               |       |
| A5        | 66  | Right            | Ya | Y               |       |
| A6        | 75  | Bilateral (same) | Ya | Y               |       |
| A8        | 48  | Bilateral (same) | Y  |                 |       |
| A9        | 66  | Left             | Ya |                 |       |
| A10       | 54  | Bilateral (same) | Ya |                 |       |
| A25       | 61  | Right            | Ya |                 |       |
| A11       | 72  | Bilateral (same) | Ya |                 |       |
| A12       | 76  | Bilateral (same) | Ya |                 |       |
| A61       | 68  | Right            | Y  |                 |       |
| A29       | 57  | Bilateral (same) | Ya |                 |       |
| A22       | 51  | Bilateral (same) | Ya |                 |       |
| A13       | 50  | Right            | Ya |                 |       |
| A14       | 62  | Bilateral (same) | Ya |                 |       |
| A15       | 45  | Left             | Ya |                 |       |
| A7        | 69  | Right            | Ya |                 |       |
| Adenofibroma |    |                  |    |                 |       |
| IC450     | 27  | Right (other)    | Ya | Y               |       |
| Cystadenoma |     |                  |    |                 |       |
| IC148     | 67  | Bilateral (other)| Ya | Y               |       |
| IC24      | 77  | Bilateral (same) | Y  | Y               |       |
| IC196     | 46  | Unilateral (unspecified) | Y | Y |       |
| IC7       | 79  | Right            | Ya | Y               |       |
| IC591     | 48  | Right            | Y  | Y               |       |
| A17       | 35  | Bilateral (same) | Ya | Y               |       |
| A16       | 50  | Right            | Ya |                 |       |
| A18       | 73  | Bilateral (same) | Ya |                 |       |
| A19       | 46  | Right            | Ya |                 |       |
| A20       | 65  | Right            | Ya |                 |       |

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**Table 1 (continued)**

| Sample ID | Age | Laterality       | CN | Gene expression | Exome |
|-----------|-----|------------------|----|-----------------|-------|
| A23       | 58  | Bilateral (same) | Y  |                 |       |
| A21       | 64  | Bilateral (same) | Y  |                 |       |
| A26       | 55  | Bilateral (same) | Y  |                 |       |
| A27       | 59  | Left             | Y  |                 |       |
| A62       | 68  | Bilateral (same) | Y  |                 |       |
| A63       | 43  | Right            | Y  |                 |       |
| A64       | 55  | Bilateral (same) | Y  |                 |       |
| A24       | 58  | Bilateral (same) | Y  |                 |       |
| Normal    |     |                  |    |                 |       |
| IC79      | 60  | n/a              | Y  |                 |       |
| IC236     | n/a | n/a              | Y  |                 |       |
| IC369     | 40  | n/a              | Y  |                 |       |

Same = same diagnosis both ovaries. Other = different diagnosis in contralateral ovary. n/a, information not available. Y, included in this manuscript

* in Hunter et al. 2011
identify any differentially expressed genes. Comparison
of samples based on the presence or absence of CNA, or
the presence of specific CNA compared to an absence of
genomic aberrations (with and without tumour subty-
ping), did not identify differentially expressed genes that
remained significant following multiple testing correc-
tion. As these samples are difficult to enrich for neoplas-
tic cells due to a mixture of cell types in the stroma the
expression signal from the tumour cells will be diluted,
therefore a less stringent approach was taken to iden-
tify candidate genes by taking the most significantly
altered genes $p < 0.001$ with a fold change $> 2.0$. Through
this approach 17 genes were found to be differentially
expressed based on the presence of specific CNA (gain
9q and 12, loss of 16q) compared to samples with no
genomic CNAs (Table 2).

**Exome data**

Exome sequencing was performed on the stromal DNA of
seven cystadenofibromas, one adenofibroma and one cys-
tadenoma (all with CNAs), and two cystadenofibromas
and one cystadenoma with no CNAs. Exome sequencing
identified 83 putative somatic variants, with an average of
7 mutations per case (range 2–20). It is difficult to enrich
for the subpopulation of neoplastic fibroblasts in the
stroma, as indicated by the low variant allele frequency of
the majority of the variants (Additional file 2: Table S2),
and subsequently difficult to validate findings by Sanger
sequencing. We undertook Sanger validation of a sub-
set of variants for each case. No recurrent mutations or
recurrently mutated genes were identified that went on to
validate. In total, 20 somatic variants were able to be vali-
dated by Sanger sequencing (Table 3). Of the validated
variants, a single nonsense mutation was identified in the
DMD gene. The remaining 19 validated variants were all
missense variants, the functional impacts of which were
assessed using transFIC (Transformed Functional
Impact for Cancer) (Table 3). No variants from the three
tumours with no CNAs validated by Sanger sequencing.

The ability to detect variants may be confounded by
normal DNA contamination. There was a positive corre-
lation between the number of variants detected (before

| Gene     | Cytoband | Fold-change | P value      | Function                                                                 |
|----------|----------|-------------|--------------|--------------------------------------------------------------------------|
| **9q genes gain vs no gain** |           |             |              |                                                                          |
| HAPLN1   | 5q14.3   | +5.2        | 0.000008     | ECM protein and ERK signalling; overexpressed in metastatic melanoma and mesotheliomas |
| PRAME    | 22q11.22 | +3.6        | 0.000342     | Repressor of retinoic acid receptor. Overexpressed in multiple neoplasms (including melanoma) |
| SLC17A3  | 6p22.2   | +3.3        | 0.000081     | Voltage-driven transporter. Affects serum uric acid levels                |
| CKB2     | 9q22.2   | +3.3        | 0.000232     | CDC28 protein kinase regulatory subunit 2. Overexpressed in numerous neoplasms, overrides the intra-S-phase DNA damage checkpoint |
| ANOS1    | Xp22.31  | +2.8        | 0.000297     | ECM protein. Putative cell adhesion molecule, upregulated in some tumour types |
| RNF182   | 6p23     | +2.5        | 0.000110     | E3 ubiquitin ligase. Overexpressed in Alzheimers                        |
| SLC17A1  | 6p22.2   | +2.3        | 0.000711     | Sodium-dependent phosphate transporter. Affects uric acid levels          |
| CRB1     | 1q31.3   | +2.1        | 0.000466     | Photoreceptor protein                                                    |
| SYT14    | 1q32.2   | +2.1        | 0.000601     | Family of proteins involved in synaptic transmission                     |
| C6orf115 | 6q24.1   | +2.0        | 0.000848     | Uncharacterised protein                                                  |
| APOD     | 3q29     | −2.6        | 0.000762     | Putative lipoprotein metabolism. Inverse correlation between expression and colorectal tumour progression. Associated with neurodegeneration |
| CLU      | 8p21.1   | −2.4        | 0.000751     | Secreted anti-apoptotic chaperone protein. Overexpressed in many tumour types and associated with neurodegeneration |
| SLFN11   | 17q12    | −2.3        | 0.000237     | Putative DNA/RNA helicase. Expression of other family members inhibits growth of fibroblasts and thymocytes. Sensitises cancer cells to DNA damaging agents |
| **chr12 genes gain vs no gain** |           |             |              |                                                                          |
| NDST3    | 4q26     | +2.9        | 0.000814     | N-deacetylase/N-sulfotransferase 3. Golgi apparatus protein, associated with schizophrenia and bipolar disorder |
| PRELP    | 1q32.1   | −2.2        | 0.000646     | Connective tissue ECM protein. Abnormally expressed in chronic lymphocytic leukaemia cells |
| **16q genes loss vs no loss** |           |             |              |                                                                          |
| PRAME    | 22q11.22 | +6.4        | 0.000347     | Repressor of retinoic acid receptor. Overexpressed in multiple neoplasms (including melanoma). |
| GLRA2    | Xp22.2   | +2.7        | 0.000412     | Glycine receptor alpha 2, neutrophil and p38 MAPK associated              |
| GABRA5   | 15q12    | +2.5        | 0.000136     | GABA receptor alpha 5, associated with schizophrenia and bipolar I disorder |
| SLFN11   | 17q12    | −3.6        | 0.000336     | Putative DNA/RNA helicase. Expression of other family members inhibits growth of fibroblasts and thymocytes. Sensitises cancer cells to DNA damaging agents |
| Sample | CHR | POS   | REF | ALT | Consequence | Gene  | Amino acids | Condel           | PolyPhen          | SIFT          | SiftTranfsicLabel | Validation |
|--------|-----|-------|-----|-----|-------------|-------|-------------|------------------|------------------|--------------|-------------------|------------|
| A42    | 11  | 821679| T   | G   | MS          | PNPLA2| F/C         | Deleterious (0.702) | Prob_damaging (0.984) | Tolerated (0.11) | Low_impact          | Somatic    |
| A42    | 19  | 897480| G   | A   | MS          | R3HDM4| P/L         | Deleterious (0.481) | Prob_damaging (0.996) | Tolerated (0.37) | Low_impact          | Somatic    |
| A4     | 2   | 197090514| T | C   | MS          | HECW2 | Y/C         | Deleterious (0.935) | Prob_damaging (0.999) | Deleterious (0)    | High_impact         | Somatic    |
| A4     | 5   | 35068332| C  | A   | MS          | PRLR  | A/S         | Neutral (0.019)    | Benign (0.026)     | Tolerated (0.38)  | Medium_impact       | Somatic    |
| A4     | 16  | 9943623| C   | T   | MS          | GRIN2A| V/I         | Neutral (0.000)    | Benign (0.002)     | Tolerated (1)     | Low_impact          | Somatic    |
| A4     | 19  | 4448308| C   | G   | SRV         | UBXN6 | .           | .                | .                | .              | .                  | .          |
| A4     | 19  | 38692604| G  | C   | MS          | SIPA1L3| G/A        | Neutral (0.001)    | Benign (0.002)     | Tolerated (0.82)  | Low_impact          | Somatic    |
| A17    | X   | 31222107| C  | A   | NS          | DMD   | E/*         | .                | .                | .              | .                  | .          |
| IC158  | 3   | 47127761| T  | C   | MS          | SETD2 | H/R         | Deleterious (0.808) | Prob_damaging (0.96) | Deleterious (0.01) | Medium_impact       | Somatic    |
| IC158  | 1   | 44156598| C  | T   | MS          | KDM4A | P/L         | Deleterious (0.881) | Prob_damaging (0.987) | Deleterious (0)    | High_impact         | Somatic    |
| IC158  | 7   | 96639132| C  | T   | MS          | DLX6  | R/C         | Deleterious (0.877) | Prob_damaging (0.985) | Deleterious (0)    | High_impact         | Somatic    |
| IC158  | 7   | 100484701| G  | A   | MS          | SRRT  | V/M         | Deleterious (0.892) | Prob_damaging (0.992) | Deleterious (0)    | Medium_impact       | Somatic    |
| IC158  | 14  | 102504858| G  | T   | MS          | DYNC1H1| G/V        | Deleterious (0.886) | Prob_damaging (0.99) | Deleterious (0)    | High_impact         | Somatic    |
| IC158  | 16  | 21726339| G  | A   | MS          | OTOA  | A/T         | Neutral (0.021)    | Benign (0.042)     | Tolerated (0.37)  | Low_impact          | Somatic    |
| IC467  | 12  | 49422612| T  | C   | MS          | KMT2D | K/R         | Deleterious (0.543) | Prob_damaging (0.994) | Deleterious (0)    | NA              | Somatic    |
| IC467  | 17  | 11603150| A  | G   | MS          | DMAH9 | K/E         | Deleterious (0.832) | Prob_damaging (0.942) | Deleterious (0)    | Medium_impact       | Somatic    |
| IC467  | 19  | 51582924| C  | A   | MS          | KLK14 | R/M         | Neutral (0.346)    | Benign (0.231)     | Tolerated (0.06)  | Medium_impact       | Somatic    |
| IC467  | 19  | 54313656| C  | A   | MS          | NLRP12| E/D         | Neutral (0.028)    | Benign (0.113)     | Tolerated (0.37)  | Low_impact          | Somatic    |
| IC467  | X   | 58111262| C  | T   | MS          | NLGN4X| A/T         | Neutral (0.199)    | Poss_damaging (0.47) | Tolerated (0.21)  | Low_impact          | Somatic    |
| IC467  | X   | 77112855| T  | C   | MS          | MAGT1 | N/S         | Neutral (0.002)    | Benign (0.014)     | Tolerated (0.76)  | Low_impact          | Somatic    |

MS Misense, NS nonsense, SRV splice receptor variant
validation) and the average allele frequency (Spearman’s $r = 0.76$, $P = 0.01$, Additional file 3: Figure S1). The mean sequencing depth was 121.3 reads (88.6–186.8) for germline samples and 122.7 reads (72.8–163.6) for somatic samples, therefore the detection of low frequency variants is not substantially compromised by limited depth of coverage.

Discussion

The findings of this study are consistent with previous karyotyping and FISH studies that identified trisomy 12 as the most common chromosomal abnormality identifiable in ovarian fibromas [8–10]. Pure ovarian fibromas were found to harbour chromosomal abnormalities more frequently than benign serous ovarian tumours (88% vs. 33%), further supporting our hypothesis that a subset of benign serous tumours are actually fibromas that coincidentally have an associated epithelial cyst. However, benign serous tumours more frequently harboured trisomy 12 as the sole aberration (47% of tumours with aberrations) compared to fibromas (30% of tumours with aberrations). Fibromas also more frequently harboured CNA that were rarely detected in the benign serous tumours such as 9q gain (50% cases), potentially indicating unique underlying biological drivers.

Expression analysis provided some interesting candidates that have previously been associated with neoplasms or fibroblast growth for further investigation. Genes with increased expression in tumours with CNAs compared to those without CNAs included the extracellular matrix (ECM) and signalling molecules HAPLN1 and ANOS1, the antigen and repressor of retinoic acid signalling molecule PRAME, and the cell cycle regulator CKS2. All of these genes have been previously associated with overexpression in other types of neoplasm [28–34], and PRAME and CKS2 expression have been proposed as markers of poor prognosis in high-grade serous ovarian carcinoma [33, 35].

Genes with decreased expression in tumours with CNAs compared to those without CNAs included the putative DNA/RNA helicase SLFN11, the ECM protein PRELP, the high density lipoprotein component APOD, and the secreted chaperone CLU. Although these have all been linked with altered expression in other neoplasms before, this has typically been upregulation and potentially linked to neoplastic progression [36–40], including in ovarian cancer for APOD and CLU [41, 42]. Data is inconsistent for CLU, as expression was also linked to improved prognosis in high-grade serous ovarian carcinoma [33]. Low expression of SLFN11 has been associated with resistance to chemotherapy in ovarian cancer other cancers due to its role in the DNA damage response [43].

No genes were found to be recurrently mutated, however, two tumours had mutations in histone methyltransferases (SETD2 and KMT2D) and one also had a mutation in a demethylase (KDM4A), all previously associated with neoplasia and all mutations predicted to be deleterious. Other mutated genes have also been associated with neoplasia, such as HECW2, SRRT and KLK14, with predicted medium to high deleterious impact.

Limitations

- Use of Affymetrix Human Gene 1.0 ST array is limited to the probes on the array at the time.
- Insufficient power to detect differentially expressed genes due to $n=3$ normal ovaries.
- Limited ability to detect mutations due to normal contamination.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s13104-020-05194-z.

Acknowledgements

The AOCS acknowledges the cooperation of the participating institutions in Australia and acknowledges the contribution of the study nurses, research assistants and all clinical and scientific collaborators to the study. The complete AOCS Study Group can be found at www.aocsstudy.org. We would like to thank all the women who participated in these research programs.

Authors’ contributions

Study design: KLG and IGC; Experiments: SMH and SMR; Data analysis: SMH, GVD, KLG, MAD, RL, JL; Preparation of tables and figures: KLG, GVD, SMH; Pathology review: PA; Collection of samples: DDLB; Drafting of manuscript: SMH, GVD, KLG and IGC. All authors reviewed and revised the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by the Victorian Breast Cancer Research Consortium (VBCRC) and the National Health & Medical Research Council of Australia (NHMRC, ID 628630) and the Emer Casey Foundation. The Australian Ovarian Cancer Study Group was supported by the U.S. Army Medical Research and Materiel Command under DAMD17-01-1-0729, The Cancer Council Victoria, Queensland Cancer Fund, The Cancer Council New South Wales, The Cancer Council South Australia, The Cancer Council Tasmania and The Cancer Foundation of Western Australia (Multi-State Applications 191, 211 and 182) and the National Health and Medical Research Council of Australia (NHMRC, ID400413 and ID400281). The Australian Ovarian Cancer Study gratefully acknowledges additional support from Ovarian Cancer Australia and the Peter MacCallum Foundation.

Availability of data and materials

Gene Expression Omnibus GSE67189—Molecular characterization of ovarian serous cystadenomas and fibromas [Copy number], GSE67223—Molecular characterization of ovarian serous cystadenomas and fibromas [Expression]
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Title:
Molecular comparison of pure ovarian fibroma with serous benign ovarian tumours

Date:
2020-07-22

Citation:
Hunter, S. M., Dall, G. V., Doyle, M. A., Lupat, R., Li, J., Allan, P., Rowley, S. M., Bowtell, D., Campbell, I. G. & Gorringe, K. L. (2020). Molecular comparison of pure ovarian fibroma with serous benign ovarian tumours. BMC RESEARCH NOTES, 13 (1), https://doi.org/10.1186/s13104-020-05194-z.

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