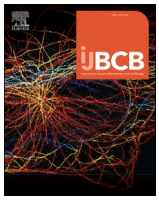
International Journal of Biochemistry and Cell Biology 157 (2023) 106383

Contents lists available at ScienceDirect

International Journal of Biochemistry and Cell Biology

journal homepage: www.elsevier.com/locate/biocel



Molecular profiling in desmoplastic small round cell tumours

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ARTICLE INFO

Keywords:
Soft tissue sarcoma
Desmoplastic small round cell tumour
Molecular profiling
Drug discovery
Biomarkers

ABSTRACT

Desmoplastic small round cell tumour (DSRCT) is an ultra-rare soft tissue sarcoma that is characterised by aggressive disease and dismal patient outcomes. Despite multi-modal therapy, prognosis remains poor and there are currently no effective targeted therapies available for patients with this disease. Advances in comprehensive molecular profiling approaches including next generation sequencing and proteomics hold the promise of identifying new therapeutic targets and biomarkers. In this review, we provide an overview of the current status of molecular profiling studies in DSRCT patient specimens and cell lines, highlighting the key genomic, epigenetic and proteomic findings that have contributed to our biological knowledge base of this recalcitrant disease. In-depth analysis of these molecular profiles has led to the identification of promising novel and repurposed candidate therapies that are suitable for translation into clinical trials. We further provide a perspective on how future integrated studies including proteogenomics could further enrich our understanding of this ultra-rare entity and deliver progress that will ultimately impact the outcomes of patients with DSRCT.

1. Introduction

Desmoplastic small round cell tumour (DSRCT) is an aggressive neoplasm predominantly affecting male adolescents and young adults (Mello et al., 2021). With an estimated incidence between 0.2 and 0.5 cases per million per year, it is an ultra-rare soft tissue sarcoma and is therefore exceptionally challenging to characterise its disease biology and generate clinical evidence for new therapeutic options (Martínez-Trufero et al., 2021; Stacchiotti et al., 2021).

DSRCT is characterised by the recurrent t(11;22)(p13:q12) chromosomal translocation that fuses the Ewing sarcoma RNA binding protein gene (*EWSR1*) with the Wilm's tumour suppressor gene (*WT1*) (Gerald and Rosai, 1989; Ladanyi and Gerald, 1994; Sawyer et al., 1992). The EWSR1-WT1 fusion protein is the driver of DSRCT which has pleotropic effects including the upregulation of proteins involved in tumorigenesis, such as platelet-derived growth factor receptor alpha (PDGFRα), insulin like growth factor1 receptor (IGF-1R), neurotrophic tyrosine kinase receptor 3 (NTRK3) and vascular endothelial growth factor (VEGF) (Mello et al., 2021; Ogura et al., 2021). Transcription factors such as *MYC*, paired box gene 2 (*PAX2*) and equilibrative nucleoside transporter 4 (*ENT4*) are also upregulated (Mello et al., 2021).

In general, DSRCT originates from the serosal surface of the abdominal cavity with the most common primary sites being the peritoneum, abdomen and pelvis (Lettieri et al., 2014). It often presents as advanced disease, with multiple intra-abdominal tumours, frequently with nodal and synchronous liver involvement (Martínez-Trufero et al., 2021). Prognosis is poor, with a median survival of 25 months, and 3- and 5-year survival rates from 44% to 15% respectively (Lal et al., 2005). Clinical management includes a combination of chemotherapy, radiation, and surgical resection (Martínez-Trufero et al., 2021). DSRCT is currently treated using the same regimen as Ewing sarcoma, and there are no subtype-specific tailored therapies available. The preferred first-line therapy for patients without extra-abdominal metastases is multi-agent intensive chemotherapy and aggressive debulking surgery. Most combinations are based on alkylating agents, with vincristine/-doxorubicin/cyclophosphamide (VDC) alternating with cycles of ifosfamide/etoposide (IE) being a commonly used regimen (Kushner et al., 2016; Farhat et al., 1996; Subbiah et al., 2018). However, there is currently no consensus regarding the most effective regimen. Common second line therapies include metronomic chemotherapy with topoisomerase-containing agents or trabectedin (Brunetti et al., 2014). Newer treatment agents, such as tyrosine kinase inhibitors and immunotherapies have shown promise in small case series (Ogura et al., 2021;

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https://doi.org/10.1016/j.biocel.2023.106383
Received 15 October 2022; Received in revised form 20 January 2023; Accepted 30 January 2023
Available online 1 February 2023

Thway et al., 2016; Frezza et al., 2014; Tap et al., 2012; Bexelius et al., 2020).

Despite the development of new therapeutic agents and advances in multi-modal therapy, the outcome for DSRCT patients remain poor due to extensive tumour spread at diagnosis and high rates of disease recurrence. Much of our existing knowledge on treatment response is based on clinical experience as opposed to mechanistic biological understanding (Katz et al., 2018). The biological causes underlying uniformly poor patient outcomes are not understood, and there is an urgent unmet need for more effective therapeutic options (Merry et al., 2021).

Recent studies using comprehensive molecular profiling of DSRCT have compared molecular similarities and differences with other sarcoma subtypes, identified potential intrinsic subgroups, and defined candidate biomarkers of clinical relevance. In this review, we describe recent molecular studies conducted to better characterise DSRCT biology and their utility for defining new drug targets and prognostic/predictive biomarkers.

2. Genomic studies

Here we discuss genomics-based studies including targeted, whole exome and whole genome sequencing analyses that have been applied to DSRCT (summarised in Table 1). Due to its rarity, molecular profiling studies are often limited to single patient case reports or single-centre retrospective cohorts with relatively small case series. The first comprehensive genomic characterisation of DSRCT was performed by Ferreira et al., where targeted sequencing, array comparative gene hybridisation (CGH), whole genome sequencing, and whole exome sequencing (WES) was performed on a single case (Ferreira et al., 2016). The authors identified 12 protein-affecting somatic mutations and 14 germline events involved in mesenchymal cell differentiation-related processes such as muscle development, cell adhesion, and cell cycle. Seven of the genes harbouring somatic mutations are known to be regulated by lymphoid enhancer-binding factor 1 (LEF1), a transcription factor regulated by WT1. Array CGH detected few copy number alterations (CNA), with gains in chromosomes 5 and 18, and 11p, 13q, and 22q deletions.

Table 1
Summary of genomic studies described herein.

Study	DSRCT samples	Key findings
(Ferreira et al., 2016)	1 patient tumour	1. Identified alterations of genes involved in muscle development, cell adhesion, and cell cycle processes. 2. Seven of the mutated genes are normally known to be regulated by LEF1. 3. Chromosomal gains: 5, 18. Chromosomal losses: 11p, 13q, 22q.
(Devecchi et al., 2018)	6 patient tumours	1. Identified alterations of genes involved in the DDR and MErT/EMT pathways. 2. Chromosomal gains: 1. Chromosomal losses: 6.
(Chow et al., 2020)	83 patient tumours	1. Low MTB and MSI across all patient samples. 2. Identified recurrent alterations for *FGFR4*, *TP53*, *ARID1A*, *MSH3*, *MLL3* and various DDR pathway genes.
(Wu et al., 2022)	22 patient tumours	1. Identified recurrent alterations in *MUC* and *ARID1A*. 2. Identified alterations in genes involved in PI3K/AKT signalling, cell adhesion, cell proliferation, and angiogenesis pathways. 3. Chromosomal gains: 1q, 5, 7, 18, 19, 20, 22. Chromosomal losses: 4, 6q, 11, 16. 4. Multi-site tumours from individual patients show similar CNA and mutational profiles.
(Slotkin et al., 2021)	68 patient tumours and 24 PDX models	1. Low MTB and MSI across all patient samples. 2. Identified recurrent alterations in *FGFR4*, *ARID1A* and *HRAS*. 3. Chromosomal losses: 11p, 11q, 16q. 4. PDX showed similar mutation and CNA profiles to corresponding patient tumours, but had additional alterations in *TERT*, *TP53* and *BRAF*.

Devecchi and colleagues performed WES on specimens from 6 patients (Devecchi et al., 2018). The tumour mutational burden (TMB) ranged from 8 to 33 mutations per case, with an average of 23 mutations. In total, 137 unique somatic mutations in genes related to the DNA damage response (DDR) network and mesenchymal-epithelial reverse transition/epithelial-mesenchymal transition (MErT/EMT) were identified. CNA analysis found recurrent chromosome 1 gains and chromosome 6 losses in half of the cases. This did not match the results of Ferreira et al., suggesting interpatient differences (Ferreira et al., 2016).

Chow et al. analysed 83 tumour specimens using the FoundationOne Heme test and found fewer mutations per case than Devecchi et al. (2018) and Chow et al. (2020). The number of alterations per patient ranged from 1 to 28, with an average of 8 mutations. None of the patients were considered to have high TMB ($\geq$20 mutations/megabase) or microsatellite instability (MSI). Unlike the findings from Devecchi et al., several recurrent genetic alterations were found, indicating potential therapeutic targets. This included fibroblast growth factor receptor 4 (*FGFR4*), tumour suppressor genes *TP53* and AT-rich interactive domain-containing protein 1 A (*ARID1A*), and other genes such as MutS Homolog 3 (*MSH3*) and myeloid/lymphoid or mixed-lineage leukemia protein 3 (*MLL3*). Interestingly, mutation of 12 DDR pathway genes were identified across the cohort.

WES was performed on 22 tumours from 14 patients by Wu et al. (2022). This analysis showed a low mutation rate, with a median of 23 non-silent mutations per tumour with 460 non-silent mutations were identified in total. Recurrently mutated genes include mucin genes (*MUC*) and *ARID1A*. The mutated genes were found to be associated with phosphatidylinositol-3-kinase (PI3K)/AKT signalling, cell adhesion, cell proliferation, and angiogenesis pathways. The majority of CNAs involved entire chromosome arms or whole chromosomes. Gain of chr1q and loss of chr6q was seen in 55% and 30% patients respectively, corresponding with the findings of Devecchi et al. Recurrent gains were also identified in chromosomes 5, 17, 18, 19, 20, and 22 and losses in chromosomes 4, 11, and 16. When comparing multiple samples from individual patients, it was found that CNA profiles was very similar across tissue sites, and no specific mutations was consistently required for early DSRCT oncogenesis other than *EWSR1-WT1*.

Slotkin et al. analysed 68 matched tumour/normal samples from 53 patients using the MSK-IMPACT assay (Slotkin et al., 2021). TMB was low across all samples (0–3.9 mutations/Mb) and none showed MSI. Recurrent genetic alterations were uncommon, but observed in genes such as *FGFR4*, *ARID1A* and *HRAS*. Compared to previous findings by Chow et al., overall mutation rates were much lower as the current analysis used matched germline normal controls. CNA analysis showed that recurrent loss of heterozygosity was most commonly observed in chromosome arms 11p, 11q, and 16q. The MSK-IMPACT assay was also used to analyse 24 DSRCT patient-derived xenografts (PDX) from 10 patients. Mutational and CNA profiles were mostly reflective of the original patient tissue, but several PDX had additional mutations in genes such as telomerase reverse transcriptase (*TERT*), *TP53* and *BRAF*.

In summary, these genomic studies indicate that DSRCTs have low TMB, are relatively homogenous at the genomic level and identifies several recurrently mutated genes and CNAs in key pathways, including targets in the DDR pathway genes which may represent future viable therapeutic targets.

3. Epigenetic studies

Hingorani and colleagues used RNA-seq and ChIP-seq to characterise

14 DSRCT patient tissues and one cell line (Hingorani et al., 2020) (Table 2). Single sample gene set enrichment analysis (ssGSEA) and clustering of the transcriptomic data showed that the DSRCT tissues separated into two distinct clusters. The most significantly differentially enriched gene sets between the two clusters are DDR and muscle development. Using publicly available gene expression array data, the authors also demonstrated using principal component analysis (PCA) that DSRCT tissues clustered independently of other fusion-gene positive sarcomas arising in young adults, such as alveolar soft part sarcoma and Ewing sarcoma. Mining the gene expression array data, the authors showed that *IGF2* expression in DSRCT was significantly higher compared to other fusion gene positive sarcomas, with the exception of alveolar rhabdomyosarcoma. ChIP-seq using an antibody against WT1 showed that the EWSR1-WT1 fusion protein directly binds to the *IGF2* locus, though silencing the expression of the fusion gene in the DSRCT cell line did not reduce IGF2 protein expression. ChIP-seq further showed that EWSR1-WT1 directly binds the *FGFR4* locus. Silencing the expression of *EWSR1-WT1* in the DSRCT cell line decreased FGFR4 protein expression. In addition to *IGF2* and *FGFR4*, the transcriptomic data and immunohistochemistry analysis also showed high expression of targetable immune checkpoints CD276 and CD200 in DSRCT samples which may serve as potential immune-oncology therapeutic targets.

To further evaluate the expression level of *FGFR4* in DSRCT, RNA-seq data from a cohort of 154 paediatric malignancies (DSRCT n = 8) was analysed by Slotkin et al (Slotkin et al., 2021). Whilst none of the DSRCT samples had *FGFR4* alterations, *FGFR4* gene expression levels were significantly higher in DSRCT compared to other sarcoma subtypes. To test the potential use of FGFR4 as a therapeutic target, a panel of four selective and broad spectrum FGFR inhibitors were evaluated in the JN-DSRCT cell line. JN-DSRCT does not harbour *FGFR4* mutation or amplification, but RNA-seq data showed the cell line had high expression of *FGFR4*. Only one of these inhibitors ponatinib showed any activity. This suggests that, despite *FGFR4* overexpression, FGFR4 inhibition is ineffective against DSRCT cells at least in the absence *FGFR4* amplification or activating mutations.

In another study, RNA-seq data from 117 sarcomas (DSRCT n = 22) showed that the transcriptomic profile of DSRCT is significantly different from adjacent normal tissue and other sarcoma subtypes (Wu et al., 2022). To study the immunogenic potential of DSRCT, the authors used ssGSEA scores of immune cell gene sets to characterise immune cell profiles. Compared to other subtypes, DSRCT is immune "cold" and has low activity of most infiltrating immune cells, except neutrophils and T helper 17 cells in a subset of patients. Additionally, when compared to publicly available data for other cancer types from The Cancer Genome Atlas (TCGA), DSRCT was among the cancer types with the lowest ESTIMATE immune infiltration score. With a significantly lower score than other sarcoma subtypes (e.g. dedifferentiated liposarcoma and undifferentiated pleomorphic sarcoma) that respond to immune checkpoint inhibition (ICI), the authors believe that DSRCT tumours do not have sufficient immune cell infiltrate to generate meaningful responses to ICI.

Bleijs et al. and Gedminas et al. investigated the effect of *EWSR1-WT1* loss on the transcriptome in a patient-derived cell line, and two established DSRCT cell lines (Bleijs et al., 2021; Gedminas et al., 2020). Differentially expressed genes upon *EWSR1-WT1* knock-down varied between cell line models, but in total there were 11 upregulated and 7 downregulated genes that were shared between them. Using gene set enrichment analysis, Gedminas et al. found that *EWSR1-WT1* expression was associated with strong pro-proliferative and DDR signatures while it repressed oestrogen signalling (Gedminas et al., 2020). Bleijs et al. found that the MER tyrosine kinase (*MERTK*) was one of the most down-regulated genes upon knock-down of *EWSR1-WT1* (Bleijs et al., 2021). To follow-up on this finding, the authors used the MERTK inhibitor UNC2025 and showed that it reduced proliferation in the patient-derived DSRCT cell line, suggesting that MERTK may be a potential therapeutic target for DSRCT.

In summary, transcriptomic studies have identified several

Table 2
Summary of transcriptomics, ChIP-seq and proteomic studies described herein.

Study	Approaches	DSRCT samples	Key findings
(Hingorani et al., 2020)	RNA-seq (Illumina HiSeq2500) ChIP-seq	14 patient tumours and 1 cell line	1. DSRCT patient transcriptomes separated into two clusters, mainly driven by genes involved in DDR and muscle differentiation. 2. High expression of *IGF2*, *CD276* and *CD200* across all samples. 3. DSRCT transcriptomes clusters separately from other fusion-gene positive sarcomas.
(Slotkin et al., 2021)	MSK-Solid Fusion assay (Illumina MiSeq)	8 patient tumours	1. *FGFR4* overexpression was consistent across patient samples, but selective and broad spectrum FGFR4 inhibitors had limited effect on DSRCT cells in vitro.
(Wu et al., 2022)	RNA-seq (Illumina HiSeq2500)	22 patient tumours	1. The transcriptome of DSRCT tumours and adjacent normal tissues are significantly different. 2. Compared to other cancers, DSRCT tumours are immune "cold" and have low immune infiltration scores.
(Bleijs et al., 2021)	RNA-seq (Illumina NovaSeq6000)	1 cell line	1. *MERTK* expression correlates with *EWSR1-WT1*, and when inhibited reduced proliferation of DSRCT cells in vitro.
(Gedminas et al., 2020)	RNA-seq (Illumina NextSeq500)	2 cell lines	1. EWSR1-WT1 is associated with strong pro-proliferative and DDR signatures while it repressed oestrogen signalling
(Lamhamedi-Cherradi et al., 2022)	RPPA RNA-seq (Illumina HiSeq2500)	16 patient tumours	1. DSRCT tumours showed overexpression of Akt, Syk and PKCα compared to adjacent normal tissue, and overexpression of AR and Syk compared to Ewing sarcoma tumours. 2. DSRCT tumours showed higher expression of AR than other sarcoma types. Expression of AR associated genes were more like pancreatic cancer

(*continued on next page*)

Table 2 (*continued*)

Study	Approaches	DSRCT samples	Key findings
			than other sarcoma types. 3. AR antagonists showed efficacy against DSRCT both in vitro and in vivo.
(Smith et al., 2022)	Antibody array	5 patient tumours and 5 cell lines	1. EGFR phosphorylation in both patient tumours and cell lines. 2. *EGFR* and *ERBB2* signatures enriched in DSRCT tumours compared to other sarcoma types. 3. EGFR inhibitors showed efficacy against DSRCT both in vitro and in vivo.

overexpressed genes and pathways that may act as potential therapeutic targets in DSRCT, including *FGFR4*, *MERTK* and the DDR pathway. Although initial studies indicate that DSRCTs are immune cold tumours, they do express immune checkpoints CD200 and CD276 and further studies are required to establish if DSRCT patients would benefit from immunotherapies.

4. Proteomic studies

In some more common sarcoma types, proteomics analysis have been used to describe molecular subgroups within histological subtypes, and to identify new potential therapeutic targets and biomarkers of clinical relevance (Burns et al., 2020; Chadha and Huang, 2022; Noujaim et al., 2016). Lamhamedi-Cherradi et al. studied the protein expression in 16 DSRCT patient tissues using reverse-phase protein arrays (RPPA) which measure 151 proteins and phosphoproteins (Lamhamedi-Cherradi et al., 2022) (Table 2). Compared to adjacent normal mesenteric tissue, DSRCT tumours were found to overexpress proteins such as AKT, Syk and protein kinase C alpha (PKCα). Furthermore, when compared to Ewing sarcoma patient tissues, DSRCT showed an upregulation of androgen receptor (AR) and Syk, To orthogonally confirm the increased AR expression in DSRCT, immunohistochemistry and western blotting was performed on separate DSRCT tissue cohorts and AR was found to be highly expressed in 39/60 and 5/12 samples respectively. The authors also performed RNA-seq analysis comparing 22 DSRCT with 71 sarcoma samples of 4 other subtypes, and 12 prostate cancer samples, a cancer type known to be associated with high AR activity (Heinlein and Chang, 2004). DSRCT specimens demonstrated significant upregulation of AR compared to other sarcoma subtypes, but not prostate cancer (Lamhamedi-Cherradi et al., 2022).

Based on this data, the authors evaluated the utility of AR antagonists in DSRCT preclinical models. Enzalutamide and AR-antisense oligonucleotide (ASO) both significantly slowed the proliferation of the JN-DSRCT cell line and reduced AR expression. These agents also reduced the tumour burden and improved survival in JN-DSRCT xenografts compared to placebo or control groups. This suggests a potential role of AR in the development and progression of DSRCT and may act as a candidate therapeutic target.

In another study, Smith et al. profiled the phosphorylation state of 49 receptor tyrosine kinases (RTKs) using phosphoproteomic arrays in 5 DSRCT patient tumours and 5 cell lines (Smith et al., 2022). Phosphorylation of ERBB family RTKs was observed in all five cell lines, with phosphorylation of epidermal growth factor (EGFR), ERBB4 and ERBB2 consistently high in all cell lines. Phosphorylation of EGFR was also present in patient specimens. These findings were corroborated with gene set variability analysis (GSVA) of publicly available microarray-based mRNA data of 137 translocation driven sarcomas (DSRCT n = 28), where *EGFR* and *ERBB2* signatures were found to be enriched in DSRCT compared to other sarcoma subtypes (Filion et al., 2009). Bulbul et al. performed ssGSEA on the same microarray dataset and found enriched AR and EGFR signatures in DSRCT compared to other sarcoma subtypes (Bulbul et al., 2018).

To assess EGFR as a therapeutic target for DSRCT, Smith et al. used pan-ERBB inhibitors afatinib and neratinib, and the anti-EGFR antibody cetuximab to treat DSRCT cell lines (Smith et al., 2022). The authors noted that the inhibitors reduced growth of the DSRCT cell lines but not Ewing sarcoma and synovial sarcoma cell lines. To begin to translate these findings into DSRCT patients, the authors then tested afatinib and cetuximab on immunocompromised mice bearing DSRCT cell line or PDX tumours. Whilst afatinib alone did not cause a statistically significant reduction in tumour growth, cetuximab alone and in combination with afatinib significantly reduced tumour growth in xenograft models.

In summary, proteomic studies have identified AR and EGFR pathways as potential therapeutic targets. AR inhibitor enzalutamide and anti-EGFR antibody cetuximab, currently approved to treat prostate cancer and colorectal cancer respectively, have shown promise in treating DSRCT in initial in vitro and in vivo studies. These promising studies using repurposed agents should be prospectively evaluated in clinical trials.

5. Future perspectives

DSRCT is an ultra-rare, aggressive sarcoma subtype with dismal prognosis. Although our understanding of the biology of DSRCT is improving, there is currently a lack of effective therapies. Currently, there are no agents that target the product of the *EWSR1-WT1* fusion. It is encouraging that despite its rarity, multiple molecular profiling studies have been undertaken and have led to the identification of candidate therapeutics targets and repurposed drugs that have been evaluated in the pre-clinical setting. This represents an exciting opportunity to improve the clinical management and treatment of DSRCT. For instance, AR has been identified in multiple studies as a potential therapeutic target of DSRCT. The use of combined androgen blockade treatments previously showed transient benefit for a subgroup of AR+ DSRCT patients (Fine et al., 2007). With newer AR-targeted therapies such as enzalutamide now available for other cancer types, the time is ripe for translating these biological findings into clinical trials for patient affected by DSRCT. Treatments for other identified targets, including CD276, and DDR pathway component Checkpoint Kinase 1 (CHEK1) have also showed promising results in phase I/II trials (Modak et al., 2020; Slotkin et al., 2022). It should be noted that most of the proposed therapies target downstream pathways and not the EWSR1-WT fusion itself and therefore may have limited clinical benefit. The use of antibody-drug conjugates or cellular therapies that are based on identified targets may be prove more beneficial. To that end, immunotherapies, such as EGFR and CD276 chimeric antigen receptor (CAR) T-cell therapy, are currently being evaluated in clinical trials (NCT03618381, NCT04483778, NCT04897321) (Espinosa-Cotton and Cheung, 2021).

Other Omics approaches including mass spectrometry-based proteomics and metabolomics of DSRCT remain largely unexplored. The CPTAC consortium have demonstrated the power of integrated proteogenomics in multiple epithelial cancer types (Rodriguez et al., 2021; Clark et al., 2019; Gillette et al., 2020). Some of these studies include rare and ultra-rare diseases including paediatric brain tumours, indicating that it is possible to undertake international collaborative efforts to pool together patient specimens, databases and resources for integrative large scale studies (Petralia et al., 2020). To make clinically meaningful advances in our understanding of this ultra-rare sarcoma, there is a need to develop national and international collaborations to

accelerate and coordinate DSRCT molecular profiling efforts. In particular, the application of proteogenomics to understand interpatient heterogeneity within DSRCT holds the promise of defining biomarker-matched therapies for precision oncology applications.

While conventional bulk sequencing approaches may be useful for studying intertumoural heterogeneity, new tools such as spatial transcriptomics and single cell sequencing may shed light on the intratumoural heterogeneity that is inherent in these tumours and their microenvironment and may explain why therapy is largely ineffective in this recalcitrant disease. New protocols compatible with fresh frozen and formalin-fixed paraffin-embedded (FFPE) samples are also being developed for these techniques, which will be particularly useful for rare cancers such as DSRCT (Habib et al., 2017; Foley et al., 2019; Chung et al., 2022). Using single nucleus RNA sequencing on fresh frozen specimens from 9 patients, Truong et al. presented at the Connective Tissue Oncology Society 2022 annual meeting that AR and neuroendocrine (NE) signatures appear to be inversely related in DSRCT tumour cells and may follow a similar NE reprogramming mechanism observed in prostate cancer (Truong et al., 2022). DSRCT patients were found to have an AR+ , NE+ or hybrid signature, which may help identify patients that might benefit from AR therapies in future.

Taken together, although the use of molecular profiling technologies to study DSRCT are still in early stages, collectively these studies demonstrate the power of omic techniques to increase our understanding of the biology of this disease and identify new biomarkers and drug targets. By incorporating this new knowledge with developments in preclinical modelling as well as therapeutic innovations, we anticipate that progress in the clinical management of this disease is forthcoming, ultimately leading to improvements in the outcomes of patients affected by DSRCT.

Declarations of interest

none.

Data availability

No data was used for the research described in the article.

Acknowledgements

The authors have no conflicts of interest to declare. The authors are funded by grants from Sarcoma UK, Cancer Research UK (C56167/A29363), Royal Marsden Cancer Charity, The Institute of Cancer Research, and the National Institute for Health Research (NIHR) Biomedical Research Centre at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research.

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