Genome-Wide Analysis and Characterization of an Online Sarcoma Cohort


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Introduction
Sarcomas represent an uncommon, complex and heterogeneous group of mesenchymal-derived cancers, making up as many as 50 distinct subtypes and striking just 14,000 individuals in the United States annually. As such, recruitment of an adequately sized cohort to power sarcoma genome-wide discoveries presents a double challenge. Traditional barriers to participation include proximity of clinical and research centers of care, as well as the inherent discomfort or ability to travel. The web-based research platform offered by 23andMe provides increased accessibility to patient and family participation, facilitating rapid recruitment of a relevant population and enabling a large-scale genome-wide association study (GWAS) of rare diseases such as sarcomas.

Methods
Patients with any history of ever having had a diagnosis of sarcoma or mesenchymal neoplasm were recruited through web and email campaigns, patient advocacy groups, physician offices, and events. Participants provided IRB-approved consent, completed surveys, and received updates about research progress through an online account. In collaboration with an uncompensated panel of academic experts, an online survey was developed to collect patient-reported data on demographics, family history, symptoms and treatment. Association scans were conducted across a set of 1,047,958 SNPs, using 714 unrelated sarcoma cases of European ancestry and over 88,000 unrelated population controls from the 23andMe database.

Results
RECRUITMENT and ENGAGEMENT
The 23andMe research approach has led to accrual of one of the largest sarcoma research cohorts in the world. Over 889 sarcoma patients have enrolled, 811 have been genotyped, and 668 have completed the online sarcoma survey. Over 80% of patients have been recruited by online means (33% by advocacy partner campaigns). Patients have received updates about research progress through an online account. In collaboration with an uncompensated panel of academic experts, an online survey was developed to collect patient-reported data on demographics, family history, symptoms and treatment. Association scans were conducted across a set of 1,047,958 SNPs, using 714 unrelated sarcoma cases of European ancestry and over 88,000 unrelated population controls from the 23andMe database.

DIAGNOSIS, SYMPTOMS, and TREATMENTS
- The cohort is primarily of European ancestry (89%), disproportionately female (72%) with an average age of 56 ± 15 years. The majority of participants reside in the United States. - Controls are also primarily of European ancestry (77%), 43.9% female, with an average age of 46 ± 15 years. - Time since diagnosis - MEAN 5.46 ± 6.42 years ago; MEDIAN 4 years ago. - Leiomyosarcoma (N = 176) is the most frequent subtype and the most common fibrous tumor with a suggestive association. Table 1 lists suggestive associations from GWAS for all sarcoma subtypes. - Over 37% of participants report undergoing active treatment of some type. - The top five treatments reported by participants to have been received for sarcoma include: doxorubicin + dacarbazine, temodar, doxorubicin + cisplatin, and doxorubicin + ifosfamide. - Over 95% of participants report side effects include hair loss, nausea, and low white blood cell count.

Discussion
The study demonstrates the feasibility of both rapid recruitment and longitudinal engagement of patients through a web-based research platform. A combination of online recruitment methods by sarcoma advocacy groups, 23andMe, and patients has been key to accruing one of the largest geographically and phenotypically diverse genotyped sarcoma cohorts in the world, and has enabled one of the first sizable genomic studies of this rare disease. Investigation of associations within genetically more homogeneous sarcoma subtypes remains a promising avenue for future exploration, although will require additional recruitment to achieve adequate statistical power. Web-based genetic research has the potential to change the one-size-fits-all approach to clinical research and transform how sarcoma is diagnosed and treated.

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References

Table 1. Suggestive associations (p < 1e-6) from all sarcoma and sarcoma subtype GWAS. N = 714 sarcoma cases; N = 36 uterine leiomyosarcoma; N = 169 leiomyosarcoma; N = 153 leiomyosarcoma (no uterine leiomyosarcoma); N = 56 osteosarcoma + chondrosarcoma; N = 88,000 controls for all GWAS. No suggestive associations from lipomas (GWAS).

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