

# Study identifies distinct sub-types of aggressive tumours to allow for targeted treatment

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A new study led by clinician-scientists from the National Cancer Centre Singapore (NCCS), with collaborators from research institutions

worldwide, has found that angiosarcomas have unique genomic and immune profiles which allow them to be classified into three different subtypes. With this new and improved classification system, patients can be treated using a personalised-medicine approach and it will encourage the development of novel treatments.

Angiosarcomas, a type of cancer that forms in the lining of the blood and lymph vessels, are more commonly found in Asia making up 7% of all sarcoma diagnoses. Angiosarcomas are aggressive and can spread to various regions of the body and most often occur on the scalp and face.

For angiosarcomas that have not spread, a combined approach using surgery, radiotherapy and/or chemotherapy is often the course of action for treatment. Once the cancer has metastasised, various chemotherapy treatments are typically administered, which often have poor clinical efficacy and little benefit. As a result, angiosarcomas present a challenge for clinicians and patients because treatment options are limited and prognosis is bleak.

"At NCCS, we treat around 100 patients with sarcomas a year. With a deeper understanding of the tumours, we can better treat these group of patients," said Clinical Assistant Professor Jason Chan, first author of the study and Consultant Medical Oncologist, Division of Medical Oncology, NCCS.

For the study, 68 patients diagnosed with [angiosarcoma](#) at NCCS and Singapore General Hospital between 2000 to 2015 were identified. The research team analysed the tumour samples using multiomic sequencing, NanoString immuno-oncology profiling, and multiplex immunohistochemistry and immunofluorescence.

Multiomic sequencing, which is used to find associations or pinpoint biomarkers in biological entities, like an angiosarcoma, found that 50%

of the head and neck angiosarcomas exhibited higher tumour mutation burden (TMB) and UV mutational signatures. This indicated that half of the head and neck angiosarcomas may have developed as a result of UV exposure, and are likely to respond to a type of cancer treatment known as immune checkpoint inhibitors.

NanoString profiling, a technology that profiles [gene expression](#) in tumours, revealed that patients with angiosarcomas were grouped into three clusters. Patients in the third cluster had specific enrichment of immune cells and genes involved in immune-related signalling. Tumour inflammation signature (TIS) scores were also highest in this third cluster. Cluster one, like cluster three, was found to be predominantly head and neck angiosarcomas although with a lower inflammation footprint. Cluster two exhibited higher expression of genes that typically promote tumour growth and spread. They were also mainly secondary sarcomas, meaning they had previous exposure to certain environmental or genetic risk factors.

Recent clinical studies have shown that treating tumours with high TMB and TIS scores with immune checkpoint inhibitors showed promising results. By stratifying these 68 angiosarcoma patients, the study results suggest that checkpoint immunotherapy can be used for clusters one and three, while the tumour-promoting genes that are highly expressed in cluster two could be explored as potential treatment targets using targeted therapies.

"Our results are very promising, as they show that we can potentially use existing modes of therapy, like immunotherapy to treat a subset of angiosarcoma patients," said Clin Asst Prof Chan. "The next step will be to perform further molecular and immunological dissection of angiosarcomas to get more insight into how we can best use precision medicine to target these cancers."

The findings, published in *The Journal of Clinical Investigation* in October of this year, is testament that research can directly improve patient care.

"Understanding angiosarcomas will allow oncologists to treat their patients in a more targeted way and it is also a confirmation that NCCS is continuously conducting cutting edge, translational research that has an impact on patients," said Professor Soo Khee Chee, senior author of the study and Founding Director, NCCS.

The research team plans to further the study by investigating the molecular and genomic profiles of other sarcoma subtypes. This study is part of a plan to investigate rare cancers and establish NCCS as a leading global cancer centre.

**More information:** Jason Yongsheng Chan et al, Multiomic analysis and immunoprofiling reveal distinct subtypes of human angiosarcoma, *Journal of Clinical Investigation* (2020). [DOI: 10.1172/JCI139080](https://doi.org/10.1172/JCI139080)

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