PEDIATRIC ONCOLOGY REPORT 2021

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SIDRA MEDICINE

Pediatric Oncology Report 2021

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WELCOME MESSAGE

Sidra Medicine is the primary pediatric cancer care facility in Qatar since opening the oncology clinic in 2018. The overall incidence rates of childhood cancer vary between 50 and 200 per million children across the world, which puts Qatar with 126 per million children in 2019 right in the middle of that bracket. Cancer patients presenting at Sidra consist of mainly Arab and Asian ancestry, representing 70 and 25 percent of our patients, respectively. 39 percent of these patients are diagnosed with Leukemia, 14 percent have a diagnosis of a Central Nervous System malignancy, other common diagnosis in descending order of incidence are Lymphoma, Germ cell tumors, Neuroblastoma and Sarcomas. Which is, with the exception of germ-cell tumors, in line with what is observed in the Surveillance, Epidemiology, and End Results (SEER) Program from NCI/NIH, USA ("Surveillance, Epidemiology, and End Results Program" n.d.).

Dr. Wouter Hendrickx
Sidra Pediatric Cancer Registry & Biorepository Coordinator

The Sidra Pediatric Cancer Registry program was started along with the opening of the hospital. This close collaboration between the clinical and the research branches of Sidra Medicine, provides us with detailed understanding of our patient's characteristics and epidemiology.

The Sidra Pediatric Cancer Biorepository program was established soon after the registry and aims to consent as many of our patients possible to donate their materials no longer needed for diagnosis. This repository is what enable the researchers at Sidra Medicine to perform research most relevant to the local population. It is in this project that Sidra's outstanding Pathology department joins the effort to establish a true multidisciplinary environment.

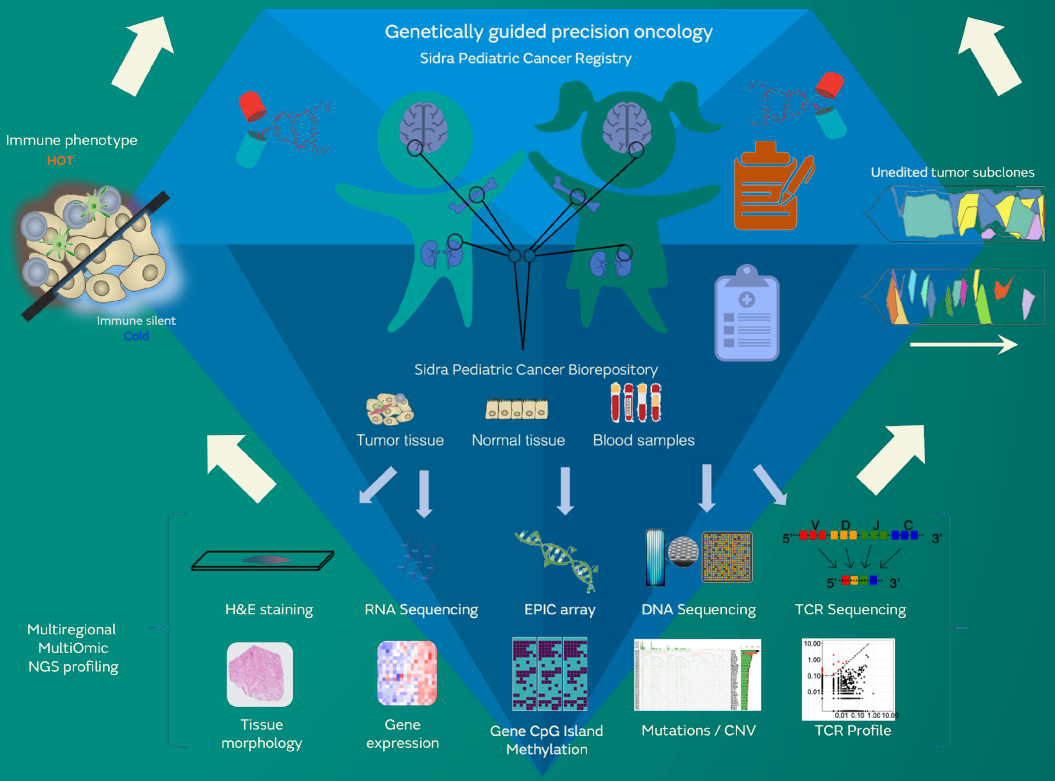
We believe these programs will allow pediatric patients to take advantage of the revolution in the treatment of cancer brought on by the applicationparticipating in local or international clinical trials of using targeted and immunotherapy. All while developingThey will allow us to gain a deeper understanding of the immune phenotype in these patients' tumors. Understanding the genetic determinants of the immune phenotypes in these cancer types,,

including, the variation in mutational load between patients, the intra-tumoral heterogeneity, and the characterization of the immune infiltrate,. This will provide us with insight in the potential for targeted and immunotherapy adaptation to these pediatric patients.

With this report we wish to share with the community this treasure of data that will enable us to, on the short term,

advice clinical grade diagnostics of rare targetable somatic mutation and facilitate patient enrollment in worldwide clinical trials. On the median term it will help us highlight new molecular targets in specific subgroups of patients, leading to the development of new biomarkers or therapeutic modalities. On the longer term this project will pave the way for personalized precision medicine for each pediatric cancer patient in Qatar.

PEDIATRIC CANCER DIAMOND



High quality samples, including blood samples, tumor and normal tissues, collected as part of Sidra's pediatric biobanking effort will be genetically and epigenetically profiled to capture the tumors immune phenotype and oncogenic heterogeneity of tumors. This multifaceted approach includes assessment of tissue morphology by hematoxylin and eosin (H&E) staining, gene expression profiling by RNA sequencing, methylome profiling by the EPIC array, somatic variant identification by DNA sequencing and SNP arrays, and T-cell receptor (TCR) profiling using the ImmunoSeq assay. A comprehensive picture of the tumor's immune phenotype and its somatic evolution will be delivered directly to the clinic, enabling genetically guided precision oncology.

MEET THE TEAM

CANCER RESEARCH INVESTIGATORS

Dr. Chiara Cugno, Dr. Wouter Hendrickx

Dr. Cristina Maccalli, Dr. Mohamed Haris

SIDRA PEDIATRIC CANCER REGISTRY AND BIOREPOSITORY COORDINATOR

Dr. Wouter Hendrickx

PATHOLOGY TEAM

Dr. William Mifsud, Dr. Erdener Ozer, Dr. Gordan Vujanic

ONCOLOGY HEMATOLOGY TEAM

Dr. Ayman Saleh, Dr. Ata Maaz, Dr. Naima Al Mulla

Dr. Chiara Cugno, Dr. Tayseer Al saad, Dr. Wafaa Abdelghani

RESEARCH LAB TEAM

Dr. Christophe Raynaud, Dr. Sathiya Narayanan, Apryl Sanchez

PRECISION RESEARCH INFORMATION MANAGEMENT ENVIRONMENT (PRIME) TEAM

Shafqat Baig, Mehshad Hamza

Mohammedhusen Khatib, Tariq Abu Saqri, Mohamed Jama

GENOMICS CORE TEAM

Lisa Sara Mathew, Li Liu, Kun Wang,

Guishuang Wang, Li Wang, Dr. Stephan Lorenz

CLINICAL RESEARCH COORDINATION

Blessing Dason, Aisha Khalifa, Asma Jamil

BIOINFORMATICS TEAM

Dr. Shimaa Sheri, Fazulur Vempalli, Dr. Tariq Masoodi

DIRECTOR SIDRA CANCER PROGRAM

Dr. Davide Bedognetti

NURSING TEAM

Mohammed Anas, Rachel Park

BREAKING THE STEREOTYPE

Family holds a significant place as a sacred institution within the Arab culture. In times of distress, such as the news of a child diagnosed with cancer, it is the family that pushes for the best possible treatment for rapid recovery. In Qatar, it has long been the belief that the best treatment for cancer is done abroad but as times are changing so are perceptions.

The division of Pediatric Hematology-Oncology at Sidra Medicine opened in May 2018. It was designed to care for all children and adolescents from birth up to 18 years of age. Sidra Medicine is revolutionizing the medical landscape of Qatar by building infrastructure that allows for state-of-the-art treatments using the best diagnostic tools available while also implementing refined research methodologies.

Dr. Davide Bedognetti- acting Executive Director of Translational Medicine and Director of the Cancer Program- is confident that the organization is internationally competitive and quickly gearing up to meet the standard of care and needs for clinical research. "Here at Sidra Medicine, we have the best pathologists and oncologists for pediatric cancer who have years of experience and are leading members in international committees on different tumors," said Dr. Bedognetti.

Being a hub for pediatric oncology gives the opportunity to treat every child diagnosed with cancer in Qatar. In the present, the aim is to characterize every single tumor at the deepest level of accuracy using advanced technology. Some patients do not respond to existing traditional cancer drugs and a personalized treatment solution is necessary. This is where research comes in- applying advanced diagnostics to propose effective treatments that are otherwise not available as a standard of care.

Dr. Ayman Saleh is the Division Chief of Pediatric Hematology-Oncology. Recently, he has noticed that more patients are seeking treatment for their cancer-stricken children at Sidra, rather than travelling abroad. This is directly related to the expanded services where Sidra Medicine started caring for these severe types of diseases. The oncology clinic is staffed with people from different backgrounds sharing their experience and skills to build a multidisciplinary atmosphere for medical innovation.

Sidra Medicine is establishing a bone marrow and stem cell transplant service for children in the same age group of newborns to 18 to be provided this service locally. There is also a specialized clinic to prepare and care for patients pre- and post-transplant. The clinic takes care of children within 100 days of their transplantation.

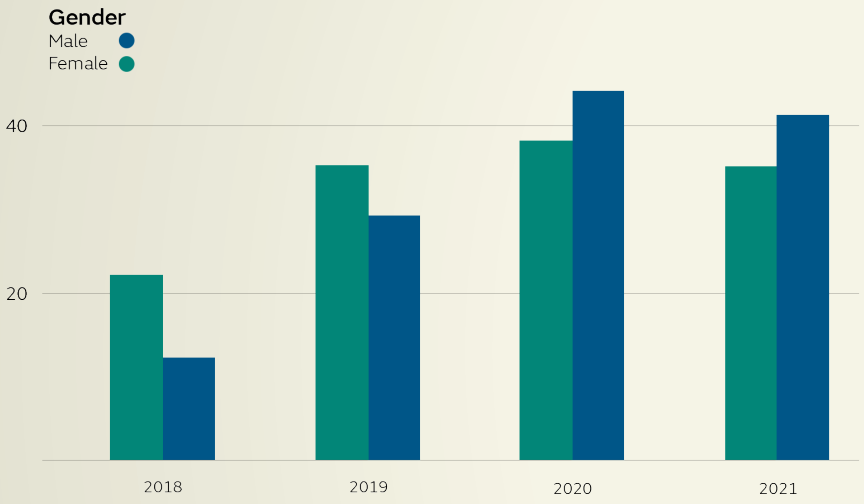
At Sidra Medicine, great care is taken for the timely diagnosis of a patient. The "expedite genomic oncology pipeline" (eGOP) is used when standard diagnostic means are insufficient to provide the optimal treatment. Results and diagnosis is conducted by the research team and then communicated within a few weeks to help guide the clinicians in deciding a personalized treatment for each specific patient. In 2022, the team was awarded the Internal Research Fund.

The awarded project introduces a new technology called spatial transcriptomic, which sees the localization of expression of different genes. This technology was recently acquired, and it is the first of its kind in the Middle East.

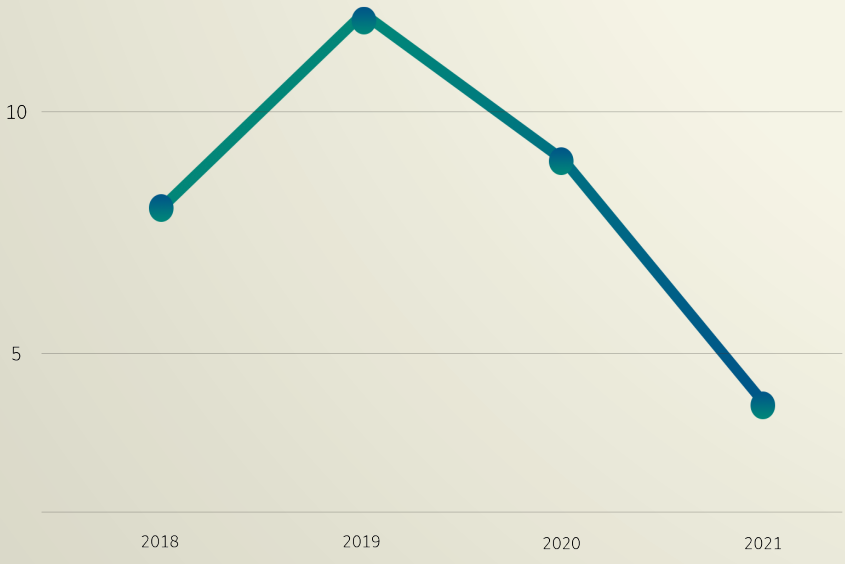
"We have active involvement from both clinical staff and research faculty that promotes better clinical trial units for pediatric cancer, while constantly maturing and customizing the program for targeted therapy and precision medicine," said Dr. Saleh. With the rate of progress and insight from professionals in the division, the future for Qatar's fight against cancer is in capable hands. The pediatric oncology-hematology division is making huge strides in breaking stereotypes to ensure residents receive world-class cancer treatment for their families without the need to travel abroad.

SIDRA MEDICINE PEDIATRIC CANCER REGISTRY

Cancer registry by diagnosis year

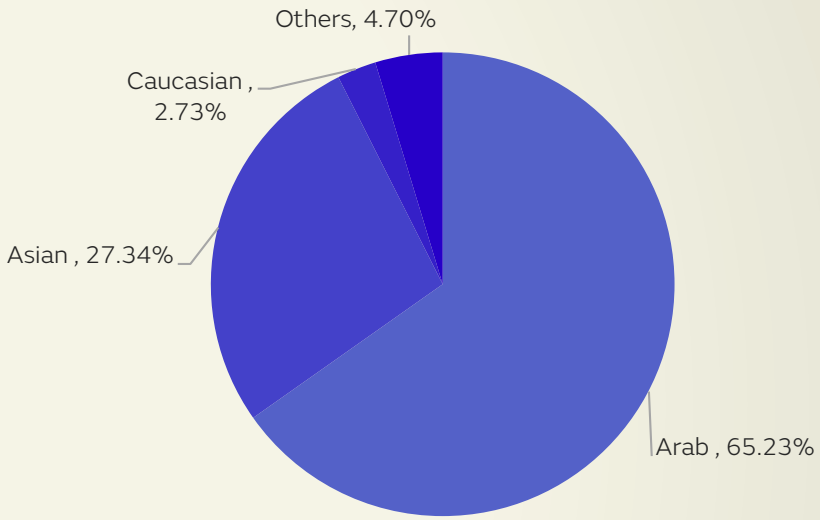


Cancer patients treated abroad by year

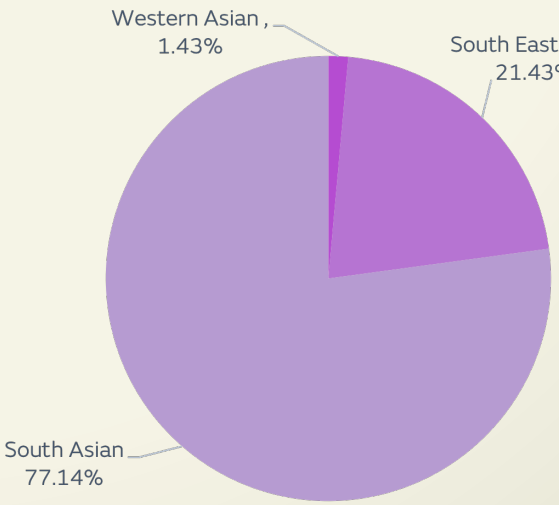


Ethnicity of our patients

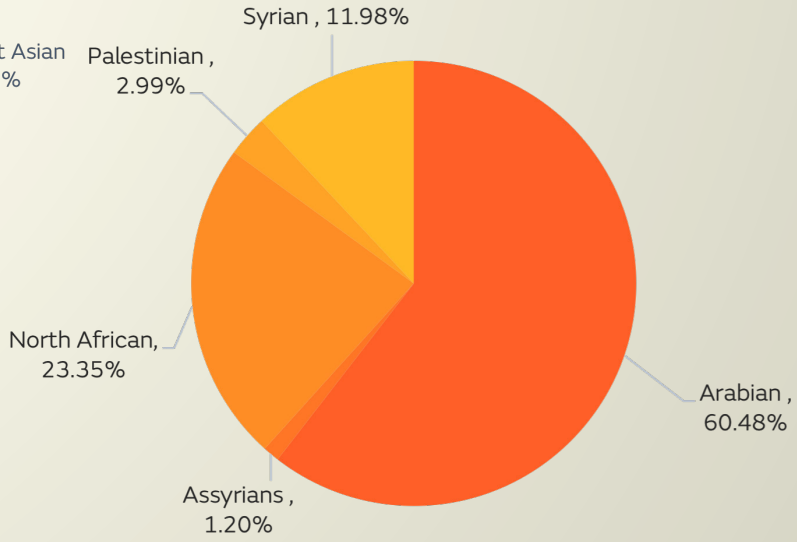
All population



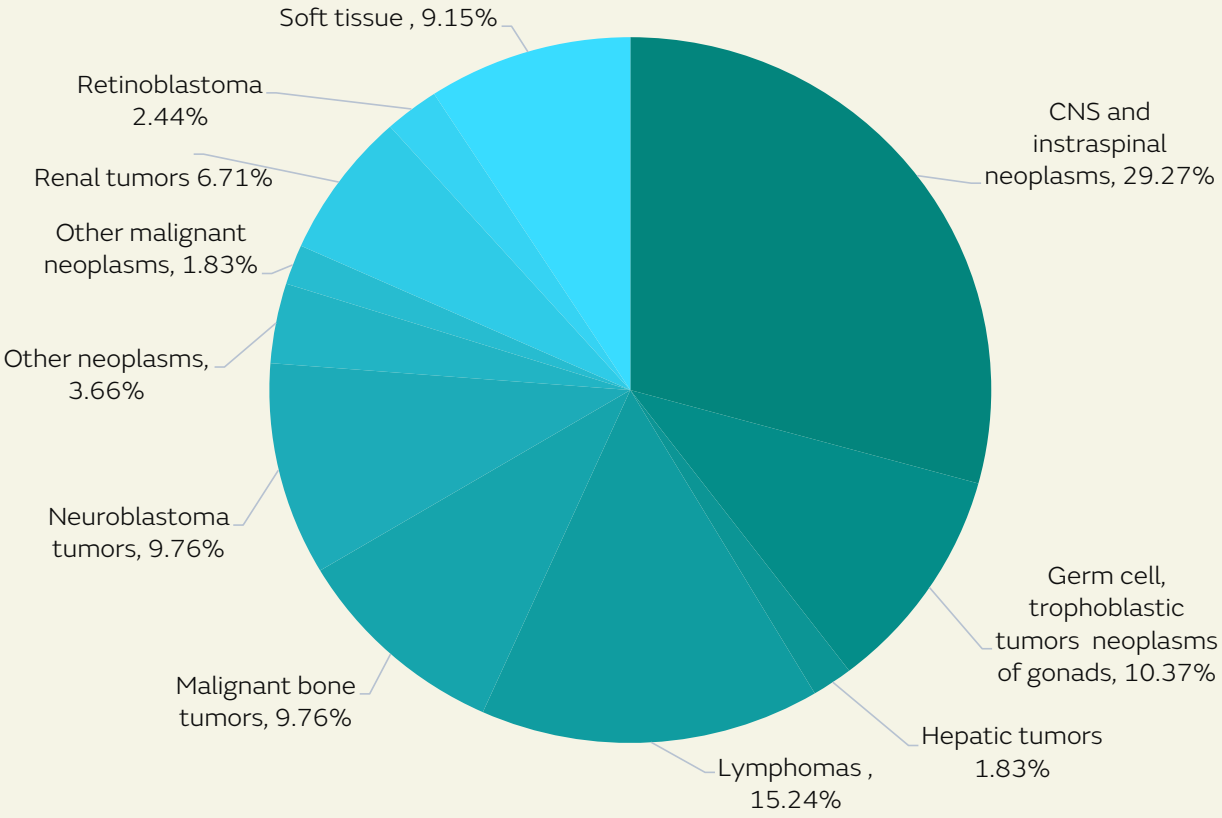
Asian population



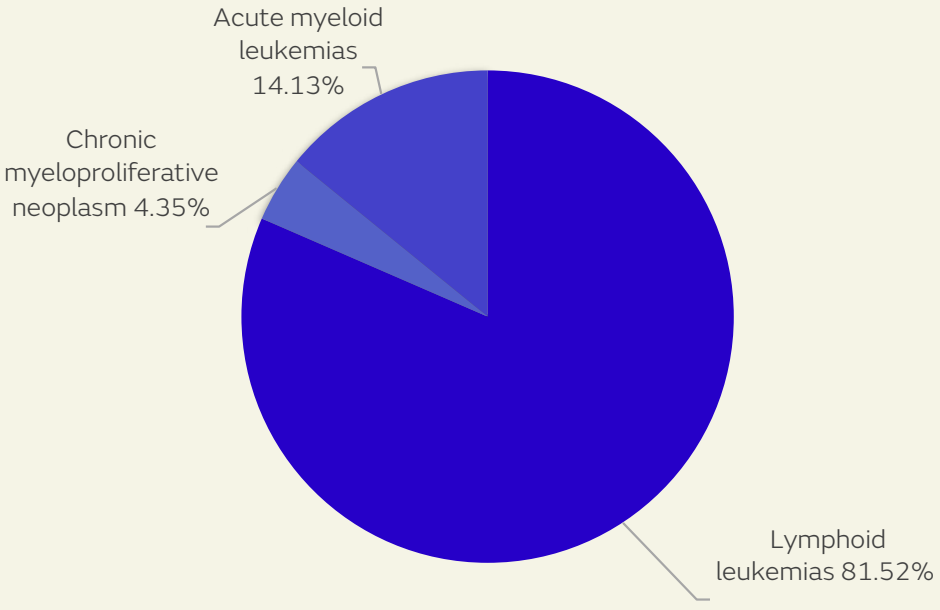
Arab population

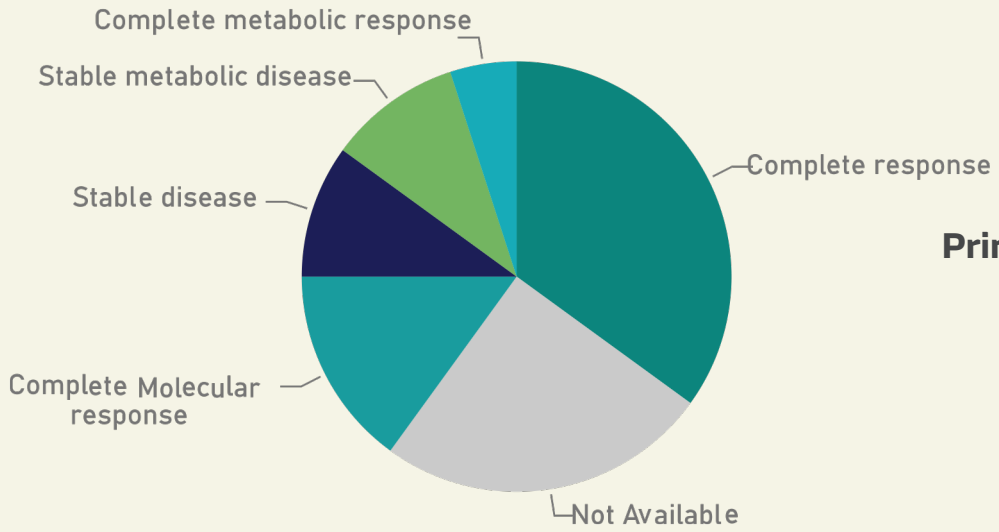


Types of Pediatric Solid Cancer Presented at Sidra Medicine 2018-2021

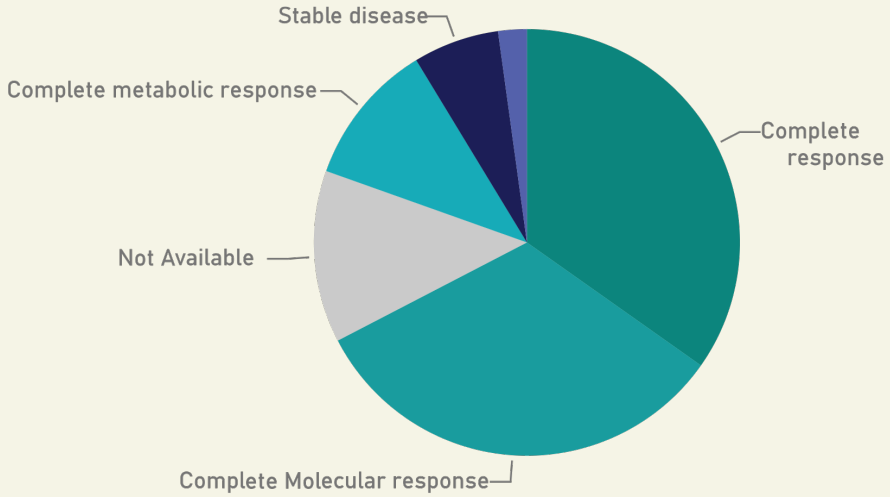


Types of Pediatric non-Solid cancer Presented at Sidra Medicine 2018-2021

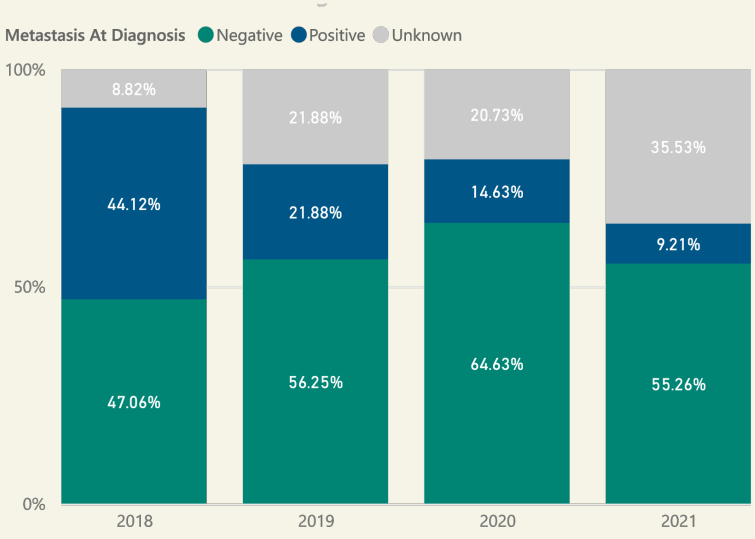




Primary response in 2018



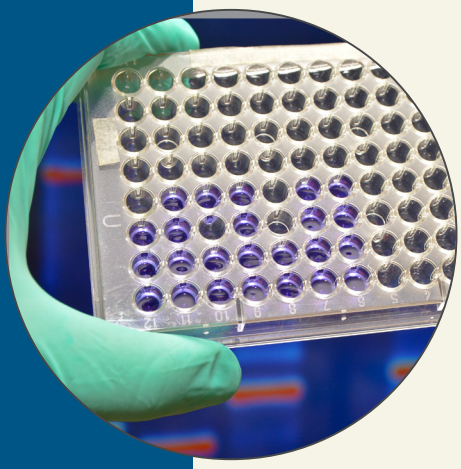
Primary response in 2019



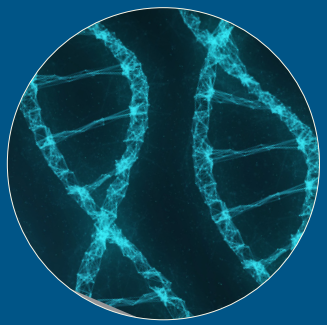
Patients with metastasis at diagnosis

A RACE AGAINST TIME

An hourglass can offer the right symbolism for the worldwide phenomenon that is cancer- a disease where time is of utmost importance. In children, some cancer cells can double in one day, so outcome is dependent on timely intervention and correct diagnosis. There are lives that hang in the balance where every hour that passes constraints the window of opportunity for effective medical response. In such a quagmire, personalized medicine may offer alternatives once thought to be unrealistic.



Dr. Chiara Cugno, director for the Advanced Cell Therapy Core at Sidra Medicine, is a pediatric oncologist and hematologist serving a dual role as both researcher and clinician. Her patient pool consists of pediatric cancer patients from all over Qatar that are referred to Sidra as the only third-level center for pediatric cancer in the country, covering treatment, diagnosis, and follow up. Dr. Cugno holds specific expertise in pediatric leukemia and hematopoietic stem cell transplantation and is a firm believer in advanced diagnostics and treatments as part of personalized medicine.



Genetic sequencing, a method to determine the entire genetic makeup of the cells, holds the promise tohelp treating and curing cancer patients. It underscores the importance of strengthening the relationship between both sides of medicine: the research and clinical. “Sequencing can allow to unveil tumor-specific mutations that can guide the applications of targeted treatments.

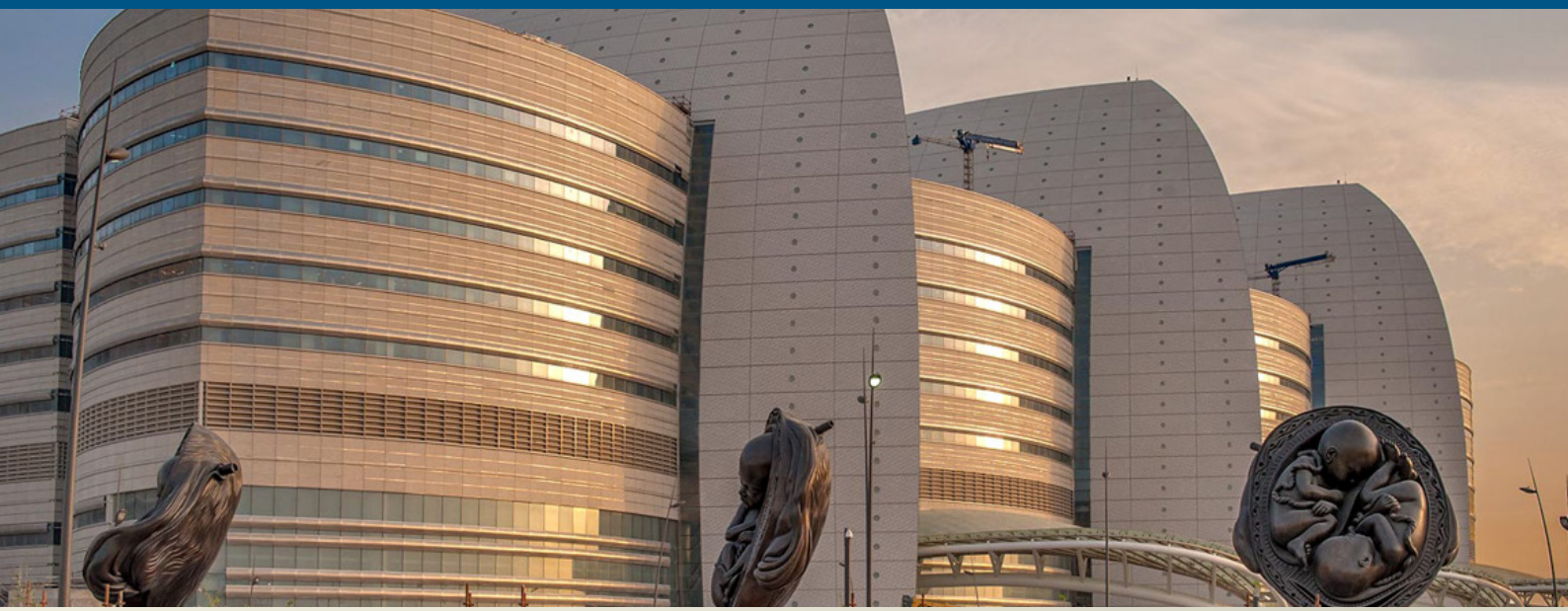
The clinical question that we have to answer is important, otherwise the researcher would venture blindly," says Dr. Cugno.

There are endless applications of personalized medicine but two are currently being established in treating pediatric cancer patients at Sidra. One is in the case of relapsed or refractory tumors (i.e., tumor recurring after treatment or not responding to therapy) which leave the patients with low chance of survival. There are now efforts being made to sequence the tumor tissue from the patient in a timely manner and identify potential mutations that can be treated by a specific drug. This is called targetable alteration. When standard treatments fail, this might offer an alternative weapon to use against cancer, which Dr. Cugno perceives as life-changing for the patient.

The second application is in the field of pharmacogenomics, i.e., how our genetic make-up influences the response to drugs. Our Team- says Dr. Cugno- is leading a research aimed to better understanding the response to chemotherapy in the Arab population.

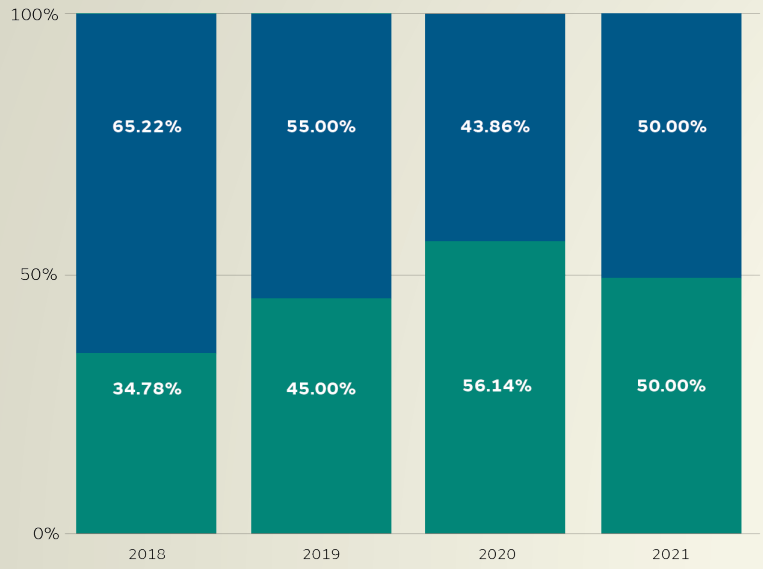
Common clinical experience shows that several children from this region suffer from severe toxicity following chemotherapy. There could be a genetic background predisposing to increased toxicity which might warrant a modulation the standardized treatment, and the customization of chemotherapy protocols for Arab ethnicity patients. This could lead to a more sustainable chemotherapy with less complications, shorter hospitalizations, and better final outcome.

Sidra Medicine is an internationally competitive organization and is proactive in the global fight against cancer where people like Dr. Chiara Cugno are leading the offensive. Personalized approaches are necessary weapons in the artillery for cancer treatment and can potentially provide more scientific breakthroughs in the future.



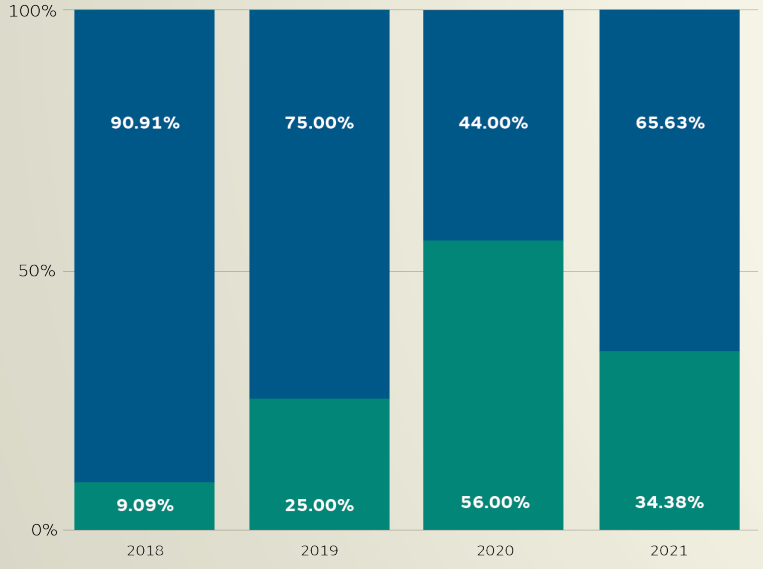
BIOBANK DATA

Consent rate of patients



Patient is Consented for Solid Cancer

No Yes



Patient is Consented for Non-solid Cancer

No Yes

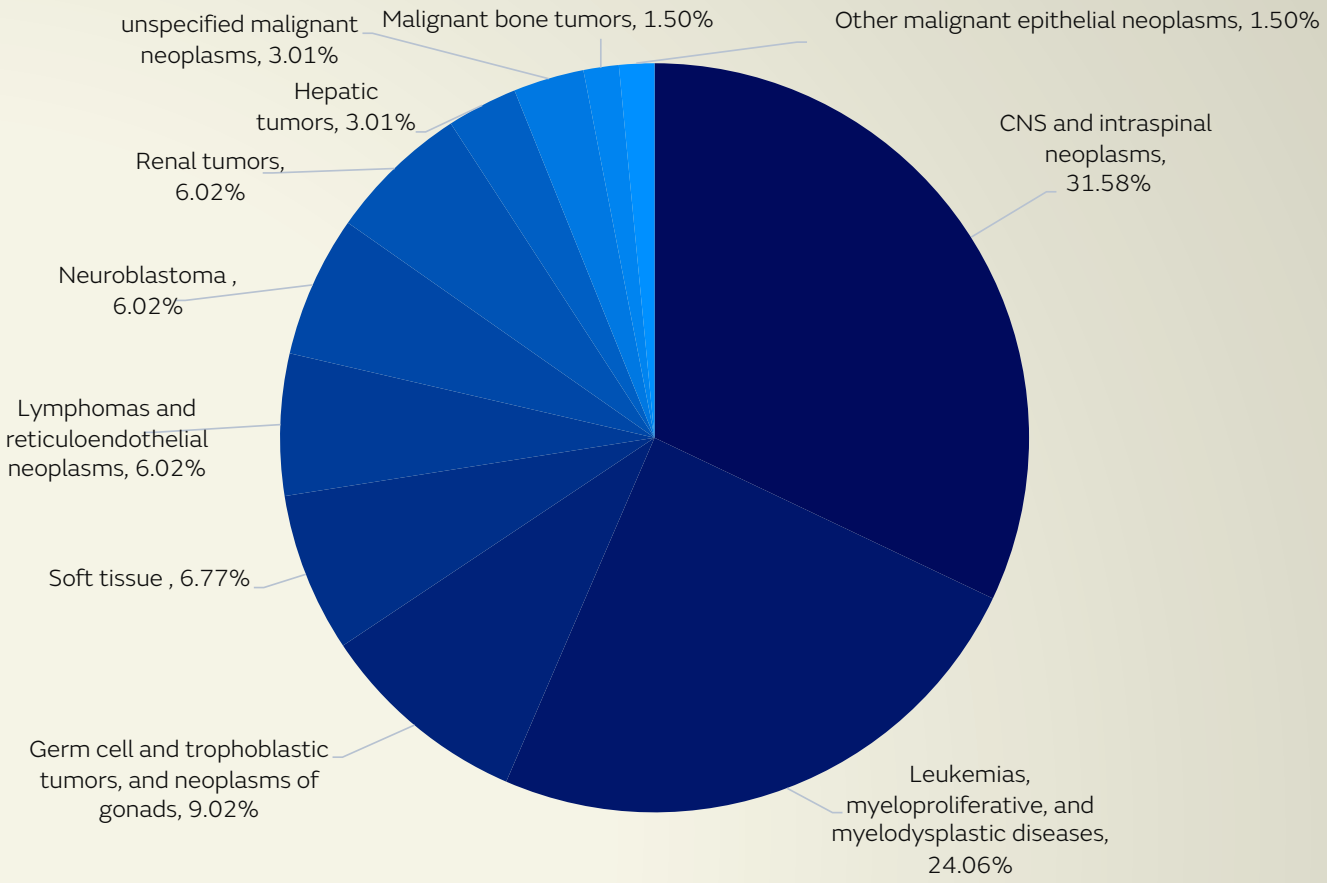
Blood Sample Available

61%

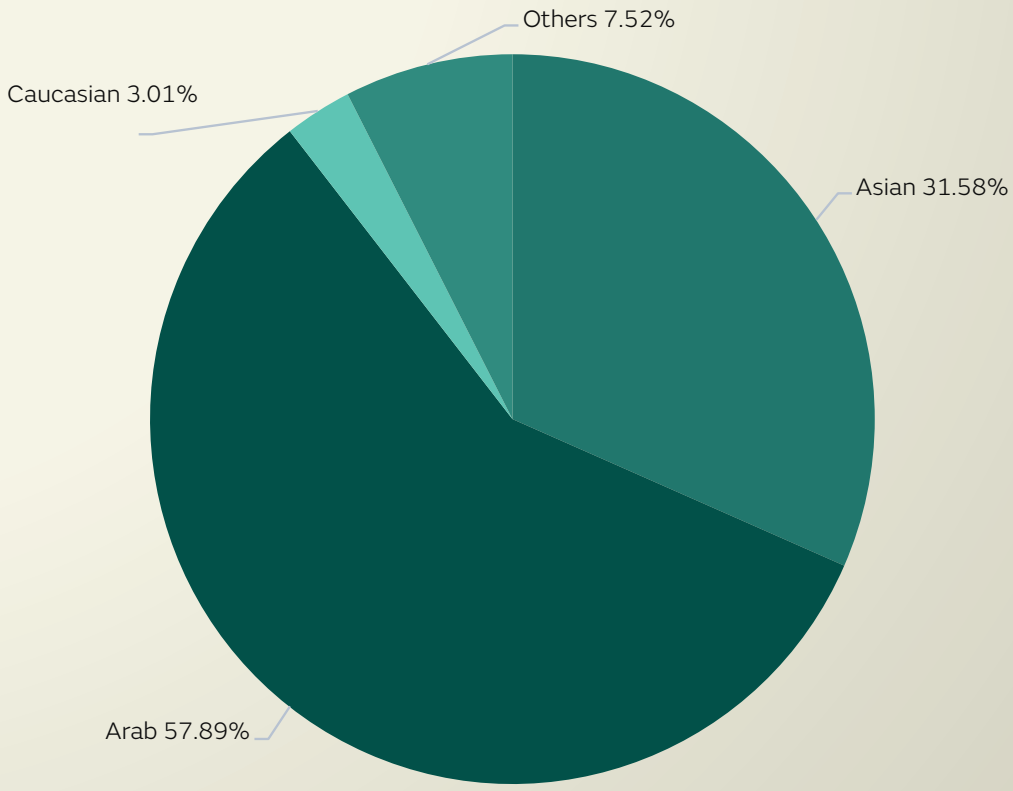
Tumour Sample Available

35%

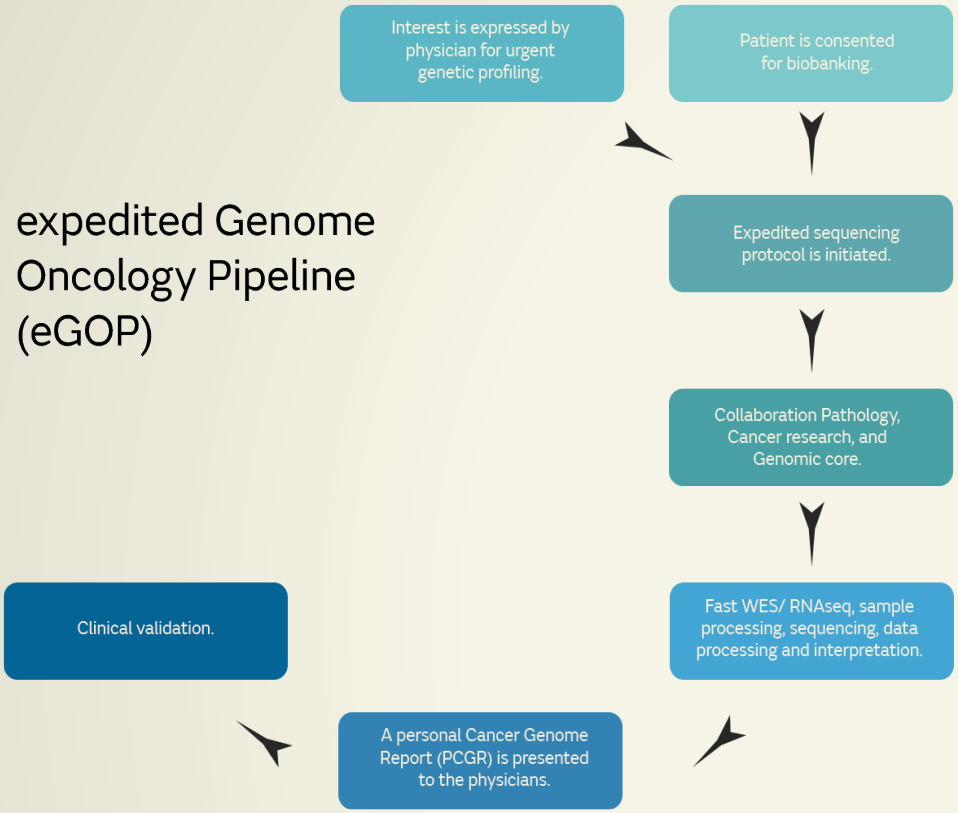
Types of pediatric cancer included in the Sidra Biobank



Biobank Ethnicity



EXPEDITED GENOMIC ONCOLOGY PROFILING (eGOP) FLOW CHART



The expedited Genomic Oncology Profiling (eGOP) procedure has been available since October 2020. This protocol is activated whenever the clinician (oncologist or pathologist) feels the need for an urgent molecular characterization to guide diagnosis and treatment. The eGOP procedure is typically requested for patients with extremely aggressive/relapsed cases and poor prognoses. The pipeline includes the rapid transfer of samples to research, DNA and RNA extraction, next generation sequencing, variant annotation, and generating the "Personal Cancer Genome Report" (PCGR) and Cancer Predisposition Sequencing Report (CPSR) to clinicians within 2-3 weeks.

eGOP Patients

Tumor type	Sample arrival	Date PCGR generation	Genes with actionable mutations
Brain (Glioma)	13-Oct-20	9 days	FGFR1
Brain (Ependymoma)	20-Oct-20	18 days	CDKN2C
Embryonal rhabdomyosarcoma	9-Dec-20	28 days	HRAS, BRAF
Embryonal rhabdomyosarcoma	15-Jun-21	12 days	NRAS, TTN, CTNNB1, NUP98, FBXW7
Alveolar rhabdomyosarcoma	8-Nov-21	11 days	None
Alveolar rhabdomyosarcoma	30-Mar-22	14 days	None
Rhabdoid tumor	31-Aug-22	17 days	SMARCB1
Brain (Glioma)	31-Aug-22	__	Under process

CANCER PUBLICATIONS 2018 - 2021

PEDIATRIC CANCER

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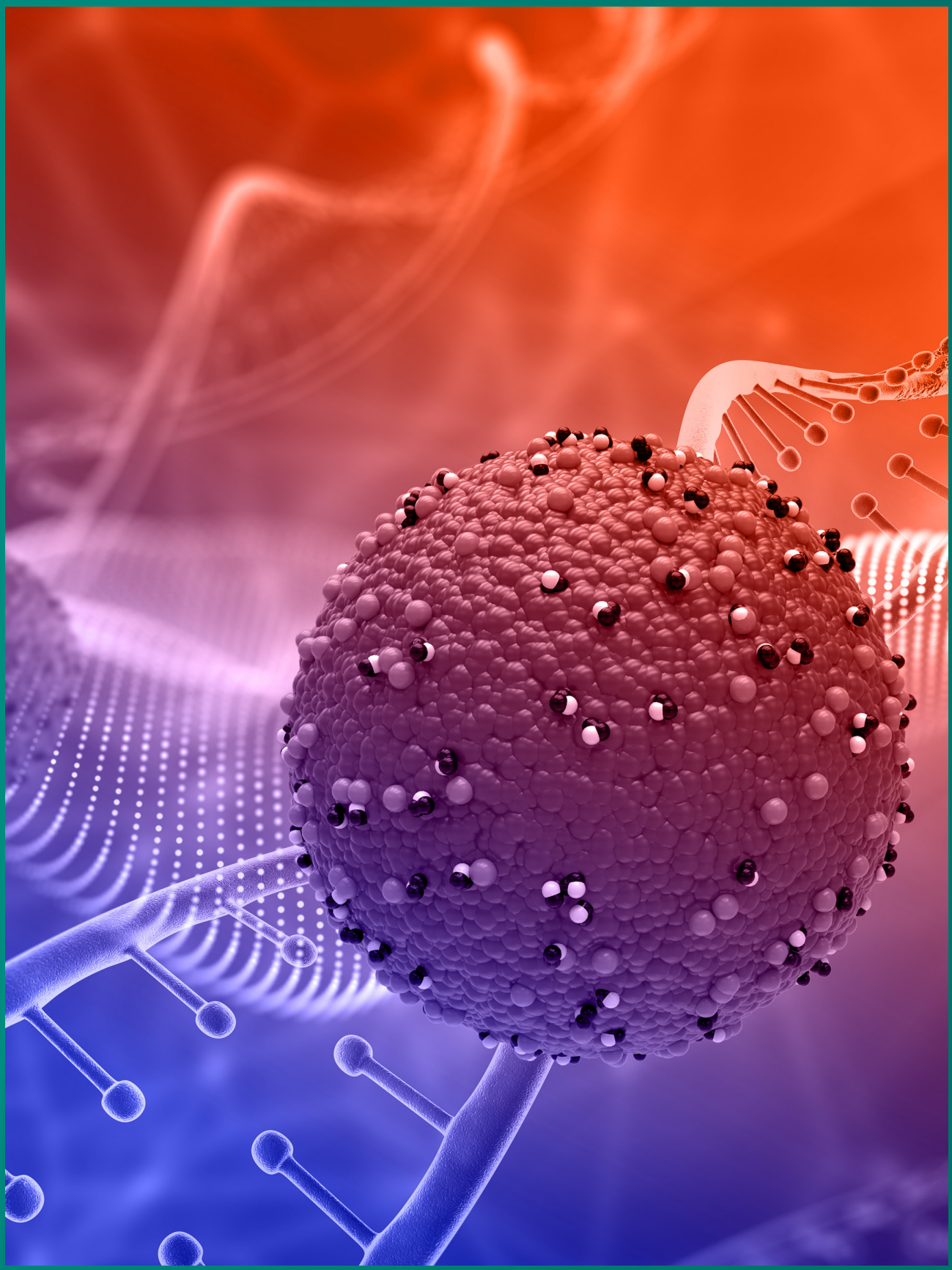

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