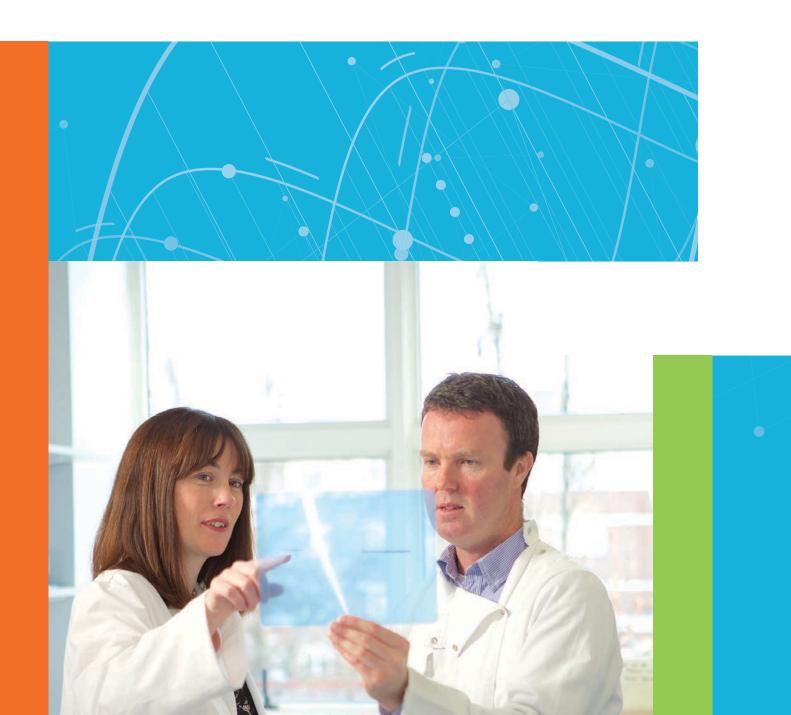


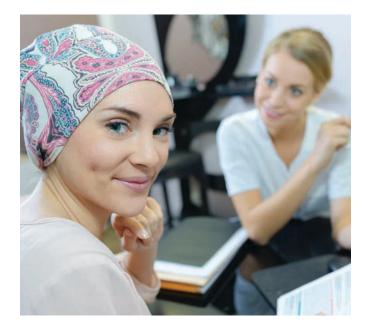
Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin



THE TRINITY ST. JAMES'S CANCER INSTITUTE

WORLD CLASS SCIENCE FOR BEST PATIENT OUTCOMES











TRINITY ST. JAMES'S CANCER INSTITUTE



TRINITY ST. JAMES'S CANCER INSTITUTE

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FROM THE PROVOST OF TRINITY COLLEGE DUBLIN, DR PADDY PRENDERGAST AND THE CEO OF ST JAMES'S HOSPITAL, MR LORCAN BIRTHISTLE

On the 17th of October, 2016, Trinity College Dublin and St. James's Hospital, with the participation of Minister for Health, Simon Harris TD, announced our intention to jointly establish a new Cancer Institute.

Since then our two institutions have worked together to consolidate cancer activities in the Trinity St. James's Cancer Institute. Our focus has been on harnessing our considerable capacity and strengths to improve the outcomes and experience for cancer patients. We will improve outcomes and experience for patients by providing research-led diagnosis and treatment, by developing a better understanding of cancer through interdisciplinary research and by educating the next generation of cancer clinicians, scientists and other healthcare professionals. Our Cancer Institute supports dissemination and other programmes with respect to the cause, diagnosis, prevention, treatment and survivorship of cancer and the continuing care of cancer patients and their families.

St. James's Hospital is a centre of excellence for the delivery of cancer care in Ireland, comparable in scale and complexity to other major European centres. It is a fully public hospital, providing equal access to all. St. James's Hospital is one of eight cancer centres in Ireland, and is the largest in terms of activity,





which encompasses 6 out of 8 national cancer programmes and a number of regional cancer services. The hospital campus houses the St Luke's Radiation Oncology Network and the largest medical oncology programme nationally, as well as the Wellcome Trust/ Health Research Board-funded Clinical Research Facility. The campus will also be home to the new National Children's Hospital, where all child and adolescent cancers will be managed and cared for.

The world class knowledge in Trinity's leading research institutes in nanoscience, biosciences and translational medicine when integrated with the clinical excellence and cancer expertise of Ireland's largest hospital will greatly decrease cancer incidence and improve patient experience. The focus on increasing the level of clinical trials will ensure that patients receive the best possible outcomes. Furthermore the extensive educational programs at undergraduate, post graduate and CPD levels will ensure that the Institute will produce the clinical talent to meet Ireland's future needs.

Our commitment is to harness all of the very considerable expert clinical and scientific resources we have available to us to benefit cancer patients and their families locally, nationally and internationally.

Dr Paddy Prendergast Provost of Trinity College Dublin

Mr Lorcan Birthistle CEO of St James's Hospital



Ultimately, the Trinity St. James's Cancer Institute will provide national leadership to decrease cancer mortality and continuously improve the cancer patient's experience and outcome.





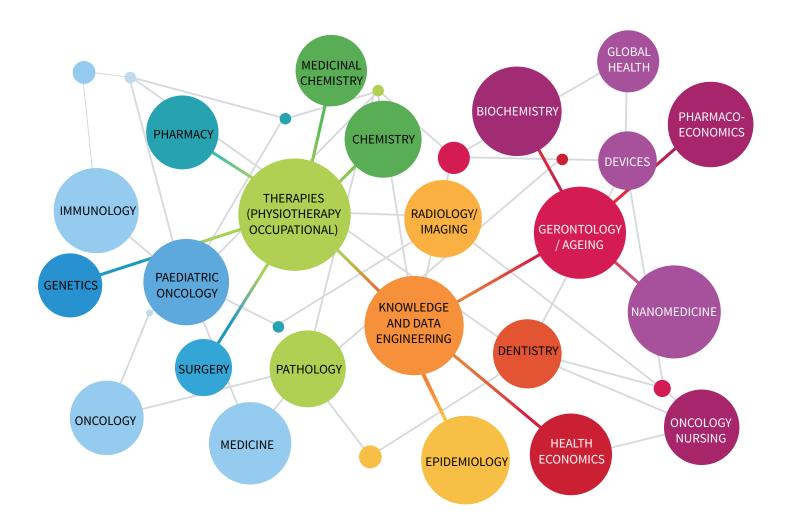
The Trinity St. James's Cancer Institute builds on the long tradition of outstanding comprehensive cancer care delivered at Ireland's largest academic health campus at St. James's Hospital in central Dublin, with the research and educational excellence of Trinity College Dublin, Ireland's leading university. Our mission is to integrate innovative and ground-breaking cancer science with compassionate, multi-disciplinary, patient focussed clinical care through translation of key research findings into incremental advances in the prevention, diagnosis and treatment of cancer.

The ambition of the Trinity St. James's Cancer Institute is to develop a comprehensive cancer centre with national services in genomics and immunology, to become a leading international institution for translational cancer research, and through its structure and national and international collaborative network to represent a standard bearer for Ireland internationally. We will continue to work across academia, and will align the efforts of government, industry, philanthropy and patient groups.

Ultimately, the Trinity St. James's Cancer Institute will provide national leadership to decrease cancer mortality and continuously improve the cancer patient's experience and outcome.

Prof Paul Browne

Director, Trinity St. James's Cancer Institute



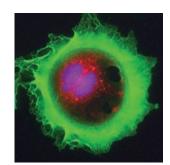
EXECUTIVE SUMMARY

In Ireland, almost **40,000** new cases of cancer are diagnosed each year; this number is expected to rise to over **55,000** per year by 2040 (NCRI, 2016). Cancer deaths alone result in lost productivity of 1.4% of Ireland's GDP annually, projected to total **€73 billion** (2011-2030). Cancer is a leading cause of death worldwide. One out of every two people will develop cancer and two out of every three people will live and work with someone with it. The National Cancer Registry estimates that the incidence of cancer in Ireland will increase by 50% from 2010 to 2025 and by 100% by 2040.



The development of the Trinity St. James's Cancer Institute is one of the most significant developments in Ireland's response to cancer for a generation: an entirely new distinctive vision that integrates basic, translational and clinical research, together with education to improve the prevention, detection and cures for cancer and to make cancer a manageable chronic disease.

St. James's Hospital is currently the largest cancer centre in Ireland, with over 4,000 new cancer cases annually. It has a well-developed highly specialised multidisciplinary team (MDT) model, and houses several national and supra-regional centres, notably for bone marrow transplantation, oesophageal and gastric cancer, lung cancer, gynaecological cancer, head and neck cancer, and lymphoma/leukaemia. The budget for cancer care from the Health Services Executive (HSE) in 2016 was €84 million, representing one quarter of the

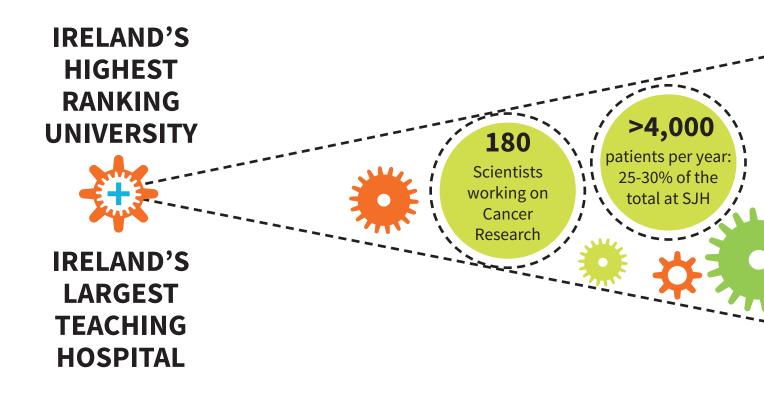


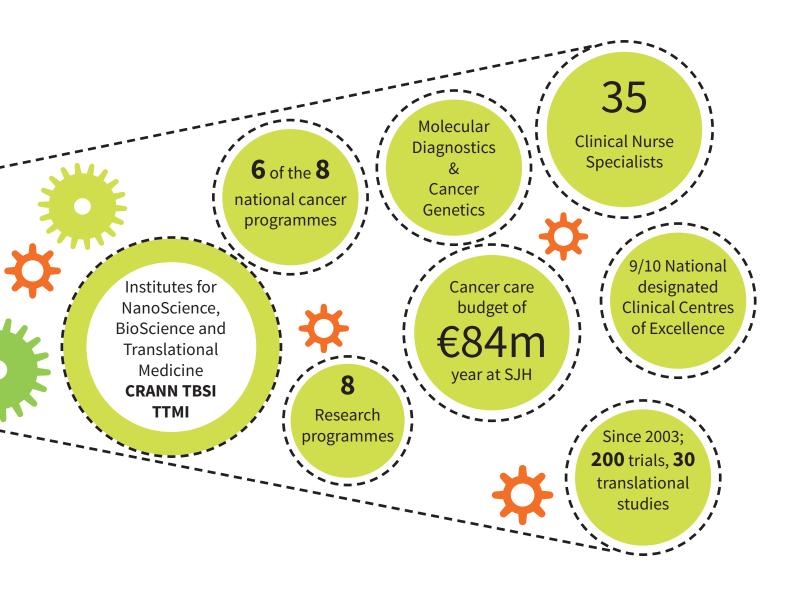
hospital's annual budget. Cancer represents between 25-30% of daily activity in the hospital, with all patients, regardless of socio-economic or health insurance status, treated within the same facilities, akin to the leading European centres.

To date, there is no comprehensive cancer centre in Ireland. Exemplar models of comprehensive cancer centres exist in the US and Europe, and there is a need and opportunity for St. James's Hospital (SJH) and Trinity to lead the development of such a comprehensive cancer centre in Ireland for the ultimate benefit of all people on this island. Trinity St. James's Cancer Institute is currently operating as a virtual entity consolidating activities across clinical cancer care, translational research and oncology education.

In July 2017, the Government announced National Cancer Strategy 2017-2026, in which the need for at least one comprehensive cancer centre was highlighted and the key role such a centre will play as part of the cancer strategy's delivery. To support this, the National Development Plan announced in February 2018 highlights the comprehensive cancer centre as one of its proposed capital investment projects.

This Cancer Institute development is in line with the Government's strategy as we proceed with the project implementation. This document outlines the existing key elements of the Institute from research to clinical trials, to education to industry engagement and to patient care.





"WITHOUT THEM, I REALLY DON'T KNOW WHAT WE WOULD HAVE DONE. THEY HELPED US THROUGH SO MUCH"

Family member supported by Palliative Care team

TRINITY ST. JAMES'S CANCER INSTITUTE

The vision of the Trinity St. James Cancer Institute is to integrate innovative and ground-breaking cancer science with patient-focussed clinical care through translation of key research findings into incremental advances in the prevention, diagnosis and treatment of cancer; providing national leadership to decrease cancer mortality and improve survival of patients with cancer in Ireland and internationally.

Strategic Objectives

- Enhance the multidisciplinary team model to improve patient care and outcomes
- Develop a national hub for Molecular Diagnostics and Cancer Genetics
- Expand clinical trials and introduce early phase clinical trial programme
- Establish a structure for dedicated education and training of cancer health care professional and scientists
- Develop the profile of Trinity St. James Cancer Institute as an exemplar of research integration with cancer care





At present there are over 180 scientists actively working on cancer projects as part of a vibrant interdisciplinary research community.

The cancer programme at Trinity and St. James's spans genetic and molecular research to clinical and translational clinical trials. At present there are over 180 scientists actively working on cancer projects as part of a vibrant interdisciplinary research community. The integrated programme unit for each cancer type is well developed and is underpinned by well-established corporate and executive structures including clinical directorates and cancer site-specific interdisciplinary teams, as well as a well-structured collaborative interface with Trinity College in cancer research and education. Cancer care follows well-defined cancer care pathways, with comprehensive multidisciplinary team (MDT) processes in place. St. James's Hospital also has an active palliative care unit on site powering purposeful and progressive relationships with hospices in the Dublin metropolitan area and cancer care facilities nationally.

Eight research programmes have designated clinical and scientific leads to organise and drive research for this area. Underlying these are translational research themes (cancer biology, cancer genomics, diagnostics, tumour immunology and immunotherapy, therapeutics and drug discovery, cancer prevention, lifestyle/obesity, survivorship and health economics), which provide the structure for multidisciplinary projects with researchers from Trinity Biomedical Sciences Institute (TBSI), Smurfit Institute for Genetics, The Centre for Research in Nanomaterials and Nanodevices (CRANN) and the Trinity Translational Medicine Institute (TTMI).



CAM (Centre for Advanced Medical Imaging)

CAMI is the first dedicated MRI research unit in Ireland, and was grant funded by The Health Research Board

CAMI provides state-of-the art functional and structural imaging to a wide range of SJH & TCD researchers. Research interests include whole body staging of cancer, functional assessment of tumours compared to positron emission tomography (PET) and early detection of disease response to chemoradiotherapy. Reflecting the broad cross-section of patients on the SJH site, research studies spanning all ages of life from birth to end of life have been performed. CAMI is situated in the main hospital and has full access to all support services and can carry out studies on all clinical and research subjects regardless of clinical status

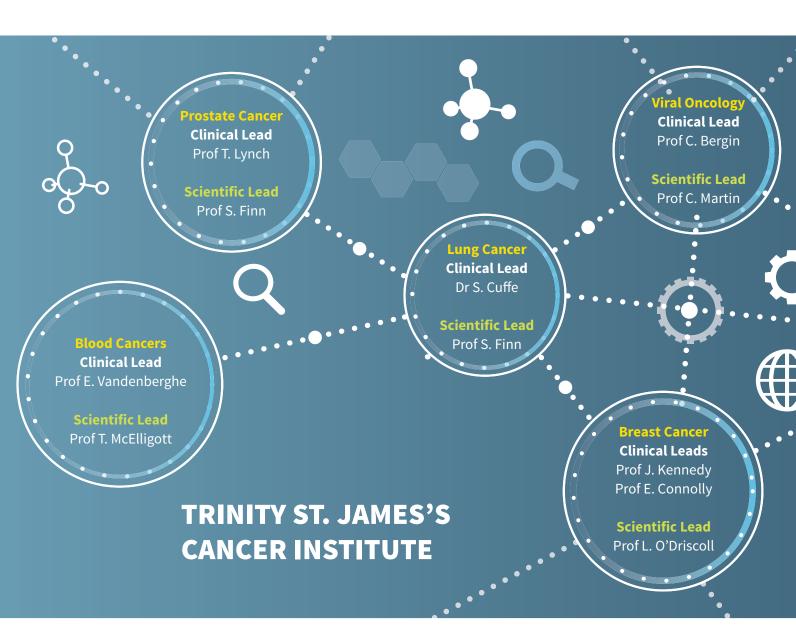


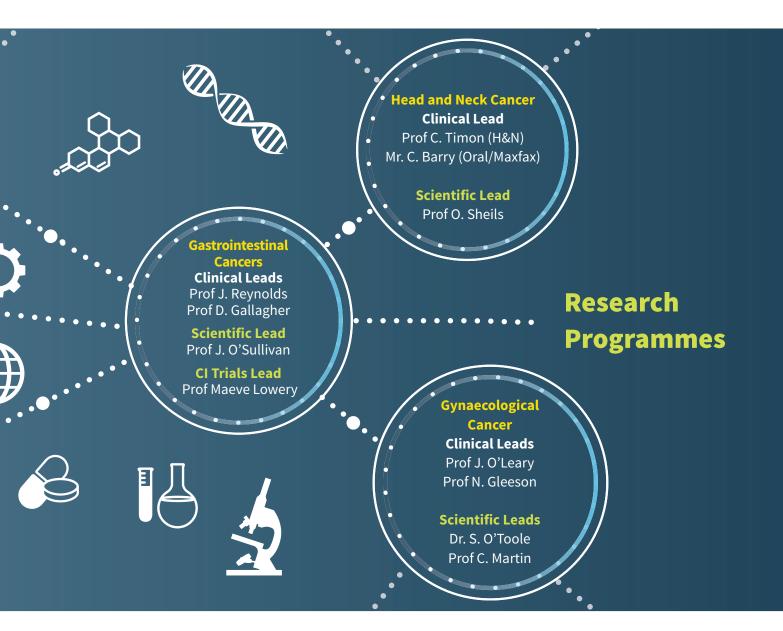


Research

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National Children's Hospital

CRANN Nanoscience Institute



Trinity Biomedical Sciences Institute

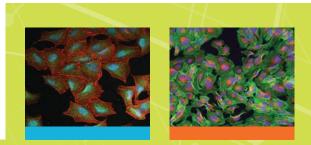
| Trinity Translational Medicine Institute



Translational research

Translational research on the St. James's Hospital campus is conducted principally in the Trinity Translational Medicine Institute (TTMI). This facility houses over 50 Principal Investigators and 150 scientists. It has 725 m2 of research facilities on campus at St. James's and is easily accessible from the operating theatres and endoscopic centre, which greatly enables translational research and supports clinical service delivery, diagnostics and patient advocacy.

Under the directorship of Prof Orla Sheils, TTMI forms a pivotal role in aligning research between TBSI, the affiliated hospitals and the Clinical Research Facility (CRF). This natural bridge of TTMI provides a seamless transition between the basic research excellence in facilities like TBSI and CRANN to the CRF. TBSI



has a suite of world-class core technologies including transgenics, category 3 facility, bioresource unit, NMR, TEM, among others. These facilities dovetail neatly with those of TTMI, which houses a genome sequencing laboratory, high content analysis and LBCAM (along with additional bioresource unit, biobanking facilities, category 3 lab and flow cytometry).

This cross-city cancer ecosystem allows for diverse research groups to collaborate in a truly translational fashion.





Audit and research activities are of paramount importance to the nursing team in St. James's Hospital (SJH) and evidence of it are apparent at different levels throughout the organisation.





Audit and Research is one of the core competencies for Clinical Nurse Specialists and Registered Advanced Nurse Practitioners throughout the organisation and priority is given to this aspect of their role. Nurses in other nursing roles are also encouraged and supported to partake in audit and research activities.

SJH has a research collaborative agreement with the Trinity Centre for Practice and Healthcare Innovation since 2012. The aim of this agreement is to enhance the research capacity of nurses working in SJH.

The Cancer Nursing Research Group within the organisation comprises of a Director of Research from the School of Nursing Trinity College Dublin (TCD), and a researcher from the Nursing Research Collaboration Group within TCD and nurses working in cancer care across SJH. The group actively encourages and support nurses to become proficient and confident in academic writing, critiquing literature, undertaking research and publishing their findings.

Cancer nursing staff continue to represent SJH and their cancer speciality at both national and international cancer conferences thereby keeping abreast and participating in current standards of cancer care.

From an international nursing perspective in 2018 the European wide ESMART research project was rolled out in SJH. This is a European nursing study monitoring chemotherapy toxicities and their effect on a patient's quality of life during chemotherapy treatment. Recruitment for the study was undertaken in the Haematology, Oncology Day Centre (HODC) and Donal Hollywood Ward (a specialised cancer ward in SJH).





"THE BREAST CANCER NURSES ADVOCATE FOR THE PATIENTS. I FOUND THE HOSPITAL ABSOLUTELY AMAZING..FROM MY SURGICAL TEAM TO MY ONCOLOGY TEAM TO RADIOTHERAPY TEAM – THERE WAS NOTHING MORE THEY COULD HAVE DONE FOR ME AND I DON'T SAY THAT LIGHTLY"

Jennifer, breast cancer patient

TSJCI Academic Collaborators (selection)





Clinical Lead Dr Sinead Cuffe Consultant Medical Oncologist, SJH



Scientific Lead Prof Stephen Finn Principal Investigator, TCD; Consultant Pathologist, SJH; Co-Director, Cancer Molecular Diagnostic Lab, SJH

Research Programmes

Lung Cancer

Lung cancer continues to increase globally. In Ireland, it accounts for more deaths per year than breast, prostate and colon cancers combined. SJH is the largest and one of the most comprehensive centres for the diagnosis and treatment of lung cancer in Ireland. Complementing our lung cancer service and established in 2004, the Thoracic Oncology Research Group has been at the forefront of translational lung cancer research, with specialist interests in novel targeted therapies, epigenetics, inflammation, drug resistance, cancer stem cells, immuno-oncology and molecular diagnostics. Clinical studies focusing on the potential use of 'liquid biopsies' in the diagnosis and treatment monitoring of patients with lung cancer form an integral part of research within the group. The SJH lung biobank is a leading contributor to a number of large pan-European lung cancer (and mesothelioma) efforts such as ETOP (European Thoracic Oncology Platform), supporting molecular epidemiology projects in collaboration with a series of leading hospitals and clinics across Europe and beyond.



Clinical Lead Prof Thomas Lynch Consultant Urological Surgeon, SJH



Scientific Lead Prof Stephen Finn Principal Investigator, TCD; Consultant Pathologist, SJH; Co-Director, Cancer Molecular Diagnostic Lab, SJH

Prostate Cancer

The Translational Prostate Cancer Group, Department of Histopathology & Morbid Anatomy, is based in the Sir Patrick Dun Laboratories on the St. James's Hospital campus. This translational multi-disciplinary research group consists of pathologists and scientists, with strong links to the physiotherapy team. The group are heavily involved in clinical trials through Cancer Trials Ireland, undertaking the translational research component of trials such as iPROSPECT and Radium 233/Enzalutamide. The group conceived and completed the first exercise intervention trial for patients with advanced prostate cancer. In addition to their exercise intervention studies, the group has four other broad research themes (i) The role of lipids in treatment response and prostate cancer-specific outcomes, (ii) Inflammatory based mechanisms for Circulating Tumour Cell (CTC) immune evasion in prostate cancer, (iii) Non-coding RNA signatures as diagnostic and prognostic tools in prostate cancer, (iv) Real world application of liquid biopsies as a means to track the natural evolution of prostate cancer and identify mechanisms of drug resistance.



Clinical Leads Prof John O'Leary Prof../Chair of Pathology TCD, Director of Pathology, The Coombe Women and Infants University Hospital and Consultant Histopathologist SJH, Dublin



Scientific Leads Dr. Sharon O'Toole Senior Research Fellow (Ovarian Cancer), TCD



Prof Noreen Gleeson Consultant Gynaecological Oncologist & Pelvic Surgeon, SJH



Prof Cara Martin Asst. Prof Molecular Pahtology, Tumour Biology and Cancer Screening (HPV-associated cancers), TCD

Gynaecological Cancer

The Departments of Histopathology and **Obstetrics and Gynaecology** work in close collaboration with clinical colleagues in SJH and the Coombe Women and Infants University Hospital in the areas of gynaecological cancer and pre-cancer. SJH Gynaecological Cancer Care Centre is the largest provider in the Republic of Ireland of treatment for gynaecological malignancies, providing a regional and national service accredited by the National Cancer Control Programme.

The departments lead several research consortia including;

- CERVIVA is a multidisciplinary research consortium working on health services and patient-focussed research in the area of HPVassociated cancers. CERVIVA research focusses on early detection and prevention of HPV-associated cancers from 4 main thematic areas; Molecular Epidemiology, Health Economics, Health Psychology and New Technologies.
- INNOVATION the Irish National Network for Ovarian Cancer Collaboration was established with a mission to integrate patient clinical pathways with cutting edge research to improve diagnosis and treatment of ovarian cancer.

A large programme in cancer metastasis in collaboration with industry is focussed on deciphering the most clinically and biologically relevant circulating tumour cells in cancer metastasis. Our other research programmes include isolation and targeting of cancer stem cells, the use of nanotechnology for ovarian cancer treatment and thrombosis in gynaecological cancer. Public outreach and advocacy form an integral part of the research programmes and close links have been established with a number of patient groups and charities.

"I HAD MY TRANSPLANT IN BURKITT'S WARD HERE IN JAMES'S. THEY ARE ABSOLUTELY FANTASTIC, THE CARE, THE ATTENTION. THEY ABSOLUTELY THINK OF EVERYTHING"

Caroline, blood cancer patient



Clinical Lead Prof Elisabeth Vandenberghe Consultant Haematologist, SJH; Co-Director Cancer Molecular Diagnostics Lab



Scientific Lead Prof Tony McElligott, Asst. Prof Molecular Haematology

Blood Cancers

Blood Cancer Research combines therapeutic clinical trials (including stem cell transplantation (SCT)) with translational research to define the molecular and cellular basis of blood cancers and provide a rational basis for 'precision medicine.' This has resulted in the introduction of companion diagnostics and targeted drugs such as imatinib, ibrutinib and eculizimab into routine Irish practise and is based on national collaboration (eg Cancer Trials Ireland) and internationally. The National Adult Allogeneic SCT unit at St James Hospital has developed a cellular therapeutic programme investigating immunomodulation in umbilical cord blood and is commencing a chimeric antigen receptor (CAR)-T programme in 2019, aligning with the UK Impact clinical trials group and European Blood and Marrow Transplant (EBMT) Registry

Current translational interests include the genetic characterization of myeloid disorders, molecular epidemiology of chronic lymphocytic leukaemia, development of NGS-based analysis in diagnosis and treatment determining mutations and the immunophenotypic and molecular tracking of disease through therapy. Pre-clinical projects include the analysis of immunotherapy and small molecules in vitro and the mediators of leukaemic cell homing/trafficking which is facilitated by biorepositories of clinically annotated patient material. Basic Blood Cancer research is led by Professor Adrian Bracken (TCD Smurfit Institute of Genetics) on the role of epigenetic mutation in Diffuse Large B-cell lymphoma with a planned translational and therapeutic arm.



Clinical Lead Prof John Kennedy Consultant Medical Oncologist SJH & St. Luke's Hospital; Clinical Prof.., TCD



Scientific Lead Prof Lorraine O'Driscoll Prof in Pharmacology Pharmacy & Pharmaceutical Sciences Trinity Biomedical Sciences Institute TCD



Prof Elizabeth Connolly Consultant Breast Surgeon SJH; Associate Prof..., TCD



Breast Cancer

Breast Cancer Research at the Trinity St. James's Cancer Institute takes place in two sites.

1. The group based in the Department of Surgery, TTMI, investigates the role of lifestyle factors including obesity and its associated metabolic syndrome in breast cancer initiation and progression. A major focus of our group is investigating the potential to reduce breast cancer risk in women with a germline BRCA 1/2 mutation. Another major research theme in our group is investigating the accuracy of breast cancer risk prediction models in the familial breast cancer setting.

2. Breast cancer research at TBSI involves a broad range of in vitro, pre-clinical in vivo and ex vivo patients' specimens' studies prior to translating relevant finds to clinical trials (with Clinical Trials Ireland). This research includes efforts to understand and so prevent mechanisms of anti-cancer drug resistance, of tumour metastasis, and of immune evasion by cancer cells. The group is also working to identify and validate reliable blood-based biomarkers for diagnosing breast cancer at the earliest stage possible and for predicting response to both classical chemotherapy and newer targeted drugs, so that treatment can be personalised as much as possible; thus, enabling patients gain most benefit with the least side effects.



Clinical Leads Upper GI Prof John Reynolds Prof of Clinical Surgery, TCD, Head of Surgery, SJH, National lead for Oesophageal and Gastric Cancer Medical Director, Trinity St. James's Cancer Institute



Lower GI Prof David Gallagher Assoc. Prof in Clinical Medicine, Medical Oncologist and Medical Geneticist



Scientific Lead Prof Jacintha O'Sullivan Prof in Translational Oncology, Dept of Surgery



GI Trials Lead Prof Maeve Lowery, Prof Translational Cancer Medicine, Consultant Medical Oncologist



Gastrointestinal Cancer

In our gastrointestinal cancer programme, there are many different research themes centred on investigating cellular, genetic, molecular and immunological factors important in driving disease progression and in regulating treatment responses in gastrointestinal cancers (Oesophageal, Gastric, Colorectal cancers). Through our drug discovery programme, we continue to develop novel drugs that possibly could be used in combination with licensed drugs to better improve patient care. We do this preclinical testing using novel ex vivo human explant models. We conduct all these translational studies using samples collected in our biobanks following patient consent with designated biobank and clinical data managers. Each patient sample is linked to detailed clinical, pathological and outcome data where new findings can be directly linked to the biology and clinical features of each tumour. Also in collaboration with physiotherapists and nutritionists, we examine the role exercise and nutritional interventions play during the cancer patient's journey from pre-neopastic GI diseases, through cancer treatment and during cancer survivorship.



Clinical Lead Prof Con Timon Consultant Otolaryngologist; Head and Neck surgeon



Mr. Conor Barry Consultant Oral & Maxillofacial and Head & Neck Cancer Surgeon



Scientific Lead Prof Orla Sheils Director of the Trinity Translational Medicine Institute (TTMI), Prof of Molecular Diagnostics and Director of Medical Ethics at the School of Medicine, Trinity College Dublin



Head and Neck Cancer

Clinical research includes factors predictive of malignant transformation of oral dysplasia to cancer and factors predictive of poor prognosis in head and neck cancer (HNC). Active self-management practices for HNC survivors to deal with challenges to their physical, functional, social, and psychological well-being post- treatment is also included. The research looks at outcomes after reconstruction, in particular use of digital technology to optimise reconstruction of the jaws post HNC ablation. Epidemiological clinical research investigates the surgical management of primary hyperparathyroidism.

Translational research involves a study of Cytokeratin 7 expression in Oropharyngeal Squamous Cell Carcinoma and its correlation as a junctional biomarker for Human Papillomavirus-Related (HPV) Tumors. A combinatorial p16 immunohistochemistry and HPV DNA ISH diagnostic has been developed, along with a next generation sequencing algorithm and pipeline for the detection and characterisation of HPV variants in patients' samples. A further project examines HPV incidence and prevalence in Men who have sex with Men (MSM). A project looking at the reclassification of thyroid cancer may have implications for the management and well-being of thyroid cancer patients. This project uses Next Generation Sequencing (NGS) in fine needle aspiration (FNA) and Liquid Biopsies of thyroid to determine markers of disease activity.



Clinical Lead Prof Colm Bergin Consultant Physician in Infectious Diseases, St James's Hospital, Dublin Clinical Prof of Medicine, Trinity College Dublin



Scientific Lead Prof Cara Martin Assistant Prof in Molecular Pathology, Tumour Biology and Cancer Screening

Viral Oncology

The Trinity St. James's Cancer Institute has an active research portfolio in the area of viral oncology. Our translational research portfolio in this area focuses on cancer screening and early detection for improved diagnosis and management of disease, and vaccine prevention of virally driven cancers across the different cancer types in different at risk populations. Our viral oncology research programme brings together basic scientists and clinical investigators to study specifically the role of human papillomavirus, hepatitis B and C viruses, and human herpes virus in cancer initiation and development, with the ultimate goal of improving diagnosis, management and treatment of associated cancers. We have a specific interest in understanding the pathogenesis of these viral infections in HIV and immune deficiency related malignancies, and developing novel biomarker screening approaches to improve diagnosis and treatment outcomes.

The university leads the international CERVIVA [www.cerviva.ie] research consortium. CERVIVA is a multidisciplinary research consortium working on health services and patient-focussed research in the area of HPV-associated cancers, including cervical, oropharyngeal and anal cancers and pre-cancers.

CERVIVA research focuses on four main thematic areas; Molecular Epidemiology, Health Economics, Health Psychology and New Technologies to improve early diagnosis and treatment.

In the area of cancer prevention, we are co-investigators on the FP7 funded PEACHI HepC Vaccine study, and the HPV MAPS Project which is assessing the impact of HPV vaccination of in men who have sex with men (MSM) and the CERVIVA-Vax Project which is assessing the impact of HPV vaccination in women.



Solid Tumour Lead Prof Stephen Finn Consultant Pathologist, SJH; Co-Director Cancer Molecular Diagnostics Lab



Haematology Lead Prof Elisabeth Vandenberghe Consultant Haematologist, SJH; Co-Director Cancer Molecular Diagnostics Lab

Cancer Molecular Diagnostics (CMD)

The Cancer Molecular Diagnostic (CMD) Laboratory is integrated with Laboratory Medicine at St James's Hospital; and with haematology and histopathology provides integrated diagnostics for both blood cancers and solid tumours, thus providing a unique service nationally. CMD is the single largest provider of molecular testing for cancer in Ireland and processes approximately 14,000 high complexity analyses annually for both blood cancers and solid tumours.

CMD provides a service to the National Cancer Control Program (NCCP) in predictive marker testing for lung and colorectal cancers, melanoma and leukaemia. Haematological cancer services which includes the National Adult Allogeneic Transplant program is based on predictive testing for targeted treatment (precision medicine), prognostic testing and monitoring patients on treatment and following transplantation provided by CMD.

New assays and diagnostic platforms are constantly being developed with a current focus on increasing the next generation sequencing (NGS) pipeline with breast cancer, acute myeloid leukaemia and lymphoma molecular profiles. Research and development is key to CMDs continuing development. CMD also provides support for cancer clinical trials and performs testing for the Cancer Trials Ireland (CTI).



Cancer Immunology and Immunotherapy is a major research and clinical strength within the Trinity St. James's Cancer Institute. The last decade has witnessed a watershed in cancer therapy, utilising the patients' own immune system to fight cancer.



While new immunotherapies have changed the way many cancers are now treated, more research is required to develop additional immunotherapies and to ensure more patients benefit from these new treatments. A full spectrum of fundamental, translational and pre-clinical research and clinical trials in the area of immunology and immunotherapy studies are ongoing at Trinity and St. James's Hospital, covering a range of malignancies. Immunology is a key strength of Trinity College Dublin with many world-renowned experts in fundamental and translational immunology. Research areas include identifying the biological mechanisms utilised by tumours to evade immune detection and promote their own survival, identifying new immunotherapies, uncovering ways to enhance response rates and identify patient cohorts whom will benefit most from cancer immunotherapies. Clinical trials at St. James's Hospital are testing cutting edge immunotherapies in patients with solid and haematological malignancies including lung, colorectal, Head and Neck and breast cancer, and these trials importantly allow patients access to new immunotherapies, with many additional trials in the pipeline. The Trinity St. James's Cancer Institute brings together the scientific and clinical expertise from both campuses to ensure cancer patients in Ireland benefit from the latest breakthroughs in cancer immunotherapy and immunology research, which has changed the face of cancer treatment for countless patients.





In the past 15 years significant breakthroughs have been made with the introduction of new cancer treatments targeting the underlying gene mutations in cancer. Cancer is a genetic disease, which is caused by changes in the genes which control the way our cells function, especially how they grow and divide.





Genetic changes that promote cancer can be inherited from our parents or can be acquired during one's lifetime, as the result of errors that occur as cells divide or from exposure to carcinogenic substances that damage DNA, such as certain chemicals in tobacco smoke, and radiation, such as ultraviolet rays from the sun. Specific gene changes or mutations are present in different cancer types and scientists have developed 'targeted therapies' which have been approved for doctors to use in the treatment of patients.

Several very successful gene targeted therapies have transformed the field of cancer treatment. However, in order to develop additional gene targeted treatments for patients with other cancer types, it is clear that more research in cancer genetics is required.

Genetics research is a key strength of TSJCI. A full spectrum of fundamental research in genetics, translational and preclinical research is ongoing. Supporting this research, St. James's Hospital are testing several cutting edge new targeted therapies in clinical trials in patients with blood and solid cancers, including lung, colorectal, head and neck and breast cancer. Importantly, these trials allow patients access to new drugs that target specific cancer genes, with many additional trials in the pipeline.

The Trinity St. James's Cancer Institute brings together the scientific and clinical expertise from both campuses to ensure cancer patients in Ireland benefit from the latest breakthroughs in targeted cancer therapies and genetic research, which are transforming the treatment outcomes for patients.



Cancer Clinical Trials



Lead Cancer Clinical Trials Unit: Prof E Vandenberghe



Lead; early phase trials program: Prof M Lowery

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Director Wellcome Trust HRB CRF: Prof M Hennessy

The Cancer Clinical Trials Unit (CCTU), St James Hospital opened in 2001 to develop a cancer clinical trials program with Cancer Trials Ireland, pharmaceutical companies and international trials groups. The CCTU has opened > 200 trials (phase I-IV), recruiting more than 3,000 patients and facilitating >30 translational studies, at a local, national and international level, with a cancer trained staff of nurses, data managers and pharmacists.

The CCTU and Wellcome Trust-HRB Clinical Research Facility ["CRF"] which opened in 2014 are aligning to provide an integrated clinical trials program at SJH; combining the CCTU team, an integrated trials pharmacy service, the CRF patient orientated environment for clinical

research and a walk-in facility for studies involving healthy volunteers. This combined program facilitates our stated aims of increasing patient trial participation to 7% of cancer patients by 2022, developing a portfolio of supportive trials for cancer patients, ensuring the seamless integration of clinical trials and translational research and sponsoring investigator initiated trials. A successful example of multidisciplinary management of patients through complex cancer treatments was carried out by physiotherapists and dietitians using a rehabilitation program focussed on exercise physiology, optimising cardiopulmonary performance, and prevention of sarcopenia. A new early phase cancer clinical trials program being developed by Prof M Lowery will benefit from the CCTU/CRF alignment.

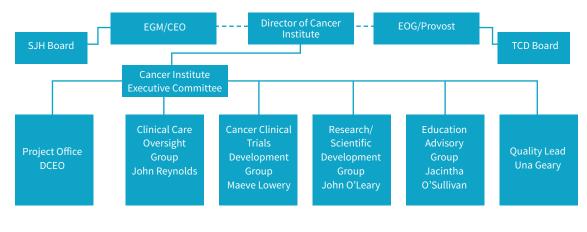






Governance model

TCD is committed to the principles underpinning an academic cancer centre model, and to realise the major opportunities for research, education, and innovation. The boards of Trinity and SJH have established a joint Development Group as a key strategic entity to lead the planning of the facility and preparation of the business plan.



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Governance structure of Trinity St. James's Cancer Institute

Cancer Institute Executive Committee

- Prof Paul Browne (Director)
- Ms. Ann Dalton (Deputy CEO SJH)
- Prof John Reynolds (Medical Director)
- Prof John O'Leary (Scientific Director)
- Dr. Una Geary (Quality Director)
- Ms. Sharon Slattery (Nursing Director)
- Prof Mary McCarron (Dean of Health Faculty)
- Prof Michael Gill (Head of School of Medicine)
- Mr. Declan Sheehan (Chair)
- Prof Jacintha O'Sullivan (Education)
- Prof Maeve Lowery (Clinical Trials)
- Mr. Simon Moores (COO at SJH)
- Mr. Niall McElwee (Director of Capital Projects SJH)
- Dr. Diarmuid O'Brien (Innovation)
- Prof James Meaney (Philanthropy)
- Dr. Patricia Doherty (Research Programmes)

EDUCATION 'Educating the next generation of leaders in cancer research'

The Trinity St. James's Cancer Institute aims to provide an integrated education and learning experience of the highest quality to fully address the needs of all learners. A number of postgraduate courses that are highly successful are already running in the various schools and institutes that comprise TSJCI, including the MSc in Molecular Medicine (approximately 25 students per year) that has been running for almost 20 years, and is formally linked to similar courses in affiliated Eurolife institutions, the MSc in Biomedical Sciences (intercalated) and our MSc in Translational Oncology, launched in 2012. This provides a broad palette of exceptional taught courses relevant to translational medicine, and it enrols approximately 20 students per year. In 2014, this course won an award from PostGrad Ireland as the best new course for multidisciplinary education and career mentoring structure.

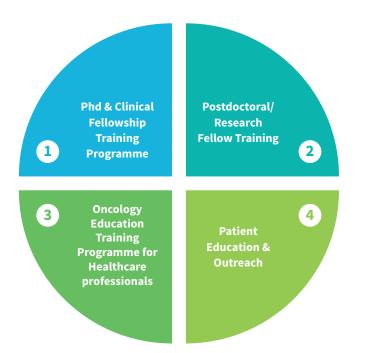




An internationally competitive education programme closely linked with our internationally competitive research strengths is under development. TSJCI aims to drive change in the education of the next generation of cancer researchers. PhD students and research fellows will be trained in innovation, IP and commercialisation of their research from an early stage, in line with SFI's Agenda 2020 and the Health Research Board strategy (2016-2020). Driving engagement with industrial, charitable partners and international leaders globally will provide collaborative opportunities for our Irish researchers and ensure that the end user (be it patient or others) is always to the fore.

This integrated education and learning platform in cancer is composed of four programmes (see below) addressing the educational needs of cancer researchers from early to advanced. A structured career development programme will map to the education structure. It also embraces the involvement of the patient with the researcher for direct public-patient engagement and involvement. The educational training of our scholars and fellows will complement the different thematic research areas in the Institute as shown above.

Programme 1 will be a structured PhD programme for both scientists and clinical fellows pursuing PhD studies. For this four year training programme, each trainee will integrate into a research training environment where the students will have two supervisors and conduct research rotations prior to choosing their specific oncology research area of interest. These competitive PhD research scholarships will also include an International Mobility Exchange as part of their research training with internationally recognised cancer institutes in Europe and in the USA.



Programme 2, will focus on training junior/senior postdoctoral fellows and senior research fellows in research areas that complement our major research themes in the Institute. Career development, mentoring and teaching opportunities will play an integral part of this training, allowing us to both retain and attract internationally competitive candidates.

In **programme 3**, structured oncology modules will be delivered to scientists and health care professionals and will cover areas such as principles of cancer prevention, diagnostics, therapeutics, survivorship and clinical trials.

Programme 4 will cover cancer patient education and outreach work within the Cancer Institute to enhance Public and Patient Involvement in cancer research.





Industry Engagement

The Trinity St. James's Cancer Institute aims to be an internationally recognised centre of excellence in basic, translational and clinical cancer research. The Institute's overarching mission is fundamentally patient focussed, with the delivery of innovative and translational cancer science advances for the prevention, diagnosis and treatment of cancer. A key cornerstone in fulfilling this strategy is the development of key partnerships; specifically, engagements with industry in collaborate research partnerships, clinical trials, staff training, educational programmes etc. The institute is continually investing in developing strategic bilateral relationships with leading pharmaceutical and life science companies.

Partnership model agreement templates are readily available with each engagement individually reviewed and structured against specific programme goals; focussed on agreed project outcomes delivered to the highest professional standards recognising the clinical setting, privacy concerns and patient involvement. Fundamental research partnership programmes are regularly undertaken, leveraging heavily on the existing research cohort with the Institute itself and across the St. James's campus and Trinity College.



TSJCI Industry collaborators (selected)



The Institute's commercial partnership offerings include;

- Availability of our clinical expertise, hospital and research biobank facilities and extensive research facilities to lead, guide and/or improve interventions aimed at early diagnosis across our eight cancer domain areas.
- Engagement in collaborative or contract research with industrial partners, working together to transform ideas into new products or commercial processes to benefit the cancer patient cohort.
- Participation in clinical trials projects involving investigation of new drugs or innovative treatment regimens. These studies are typically co-funded with support from Pharmaceutical/Healthcare companies,

or take place under existing partnership models with external agencies or by participation in European funding frameworks.

TSJCI research covers the full value chain, ranging from new scientific discoveries, licencing of these technologies to third parties and the translation of these discoveries into new treatments.



"I HAD GREAT CONFIDENCE IN THE TEAM AND I KNEW I WAS GOING TO BE WELL LOOKED AFTER SO I THOUGHT I WAS EXTREMELY LUCKY TO HAVE DISCOVERED THIS EARLY SO I HAD NO NEGATIVE THOUGHTS ABOUT MY CANCER" Eleanor, breast cancer patient

CASE STUDIES



Meet the collaborator...

Prof Bracken's research has helped define the transcriptional networks regulating well-established prognostic gene expression signatures. These transcriptional regulators consistently lie upstream of both 'prognosis' and 'proliferation' gene signatures, suggesting that a central transcriptional network underpins a shared phenotype within these signatures.

OncoMasTR a new biomarker technology which can predict the likelihood of recurrence in women who present with breast cancer.

Currently, the majority of early stage breast cancer patients are treated with chemotherapy, despite many not benefiting from such treatment. To address this problem, research led by Prof Adrian Bracken have developed OncoMasTR, a novel prognostic assay for early stage breast cancer. This technology has been exclusively in-licensed to OncoMark, an Irish biomarker small-to-medium enterprise to further develop its translational and clinical application for the improved treatment of women with breast cancer. This biomarker assay determines the risk of recurrence for early breast cancer patients, thereby aiding clinicians in determining the best treatment options for their patients. OncoMasTR will identify patients who do not require chemotherapy, thus enabling many to avoid aggressive treatments.



Meet the collaborator...

Prof O'Sullivan's group works closely with a multidisciplinary group of surgeons, oncologists and pathologists to drive translational discoveries closer to the clinic. The patient is the centre focus of all studies utilising consented human ex vivo material for drug discovery and validation. Prof O'Sullivan holds patents on the drugs investigated using the human ex vivo models and in the in vivo orthotopic models.

Quininib: Promising New Small Molecule Drugs for Treating Gastrointestinal Cancers in Translational Oncology.

Treatment algorithms and survival for colorectal cancer patients have changed dramatically over the past decade due to the advent of molecular targeted therapies such as bevacizumab, an anti-angiogenic therapy. However response rates to this anti-angiogenic therapy is only about 40% or less. Drug resistance also develops, highlighting the need for the development of newer small molecule drugs with potent anti-angiogenic activity. A drug discovery programme led by Prof Jacintha O'Sullivan at the Trinity Translation Medicine Institute at St. James's Hospital in collaboration with Prof Brendan Kennedy in UCD have identified and patented a small molecule drug Quininib, with potent anti-angiogenic activity. Therapeutic development of the patented drugs is now underway in collaboration with our industry partner, Xenopat, using orthotopic implantation of human tumors in mice to enhance our anticancer drug development and personalise cancer treatment for gastrointestinal cancer patients. Xenopat is a spin-off company of the Catalan Institute of Oncology, the Bellvitge Biomedical Research Institute and the Bellvitge University Hospital.



Meet the collaborator...

Prof O'Driscoll has a track-record in initiating and leading international collaborations of scale bringing together academics, clinicians and industry teams in this expanding area of commercially relevant research. She works extensively with industry, clinicians and academics who have an interest in the liquid biopsy; biomarkers; elucidating mechanism of disease; target identification; interactions between cancer and the immune system; drug delivery; standardisation and best practice.

Mechanistic communicators between cells -Extracellular Vesicles across all Cancer Types

Exosomes and microvesicles (collectively termed extracellular vesicles (EVs)) from blood, urine, saliva and other biological fluids is gaining increasing importance across all cancer types. The relevance of these vesicles, which are fundamentally small sacs of information, is their ability to act as mini-maps of the cells from which they have been released. Their commercial relevance to industry is:

- As a novel means of identifying new anti-cancer therapeutic targets.
- As key mechanistic communicators between cells, effectively contributing to the problem that make cancer such a challenging disease to combat (e.g. because of EVs role in metastasis/cancer spreading and in transmitting anti-cancer drug resistance).
- As important components of the liquid biopsy (e.g. as minimally-invasive methods of both diagnosing disease and predicting a patient's likelihood of responding or not responding to anti-cancer drug therapies).
- As key players in cancers avoidance of immune destruction
- EVs from non-cancer cells have potential as natural drug delivery vehicles, that can be produced in relatively large scale.



The Trinity St James's Cancer Institute aims to become an internationally designated comprehensive cancer centre for Ireland via accreditation from the Organisation of European Cancer Institutes (OECI).

The OECI is a non-governmental, non-profit legal entity established in 1979 to promote greater cooperation among European Cancer Centres and Institutes. The OECI mission is to foster high quality comprehensive cancer care, research and education, with the aim of improving patient outcomes throughout Europe.

Other OECI-accredited comprehensive cancer centres in Europe include Cambridge Cancer Centre, King's Health Partners Integrated Cancer Centre (London), Gustave Roussy (Paris) and Netherlands Cancer Institute.

The Trinity St James's Cancer Institute is driving for OECI accreditation to:

- Formally structure the organisation to coordinate and enhance interdisciplinary communications
- Enhance critical thinking in pursuit of being world leaders

- Obtain an objective external validation view of the organisation
- Enhance international credibility
- Create momentum for positive change
- Drive continuous improvement

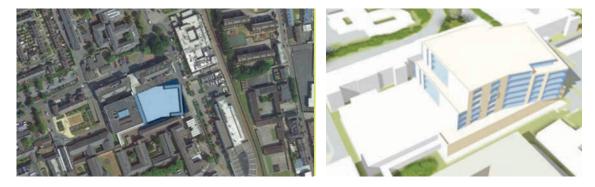
The New Building

The St. James's Hospital Master Development Plan includes proposals to consolidate substantially all cancer services on the hospital campus in a new state-of-the-art 28,000m2 facility. This new building will house cancer diagnostic and clinical services, cancer research, and cancer patient services, and will include a number of dedicated specialist cancer inpatient beds.

It is currently proposed that the new Comprehensive Cancer Centre will be adjacent to the existing Radiation Oncology Centre and developed with the second phase of the National Programme for Radiation Oncology (NPRO), which will see a major expansion of radiotherapy services and infrastructure at St James's Healthcare Campus.







The new facility will be integrated with tertiary care activities elsewhere on the St. James's Hospital campus, such as surgical suites and the adjacent radiotherapy facilities, to ensure the best possible care and outcomes for cancer patients. The new facilities within the cancer centre will also address the changing needs of cancer patients over the next decades, with a strong focus on early diagnosis, new treatments and clinical trials, ambulatory care and enhanced access to allied services after-treatment for people living with cancer

At 28,000m2, the Cancer Institute will be comparable to other major cancer centres developed within Europe.

The Institute will have an innovative configuration which will include:

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 Comprehensive oncology/haematology day wards (including single room and multi-user room therapy facilities)

- Multidisciplinary consultation rooms
- Patient education facility: multi-functional (patient/public engagement resource)
- Clinical trials offices and ancillary support suites
- Phlebotomy (with biobank/diagnostics link)
- Additional radiation oncology: Phase 2 NPRO programme build will be incorporated into centre, alongside/as
 extension of existing Phase 1 NPRO radiation oncology build. Number of linear accelerators, other equipment, to
 be determined by NPRO.
- Day surgery/procedures suite(s) and other treatment side rooms
- Diagnostics Radiology (imaging, interventional) services
- Diagnostics Laboratory: flexible design/future-proofing of laboratory diagnostic space
- Inpatient facilities will represent an extension/replacement (ward accommodation capacity and quality, with reference to improved specialist treatment, patient experience, infection control) of existing inpatient hospital facilities, and are expected to include:
- 30 high-dependency single rooms, ensuite, positive and negative pressure options (separate entry wash area, HEPA filtration etc): suitable for complex Haematology/Onconogy and Bone Marrow Transplant care
- 40 other single rooms ensuite to support the medical and surgical oncology units

2003



2014

Cancer Clinical Trials Office is launched MSc in Translational Oncology

2012

Wellcome Trust-HRB Clinical Research Facility opens at St. James's Hospital Launch of annual Burkitt Medal

Award

Launch of Cancer Week Ireland in conjunction with the Irish Cancer Society

Trinity College Dublin Strategic Plan commits to the development of integrated Cancer Institute on the SJH site

Wellcome Trust/HRB Clinical Research Facility is launched Cancer Research at Trinity College Achieves International 'A' rating

2015

TRINITY ST. JAMES'S CANCER INSTITUTE



2018

Boards of St. James's Hospital and Trinity College Dublin announce joint intention to develop a new cancer institute

2016

Appointment of Prof in Translational Oncology

2017

Trinity St. James's Cancer Institute become the first Irish members of the Organisation of European Cancer Institute

Establishment of joint Development Group to lead the planning of the facility and preparation of the business plan.

Approval by Boards of Trinity and SJH of the governance model for the Cancer Institute.

National Cancer Control Strategy (2017-2026) recommends the development of at least one national comprehensive cancer centre

Trinity St. James's Cancer Institute begins a programme of accreditation with the OECI

TTMI is launched at St James with 50 PIs and 150 Scientists

National Development Plan includes Comprehensive Cancer Centre as proposed capital investment project Accreditation Phase 1 Cancer Enterprise Unit is established

2019-22

1st Trinity St. James's Cancer Institute PhD scholarship programme begins

Comprehensive Cancer Centre designated

CEO is hired for the Institute

New Build



Acknowledgements

The Trinity St James's Cancer Institute would like to acknowledge the work done by Trinity Research and Innovation in the preparation of this document, especially Leonard Hobbs, Patricia Doherty and Audrey Crosbie. The Institute would also like to thank the Clinicians, Researchers and staff at Trinity College Dublin and St James's Hospital for giving so generously of their time in providing the many inputs to this document.



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Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin



Contact us:

For more information please contact our Senior Research Programme Officer on cancer.institute@tcd.ie WORLD CLASS SCIENCE FOR BEST PATIENT OUTCOMES