Cancer Grand Challenges

Nine new challenges – plain language summaries

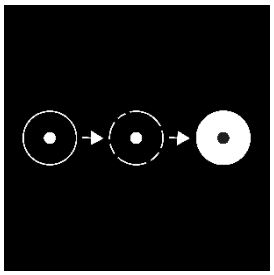
In March 2023, we announced nine of cancer's toughest challenges for the global research community to take on. These are the obstacles that continue to impede progress against cancer and that no one scientist, institution or country can solve alone.

The challenges were identified after a rigorous grassroots process, which involved workshops, consultation and debate with the global research community and people affected by cancer. This resulted in more than 300 ideas being submitted. The Cancer Grand Challenges Scientific Committee met to discuss and debate the ideas, recommending a set of complex challenges that it believes can be solved.

People affected by cancer were involved in the creation of the challenges, and members of the Cancer Grand Challenges Advocacy Panel had input in defining the plain language summaries of the nine challenges, which you can find below.

International research teams are invited to apply for funding to take on these challenges, with Expressions of Interest open until 22 June 2023. Successful teams will be announced in March 2024, and our Advocacy Panel will be involved in the selection process.

Ageing and cancer

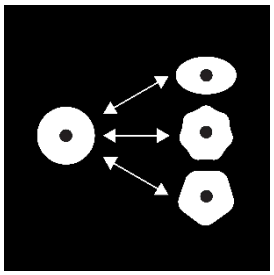


Age is a major risk factor for cancer. As we age, the cells in our bodies accumulate genetic changes called mutations, and normal cellular processes begin to go awry. As these changes build up, the likelihood of getting cancer increases. The immune system also becomes less effective with ageing and may become unable to detect and eliminate cancer cells when they arise.

Research has shown that the processes underlying ageing overlap with those of cancer development, but how distinct ageing processes increase cancer risk in different organs is unclear. Because no single ageing process explains cancer risk across all tissues, different cellular processes associated with ageing are likely to drive cancer risk in different organs.

This challenge seeks to gain a thorough understanding of the cellular and immune changes associated with ageing and how they contribute to cancer risk in different organs. This knowledge could help us to find new strategies to decrease cancer risk in ageing populations.

Cancer cell plasticity

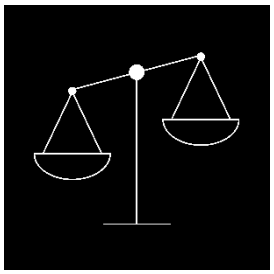


Some cells can switch from one cell type to another, and back again. This ability, called 'cell plasticity', allows cells to maintain stability through changes in their environment, such as tissue repair after injury. But plasticity in cancer cells can also push tumours to evolve and resist drugs. For example, when a tumour is treated with a drug, some cancer cells within the tumour can switch to a cell type that is resistant to that particular treatment. When the treatment is finished, these cells can cause the cancer to get worse or come back.

Cancer cell plasticity is a significant barrier to treatment success, yet the mechanisms that control it are poorly understood. Blocking or exploiting cell-switching processes could potentially stop cancer recurrence and eliminate resistant cells after initial treatment.

This Cancer Grand Challenge seeks to expand knowledge of the mechanisms that allow cancer cells to switch their identity, and of how this switching contributes to cancer progression. If we can find ways to control these mechanisms, we may be able to increase the effectiveness of current therapies.

Cancer inequities



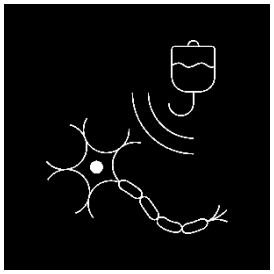
Inequities in cancer prevention, screening and treatment lead to differences in cancer incidence and mortality and are major public-health concerns.

Although most inequities are strongly influenced by social determinants and circumstances - for example when inadequate access to health care results in delayed diagnosis - data suggest that genetics and biology also have a role.

Prior research to address cancer inequities has several limitations. For example, approaches haven't considered the different contributions of genetics, biology, demographics, social drivers and circumstances, and health care delivery. In addition, most of the work that has informed understanding of what causes cancer has been done in European-ancestry populations and therefore might not be applicable to non-European populations. Similarly, most new technologies for cancer prevention, early detection, screening and treatment have not been developed or tested in diverse populations.

This challenge seeks to understand the relative contributions of genetics, biology and social drivers on cancer causes, to provide foundational knowledge for developing novel approaches to achieve equity in cancer outcomes for all people.

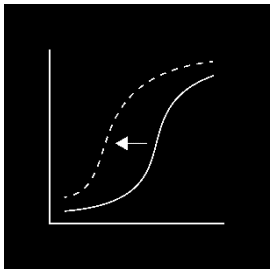
Chemotherapy-induced neurotoxicities



Chemotherapy is a cornerstone in the treatment of many types of cancer. Although these therapies kill cancer cells, they also damage healthy cells, and can cause long-lasting side effects as well as long-term damage to the nervous system. This 'neurotoxicity' can severely limit patients' quality of life and day-to-day functioning.

Our understanding of why this toxicity occurs is limited, and we don't yet have a reliable way to predict who will be most susceptible to these side effects. This challenge calls for bold and new approaches to develop this understanding, ultimately to inform how we can prevent and treat chemotherapy-induced neurotoxicity. If we can prevent and treat these side effects, much-needed improvements can be achieved for people receiving chemotherapy.

Early-onset cancers

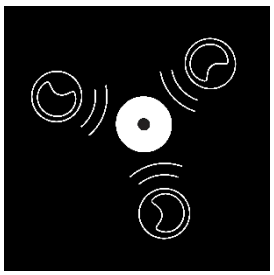


Since the 1950s, the incidence of some cancer types in adults younger than 50 years old has been rising. This trend cannot be explained by the increase in screening programmes alone. The incidence of these 'early-onset' cancers – including a variety of types, such as bone marrow, breast and colon cancer – has increased in multiple countries.

Younger generations, compared with previous generations, may be at greater risk of developing some types of cancer earlier in life, because they are exposed to different levels and types of environmental factors, such as diet, physical activity, obesity, alcohol, sleep patterns, antibiotics, stress levels, pollution and environmental contaminants.

This challenge aims to identify and understand the processes through which different biological and environmental factors cause early-onset cancers. In the future, this knowledge could be used to develop strategies to protect populations at risk.

Obesity, physical activity and cancer

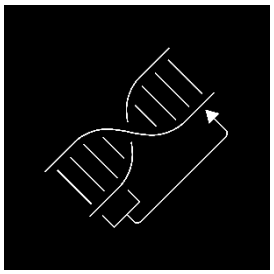


Over the past 30 years, increasing evidence has shown that physical activity and obesity influence cancer risk. Physical activity is associated with decreased risk of developing six types of cancer and obesity is associated with increased risk of developing 13 types of cancer.

Although the effects of obesity and physical activity on cancer are widely known, the specific biological processes by which they act through to influence an individual's risk of developing cancer are unclear.

This challenge seeks to gain a better understanding of how obesity and physical activity influence cancer risk at the biological level. In the future, this knowledge could allow strategies to be developed to decrease global cancer incidence.

Retrotransposable elements

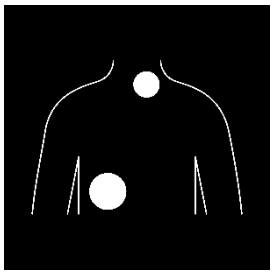


Some segments of genetic code can jump around to different locations in our DNA. These segments are derived from viruses that integrated into our genetic codes millions of years ago. 'Retrotransposable elements', one type of these mobile genetic segments, are widely scattered throughout our genetic codes, but are usually kept silent or are "trained" by cells to carry out specific functions. However, when a cell begins to transform from a normal cell to a cancer cell, silent retrotransposable elements can become reactivated, making the genetic code unstable. This instability can cause cancer.

Until recently, because we didn't have the tools to study retrotransposable elements, understanding how they contribute to cancer has been challenging. Now, newly developed cutting-edge, sequencing techniques allow us to explore how these elements cause instability within the cell and drive cancer development.

This challenge seeks to clarify how these elements contribute to cancer development and progression, so that new therapeutics can be developed to stop retrotransposable elements from contributing to cancer development.

Solid tumours in children

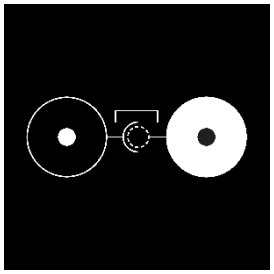


Cancer remains a leading cause of death due to disease among children globally, and outcomes for some childhood cancers have not improved in more than 30 years. Treatments for solid tumours in children still rely on decades-old chemotherapies, and often radiotherapy. Children who must endure these treatments often later experience severe side effects, such as secondary cancers; heart, nervous system and bone toxicity; and infertility.

Childhood tumours are different from those in adults, in that they are often caused by genetic changes (mutations) affecting different types of proteins from those in adults. The proteins that drive these cancers have historically been considered "undruggable" targets, and progress in effectively targeting these proteins has stalled.

This challenge seeks to find ways to 'drug the undruggable', by developing therapies that target the drivers of solid tumours in children. By developing effective targeted therapies for children with solid tumours, we should be able to improve survival and reduce the lifelong side effects caused by existing treatments.

T-cell receptors



T cells – a type of white blood cell – are an important part of the immune response to infection and cancer. T cells have receptors on their surfaces that recognise 'antigen' molecules that come from pathogens or cancer cells. After a T cell attaches to a cancer antigen, the cancer cell is 'marked' for destruction by the immune system.

Although T-cell receptors can be studied in detail, the information can't be used to work out which antigens are recognised by the receptors on a large scale. This Cancer Grand Challenge seeks to improve our understanding of how T cells interact with cancer antigens. If we can predict what antigens a T cell 'sees' based on its receptor, we can find ways to boost the effectiveness of therapies that harness the power of the immune system (immunotherapies) to fight cancer.