

CANCER CAUSES

Determine the mechanisms that cause cancer without known mutagenesis, such as obesity, in order to devise novel interventions



CONTEXT

Several carcinogens that can cause cancer have been identified, most of which have been shown to cause specific genetic or epigenetic changes that contribute to tumorigenesis. In some cases, the mechanisms underlying these mutagenic processes are well established, particularly for exposures such as tobacco and UV radiation, and in the first round of Grand Challenge we funded a team to understand more about the biological mechanisms underlying cancer-causing mutational processes.

However, there are numerous other factors that have been strongly associated with an increased cancer incidence but where the mechanisms underlying this association have not been clearly established, and there is a need to understand how these factors influence cancer development at a physiological level. Examples include (but are not limited to) obesity, chronic inflammation and physical inactivity. It may be that these lifestyle and environmental factors cause mutations via processes that we currently don't fully understand and/or they may contribute to tumorigenesis in other less direct ways, for example by the promotion of proliferation or immunosuppression. Elucidation of these complex mechanisms would allow us to determine precisely how these factors influence disease development and recurrence, and could lead to new and improved approaches to prevention and therapy.

OPPORTUNITIES AND BARRIERS

It is anticipated that teams addressing this Grand Challenge will build on existing association studies that link certain risk factors to cancer incidence, and explore the biological mechanisms underlying cancer development and progression. These mechanistic pathways are likely to be complex; for example in the case of obesity, it is possible that dietary and hormonal factors, lack of exercise and inflammation can all contribute to tumorigenesis at the molecular level to some extent. Teasing out the influence of these interrelated factors to inform intervention strategies will be challenging. The Panel would welcome applications from multidisciplinary teams of researchers that will address this problem in novel and unexpected ways.

Success in this Grand Challenge could involve the clarification/identification of a clear mechanistic link between a factor (where no clear mutagenic link currently exists) and the development of at least one type of cancer. It will also be important to demonstrate in preclinical models that targeting this mechanism could lead to preventive or therapeutic intervention.

VISION AND IMPACT

The goal of this Grand Challenge is to provide a clear mechanistic understanding of how previously identified risk factors are responsible for increased cancer incidence, which should lead to novel preventive or therapeutic interventions.