

DORMANCY

Identify and target tumour cells that remain dormant for many years after seemingly effective treatment



CONTEXT

Although some cancers are cured with current therapies, others such as melanoma, breast and prostate cancers can recur many years or even decades after seemingly effective treatment has ended. This phenomenon of tumour dormancy has been recognised for many years but remains relatively poorly understood. It is not clear for example what enables cells to remain in a dormant state, what mechanisms trigger recurrence, or why these residual tumour cells cannot be eliminated.

Only recently have single-cell sequencing technologies allowed for the identification and characterisation of small numbers of residual cancer cells. The ability to identify and characterise tumour cells in the dormant state remains a major challenge, but would facilitate further mechanistic understanding of this process, enabling us to develop ways to effectively target dormant tumour cells.

OPPORTUNITIES AND BARRIERS

This Grand Challenge specifically relates to the study of dormant cells that exist after seemingly successful treatment (i.e. following a latent period where the patient displays no clinical symptoms). This is distinct from the investigation of indolent cells that may persist for an extended period of time before progressing to malignancy, or cancers (such as chronic myeloid leukaemia) that remain 'dormant' whilst on treatment but recur when therapy is withheld.

In addressing this challenge, teams will need to first overcome the current barrier of how to identify, detect and study dormant cells. It is anticipated that this challenge will require consideration of both tumour intrinsic and extrinsic factors in order to understand how dormant cells and/or their behaviour can be effectively targeted. Importantly, findings from relevant experimental models will ultimately also need to be validated in patients.

Examples of the types of questions that could be addressed in this challenge include (but are not limited to):

- Can methods be developed to detect and isolate dormant cells; for example using rapid autopsy studies to isolate dormant cells from tissues that would otherwise be inaccessible?
- Is it possible to develop preclinical models that accurately reflect tumour dormancy in patients and provide novel insights into how dormancy is regulated?
- By understanding the mechanisms regulating tumour dormancy, can we develop approaches to eradicate dormant cells, or prevent their re-emergence?

VISION AND IMPACT

The goal of this Grand Challenge is to develop innovative approaches to accurately detect and study dormant tumour cells. It is envisaged that further biological understanding of the mechanisms that control dormancy in patients will result in new strategies to eliminate persistent or dormant cells, prolong dormancy and/or the identification of risk factors or markers of cancer recurrence either at primary or secondary sites.