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## An evolving challenge

Learning why tumours evolve is crucial, says Dr Marco Gerlinger, team leader in the ICR's centre for Evolution and Cancer



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Cancer is incredibly complex and variable: every tumour is unique and is genetically unstable, accumulating new mutations all the time. That gives cancers the ability to rapidly adapt to changing environments? so they may initially respond well to treatment, but will often develop drug resistance and start progressing once again.

Our research has begun to unravel how cancers change, adapt and evade treatment? and many questions remain. But the ICR and The Royal Marsden?s new research strategy cites cancer evolution as the key to overcoming cancer?s adaptability and drug resistance, and we are gaining insights that will be crucial in the creation of a new wave of treatments.

Cancer evolution results from the interaction of processes, some of which are predictable (such as selection) and some of which are random (such as mutation). We can?t currently assess how randomly or how predictably an individual cancer is likely to behave. We also don?t know how to make clinical decisions in situations where unpredictable behaviour dominates.

"Recently, immunotherapy has emerged as a powerful new tool that appears able to cure some cancers that are resistant to all other known therapies"

That will allow us to analyse evolutionary trajectories, helping us to more accurately predict whether patients are likely to respond to particular treatments. We don?t yet understand what tumour cells gain by acquiring genetic alterations as they progress.

We are investigating how mutations may help cancer cells survive in a crowded tumour, migrate to other parts of the body or resist attacks by the immune system.

We also need to learn what allows cancers to access these genetic changes and why some are better at evolving than others, so we are developing novel models and computer simulations to understand these processes and the evolutionary rules driving them.



We are aiming to develop biomarkers that can measure and track diversity within tumours

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- Research strategy focuses on cancer evolution [6]
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These amazing results? to which our investigators contributed hugely? provide an opportunity to discover how cancer evolution can fail and how it can be contained.

Like cancers, our immune systems have an inherent ability to evolve, and our latest clinical trials ask whether this is central to the success of immunotherapy.

As we begin to answer these questions, we will be able to establish more reliable evolutionary prediction models that will guide precision treatments. One day, we hope to control or prevent cancer evolution so that we can stop drug resistance and cancer recurrence.

We have identified the problem? the next challenge is to bring the solutions to patients.

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