International Agency for Research on Cancer

World Health Organization

10 February 2017

RESEARCH PROJECT – MUTOGRAPHS OF CANCER: DISCOVERING THE CAUSES OF CANCER THROUGH MUTATIONAL SIGNATURES

Take-home message/key point:

In a project of epic scale that spans five continents, Professor Stratton's team aims to build a deeper understanding of what causes DNA damage and how it leads to cancer. Their work could help prevent more cancers and reduce the global burden of this disease. **Cancer type:** Colorectal (bowel), pancreatic, kidney, and oesophageal cancer; has the potential to help prevent more types of cancer.

Introduction

Things in our environment and behaviours like smoking and drinking alcohol can cause cancer by damaging our cells' DNA. This damage occurs in distinctive patterns – known as "mutational fingerprints" – that are unique to the factor that caused the damage. For example, cancers caused by UV exposure have a different mutational fingerprint to cancers linked to tobacco.

Right now, scientists know of about 50 cancer-associated mutational fingerprints. But they only know what causes about half of them.

Professor Mike Stratton and his team of scientists from the UK, France and the USA, together with collaborators from the International Agency for Research on Cancer, want to fill in the missing gaps. Their Grand Challenge project aims to use cancer-associated mutational fingerprints to determine causes of cancer and reveal the biology behind how they cause different cancers to develop.

The research

In a project of epic scale that spans five continents, including countries that have high and low levels of cancer, Stratton's team want to build a much deeper understanding of DNA damage – what causes it and how it leads to cancer. They want to figure out what causes the other 25 or so cancer-associated mutational fingerprints and identify which ones are due to environmental exposures and lifestyle behaviours.

They also want to figure out exactly *how* different environmental factors and behaviours cause cancer, and at the same time search for other cancer-associated mutational fingerprints we don't yet know about.

To do this, they will study and compare the mutational fingerprints present in samples collected from 5000 pancreatic, kidney, oesophageal, and bowel cancer patients, who come from countries that have different levels of these cancers. They will also gather information about the habits, lifestyles, and environments of these patients to look for clues to what the causes might be.

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The impact

This research could dramatically improve our understanding of what causes cancer. It could also lead to better information for people on how to reduce their cancer risk and help inform government policies to reduce exposure to cancer-causing agents.

Ultimately, it could help prevent more cancers and reduce the global burden of this disease.

Team members

Name	Institute	Country
Professor Sir Mike Stratton	Wellcome Trust Sanger Institute, UK	UK
Professor Paul Brennan	International Agency for Research on Cancer	France
Dr Ludmil B. Alexandrov	Los Alamos National Laboratory	USA
Professor Allan Balmain	University of California San Francisco	USA
Professor David Phillips	King's College London	UK
Professor Peter Campbell	Wellcome Trust Sanger Institute	UK
Mimi McCord	Patient Rep	UK
Maggie Blanks	Patient Rep	UK

IARC, 150 Cours Albert Thomas, 69372 Lyon CEDEX 08, France - Tel: +33 (0)4 72 73 84 85 - Fax: +33 (0)4 72 73 85 75