# Unusual pattern of mutations induced by different kidney cancer-causing events

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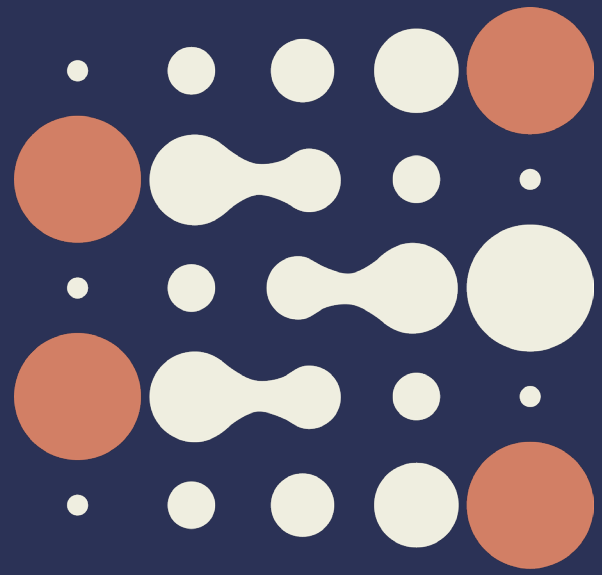


International Agency for Research on Cancer

World Health Organization

# Many cancers are caused by Environmental or Lifestyle Exposures of Unknown Cause


International cancer epidemiology studies indicate that **~80% solid cancers are preventable in principle**

We can explain 40% of this burden through known causes

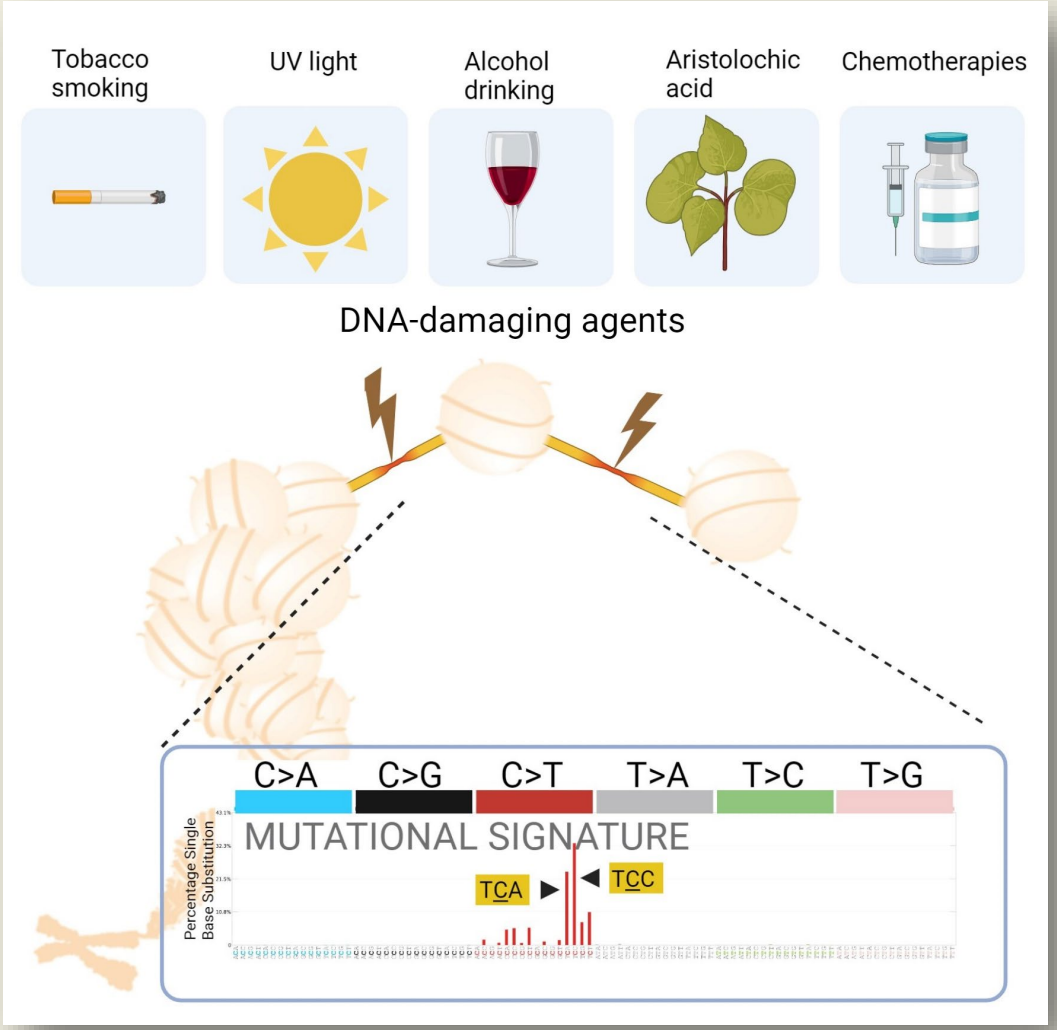
For the remaining, **we do not know causes** and, therefore, **cannot prevent them**

# Mutational Signatures offer a New Perspective on this problem

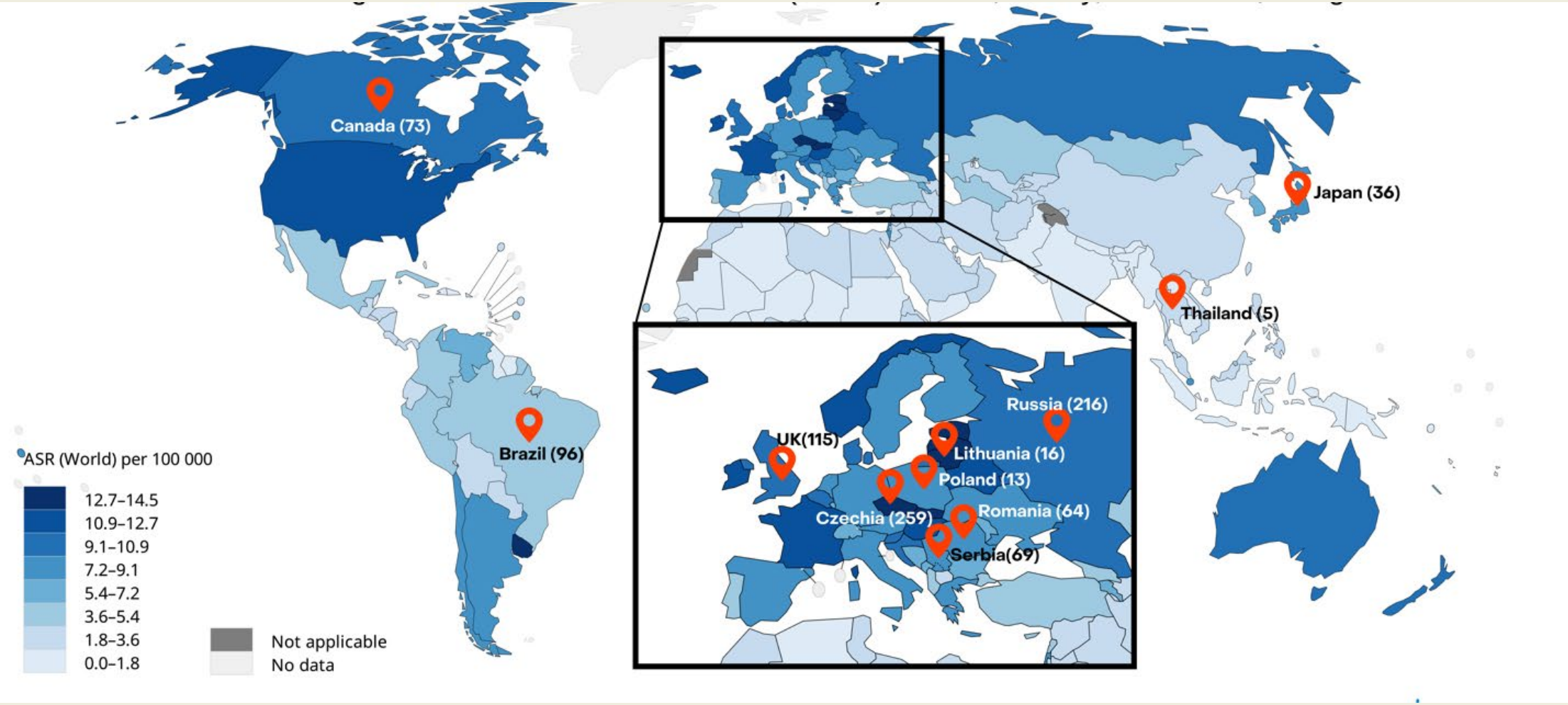
**Past mutagenic exposures** in cancer genomes that might be **still occurring today**

Common, **geographically variable**

Use **genome sequencing** of normal and cancer cells for **somatic mutations** to **survey carcinogenic exposures at a global scale**



# Capturing worldwide Renal Cancer differences in Incidence




***Mutographs* → 962 ccRCC from 11 countries of varying incidence**

*In press*, Nature

Senkin, Mutographs Team, Paul Brennan

# Two mutational patterns relevant for Kidney Cancer Prevention

High resolution mutational surveys

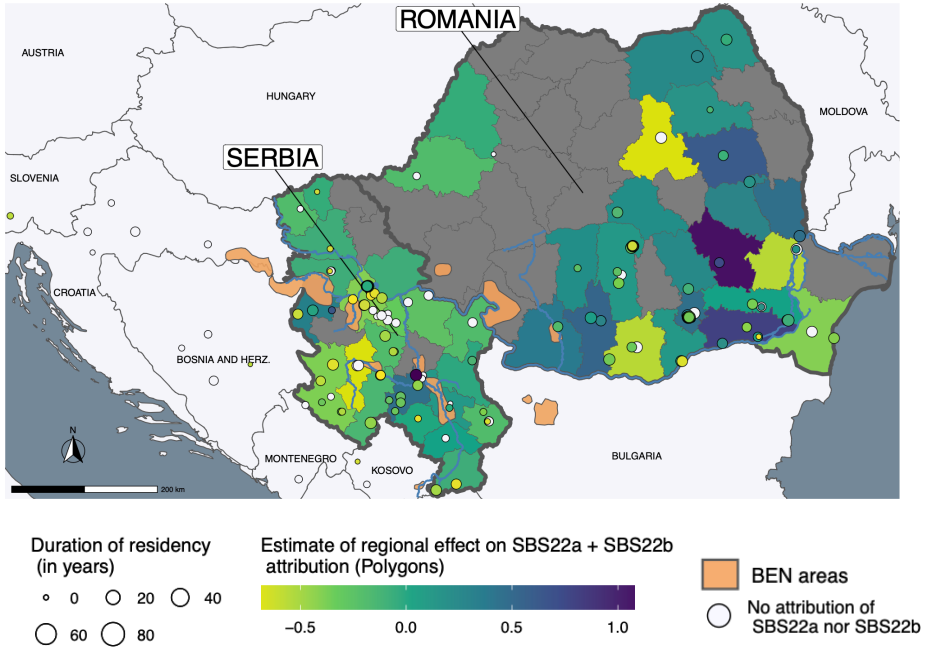
**SBS22 – Aristolochic Acid Exposure in the East-Central Europe**

**SBS12 – Unknown Origin Exposure in Japan**

# SBS22 – Aristolochic Acid Exposure in the East-Central Europe

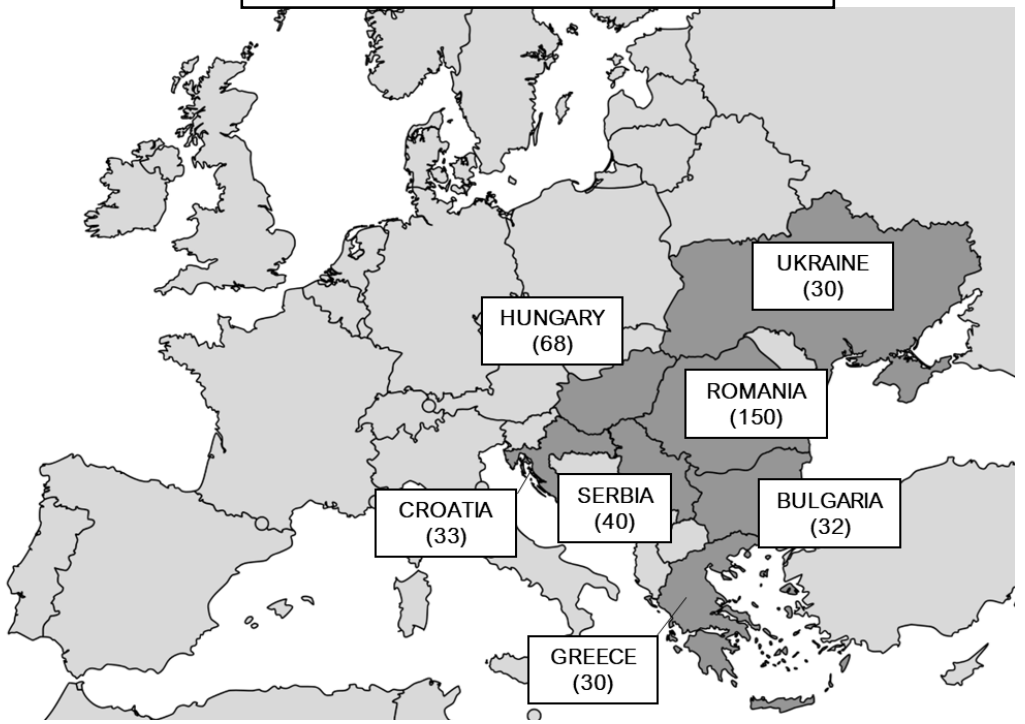
## …may be affecting millions of people across the world

### What we have done




>80% exposed Renal Cancers in Romania
Diagnosed cases from 1999 through 2006

### What we are doing



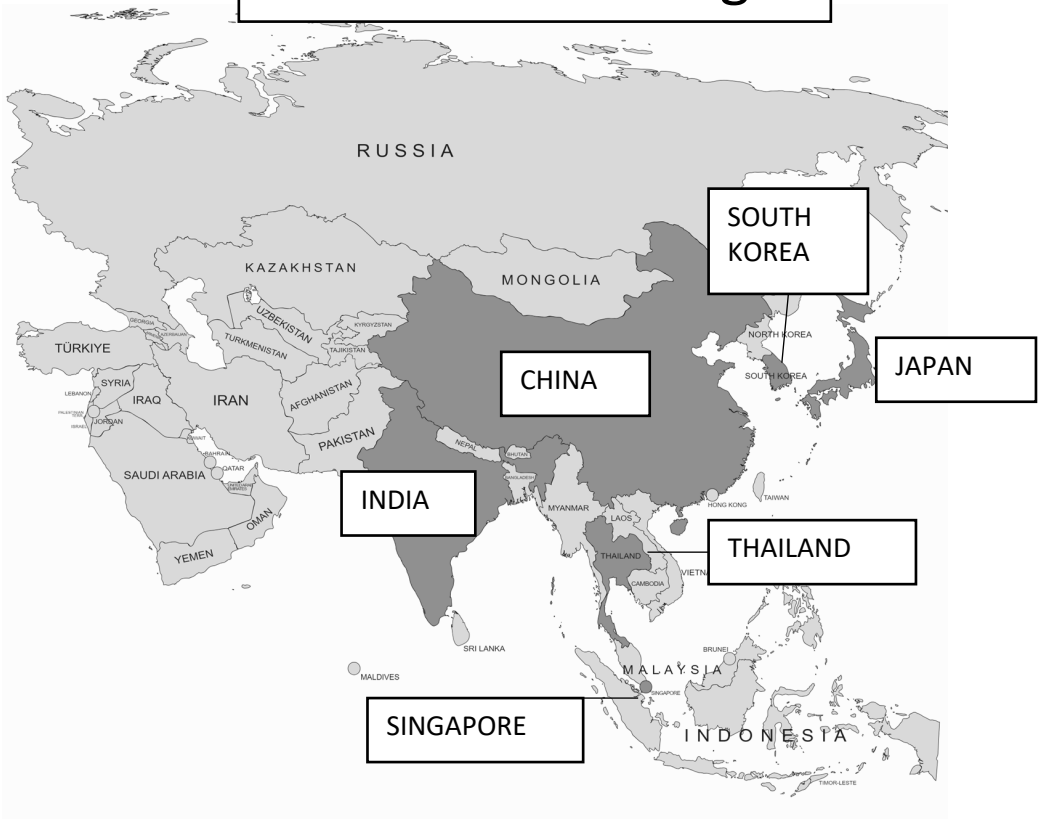

380 prospective Urinary System cancers
Tumor & normal tissue pairs, blood
Herbal remedies, animal tissue from exposed areas
Collected from 2020 through 2023

# SBS12 – Unknown Origin Exposure in Japan
## …may be ubiquitous in certain populations

### What we have done


>70% exposed Renal Cancers in Japan
>80% Residing in Tokyo prefectures
External exposure of an unknown mutagen

### What we are doing




500 prospective and retrospective renal cancers
Tumor & normal tissue pairs, blood
Exposomics

# Key take-home messages

Continuing defining the parameters of kidney cancer external exposures, which are probably affecting millions of people

*-where and how it is happening*

**→Can we use kidneys to investigate known or suspected external exposures across the world?**

**In development with Mike Stratton (Sanger Institute)**

**…Global survey 5000 Kidney cancers**

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International Agency for Research on Cancer

World Health Organization

wellcome sanger institute

UC San Diego

CANCER GRAND CHALLENGES

Team: MUTOGRAPHS