

50 Jahre
Institut für Krebsforschung

Chemische Sicherheit und Krebs-prävention

Univ. Prof. Dr. Gergely Szakács
Intstitute of Cancer Research

CANCER STATISTICS

Cases

14.1 million



New cases of worldwide cancer, 2012

Common cancers

42%



More than 4 in 10 of new cases of cancer are lung, female breast, bowel or prostate cancer, 2012, worldwide

Projection to 2030

+68%



Cancer incidence rates projected increase 2012-2030, worldwide

Deaths

8.2 million



Deaths from worldwide cancer, 2012

46%



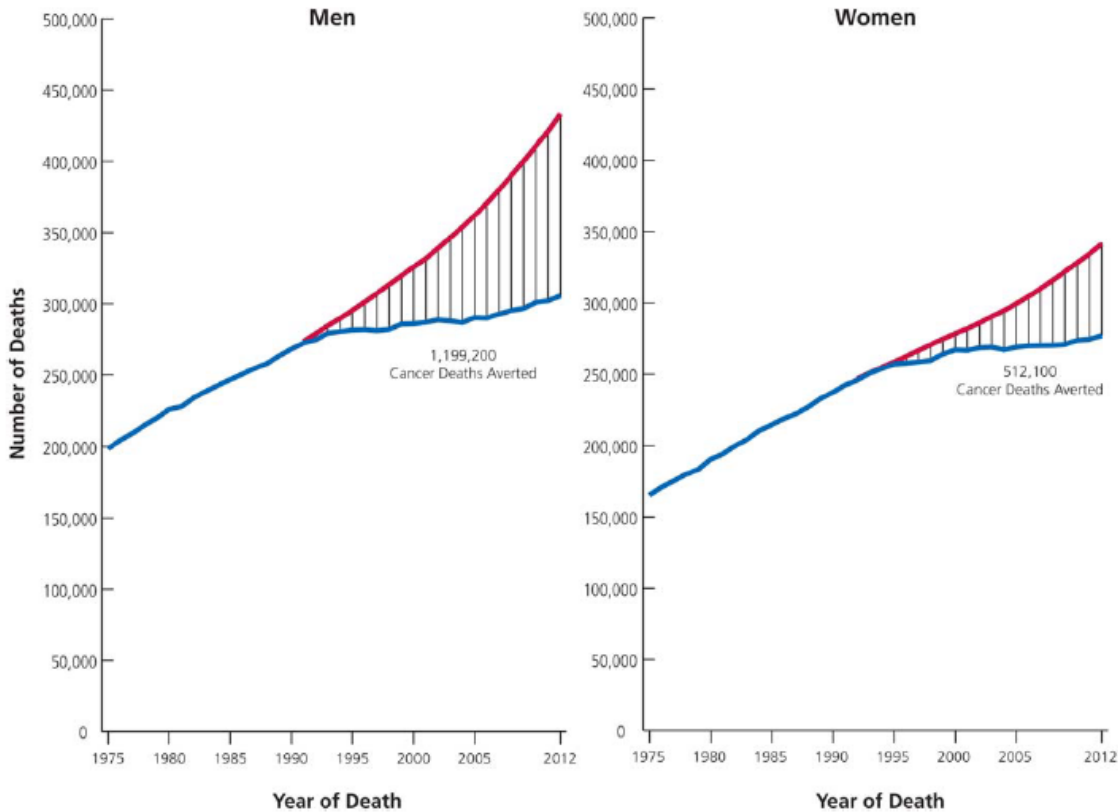
Almost half of all cancer deaths are lung, liver, stomach or bowel cancer, 2012, worldwide

LIFETIME CHANCE OF GETTING CANCER: 0-100/100000 et. al 2013

~1 in 2
for men

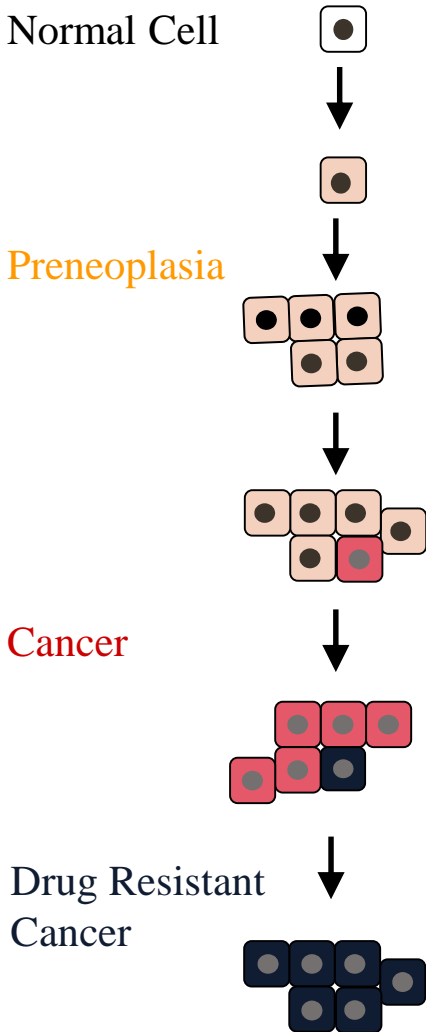
~1 in 3
for women

Number of Cancer Deaths Averted



- Prevention
- Early detection
- Better cures

What is the cause of cancer?



Cancer is caused by mutations

Hereditary

APC - Familial adenomatous polyposis (FAP)
BRCA1, BRCA2, TP53 and PTEN - Breast cancer

Somatic

- Chemicals
- Radiation
- Viral infections
- Age

How can we estimate the contribution of environmental factors?

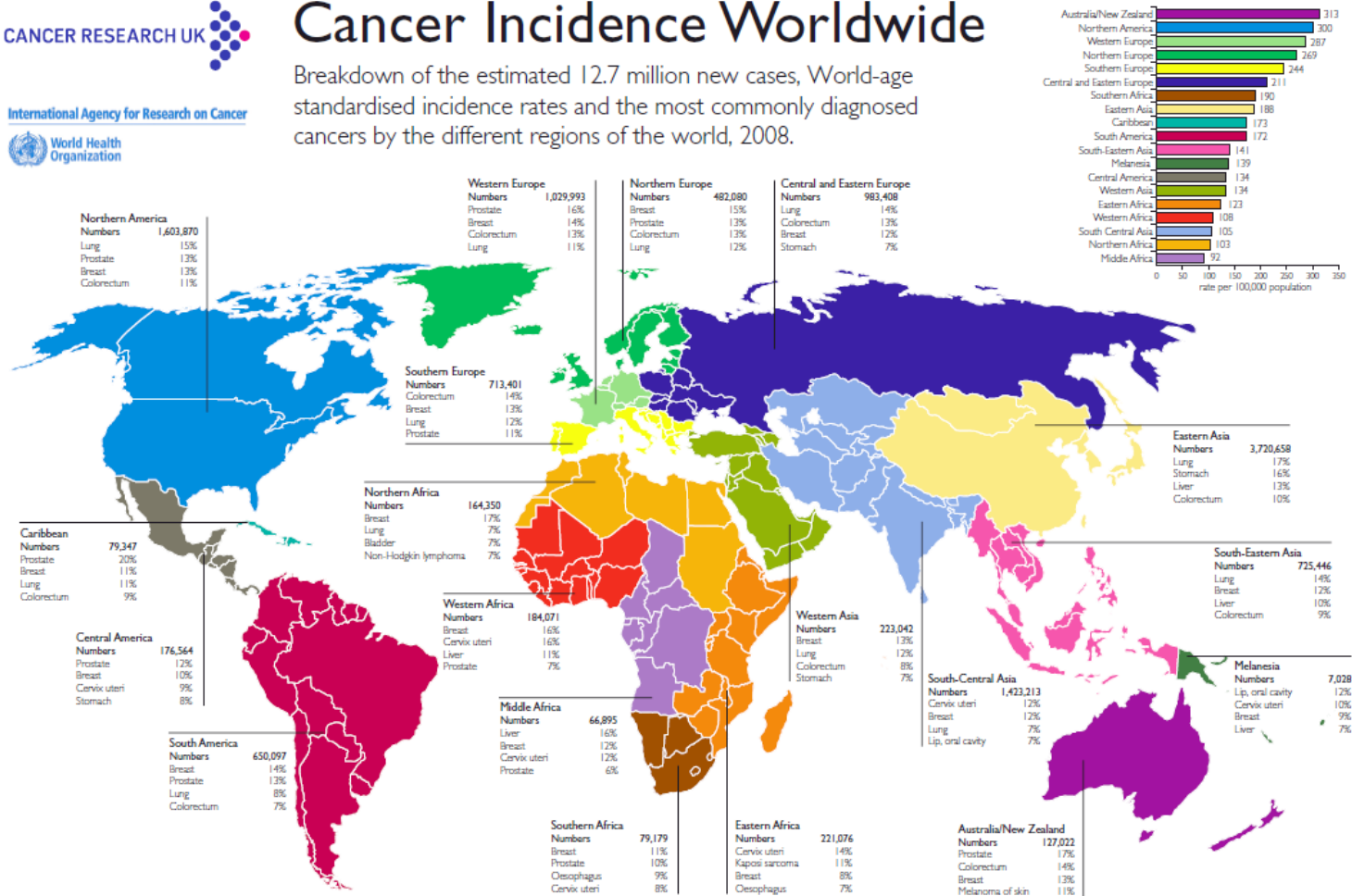


International Agency for Research on Cancer



Cancer Incidence Worldwide

Breakdown of the estimated 12.7 million new cases, World-age standardised incidence rates and the most commonly diagnosed cancers by the different regions of the world, 2008.



Source: GLOBOCAN 2008, v. 1.2, Cancer Incidence and Mortality Worldwide. IARC, 2010 (<http://globocan.iarc.fr>)
Map updated February 2011

<http://info.cancerresearchuk.org/cancerstats/>

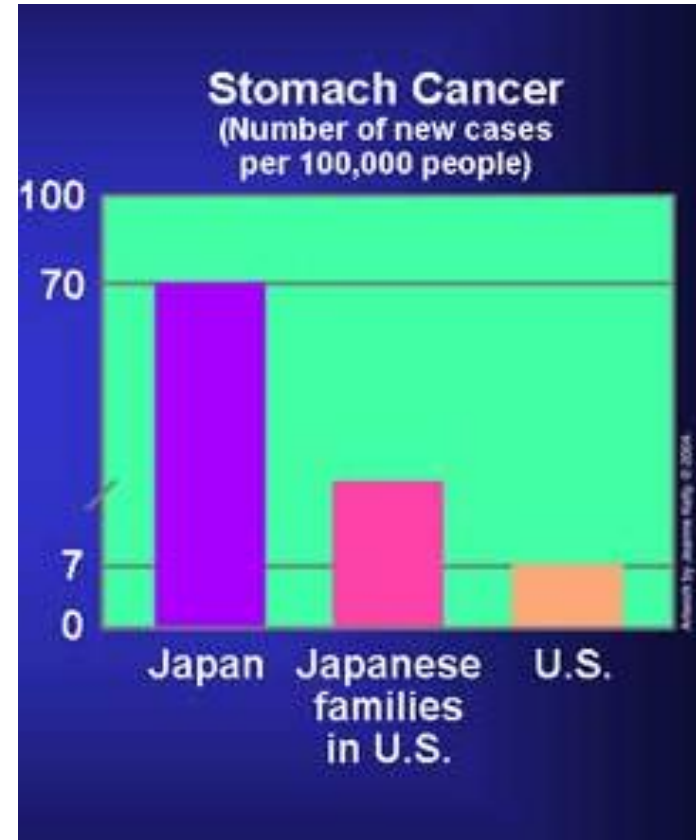
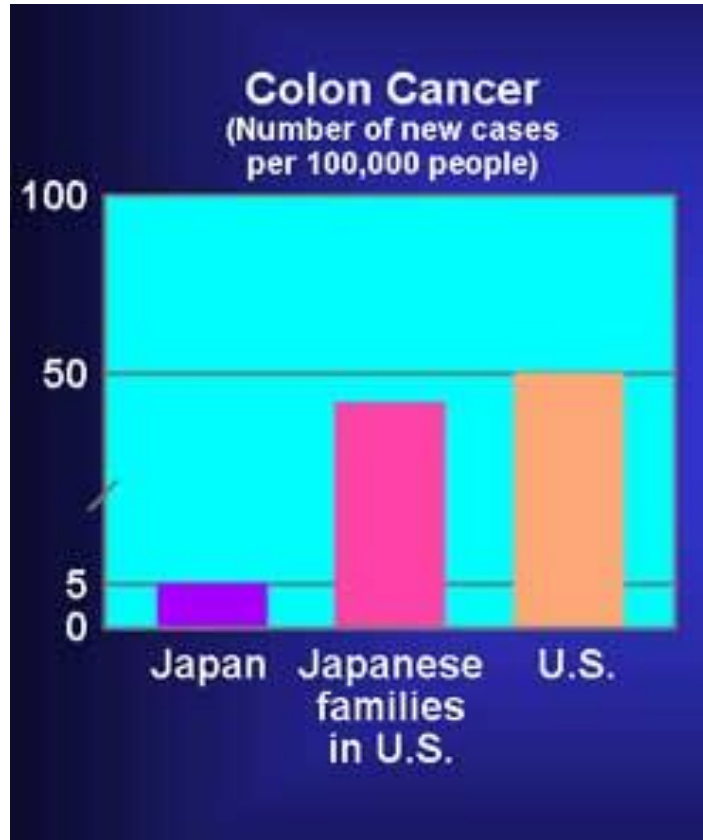
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Registered charity no. 1089464 (England & Wales)
& 5234166 (Scotland)

Cancer Research UK

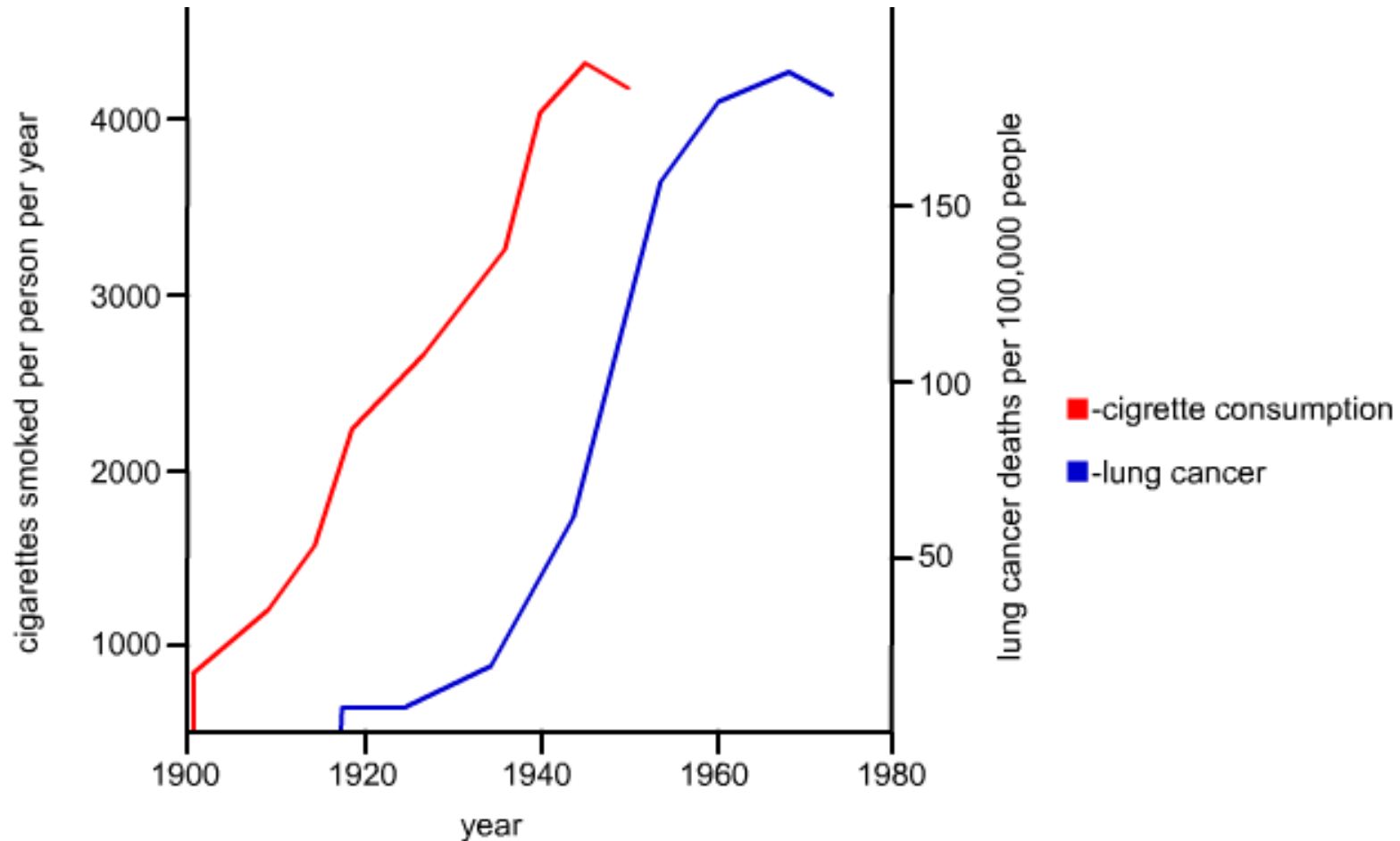


INSTITUTE OF CANCER RESEARCH
MEDICAL UNIVERSITY OF VIENNA

How can we estimate the contribution of environmental factors?



How can we estimate the contribution of environmental factors?



© ABPI 2013

Levin, M. L., Goldstein, H., and Gerhardt, P. R. (1950). Cancer and tobacco smoking: a preliminary report. *J. Am. Med. Assoc.* 143, 336-338.



How can we estimate the contribution of environmental factors?

Methods

- Combined data on 44,788 pairs of twins listed in the Swedish, Danish, and Finnish twin registries
- Cancer at 28 anatomical sites

Results

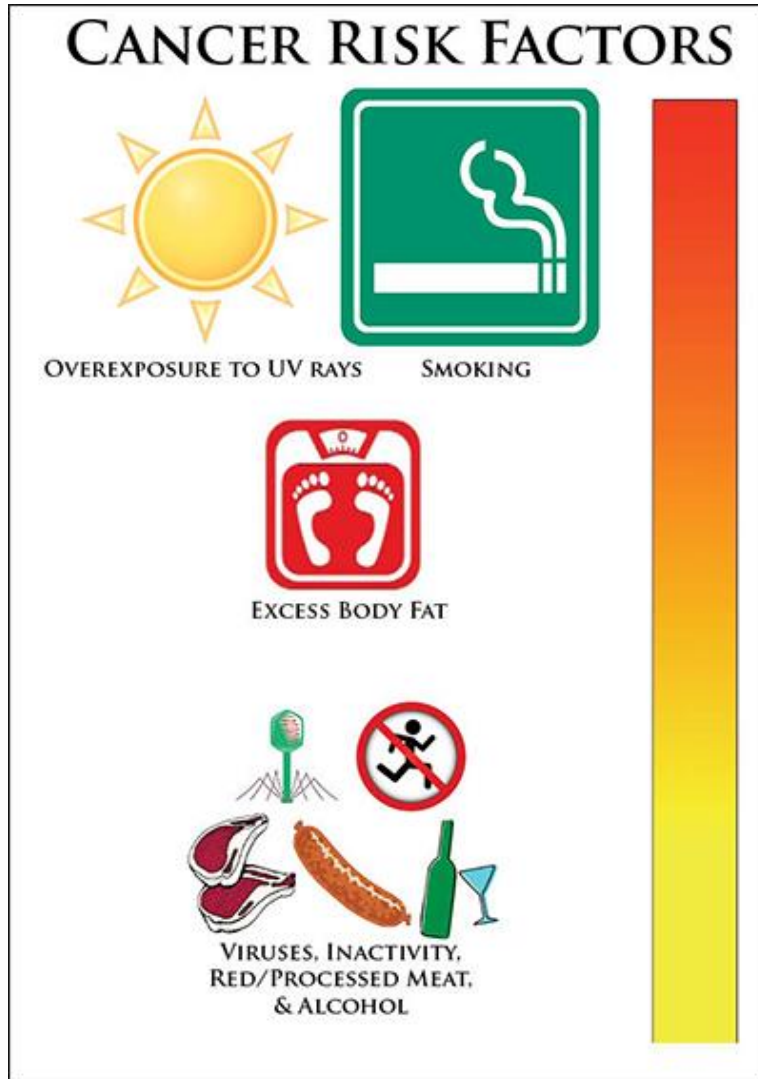
- At least one cancer occurred in 10,803 persons among 9512 pairs of twins.
- Statistically significant effects of heritable factors were observed for prostate cancer, colorectal cancer and breast cancer

Conclusions

Inherited genetic factors make a minor contribution to susceptibility to most types of neoplasms. This finding indicates that **the environment has the principal role in causing sporadic cancer.**

Lichtenstein et al (2000), *NEJM*

Environmental factors contributing to cancer



- Tobacco
- Sunlight
- Overweight
- Diet
- Alcohol
- Infections

Health professionals: Cancer may be prevented!

Seven Steps to Prevent Cancer



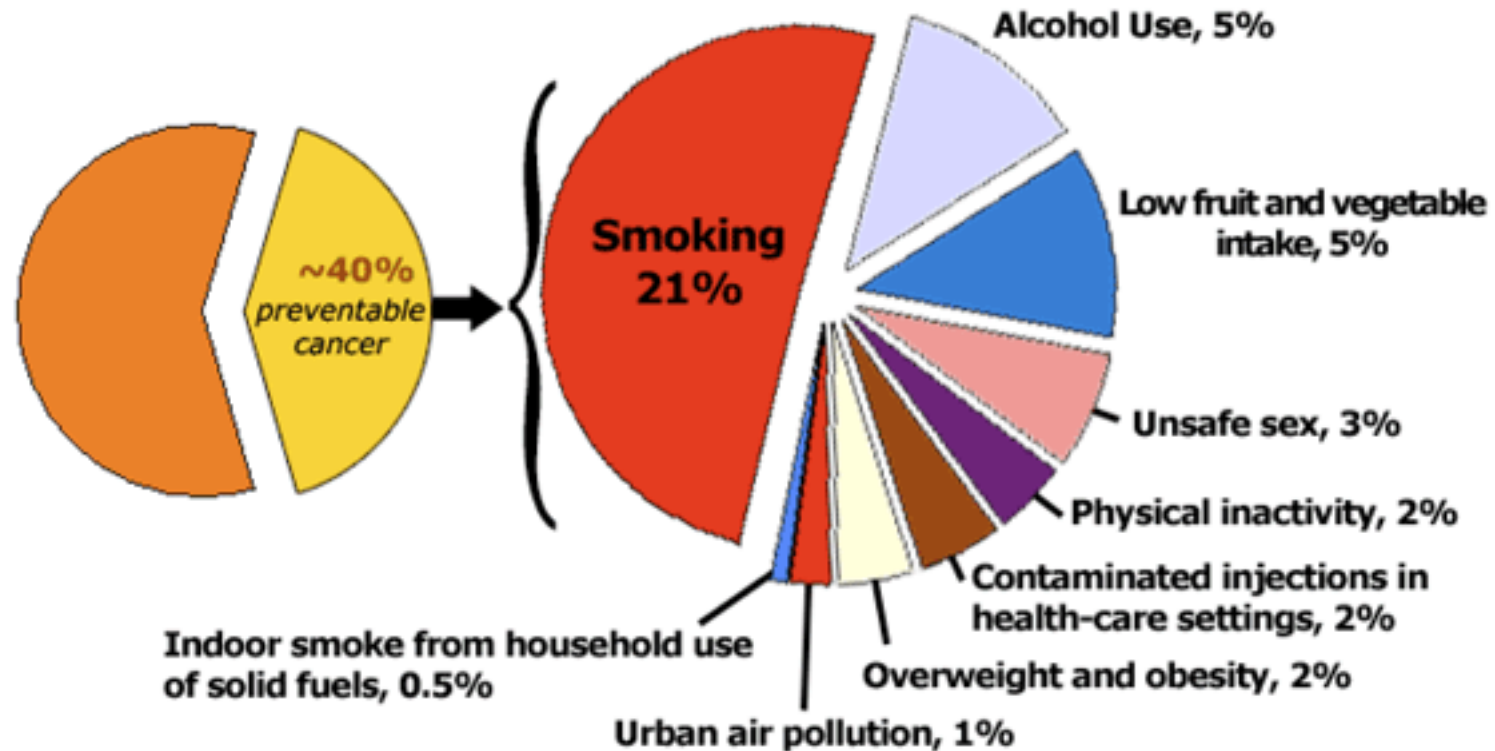
- 1 Don't use tobacco.
- 2 Protect your skin from the sun.
- 3 Eat a healthy diet.
- 4 Maintain a healthy weight and be physically active.
- 5 Practice safer sex and avoid risky behaviors.
- 6 Get immunized (HPV & hepatitis vaccines).
- 7 Know your family medical history and get regular cancer screenings.

To learn more, please visit www.preventcancer.org

What people actually think....



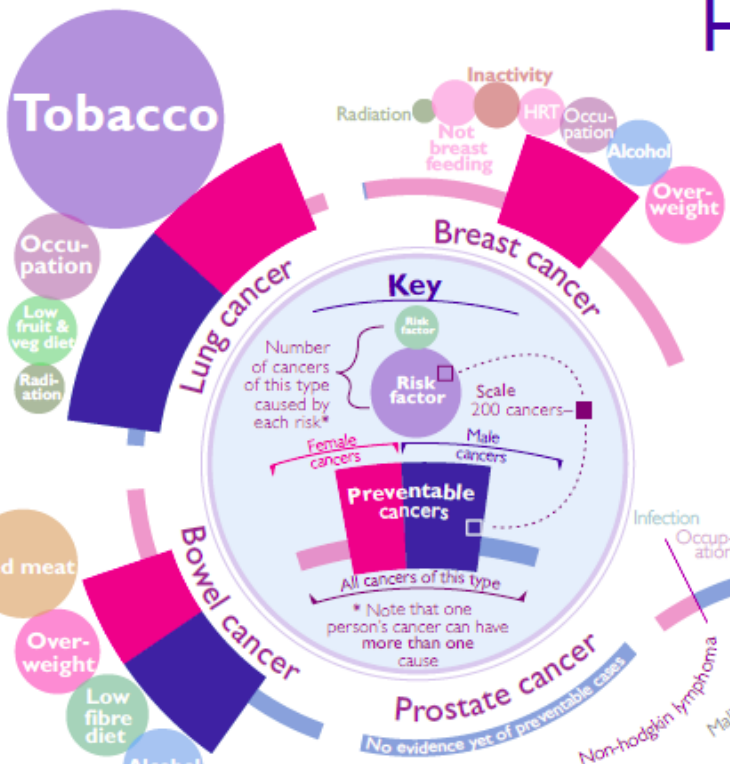
40% of all cancers could be prevented!



Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors *The Lancet*, 2005, 366:1784-1793

All cancers

- HRT** Taking any type of Hormone Replacement Therapy
- Salt** Having at least 6 grams a day
- Not breastfeeding** Breastfeeding each child for less than 6 months
- Inactivity** Being moderately active for less than 150 minutes a week
- Low fibre diet** Having less than 23 grams of fibre a day
- Radiation** Being exposed to any ionising radiation, including background levels such as those released from the earth
- Red meat** Eating any red or processed meat
- Infections** Exposure to cancer-causing infections like HPV and Hepatitis B or C
- Sunlight & sunbeds** Getting more UV than was typical for people born in 1903
- Occupation** Being exposed to cancer-causing chemicals or conditions at work
- Alcohol** Drinking any type of alcohol
- Low fruit & veg diet** Getting fewer than five portions a day
- Overweight** Having a BMI of 25 kg/m2 or over
- Tobacco** Smoking any form of tobacco, or exposure to environmental tobacco smoke

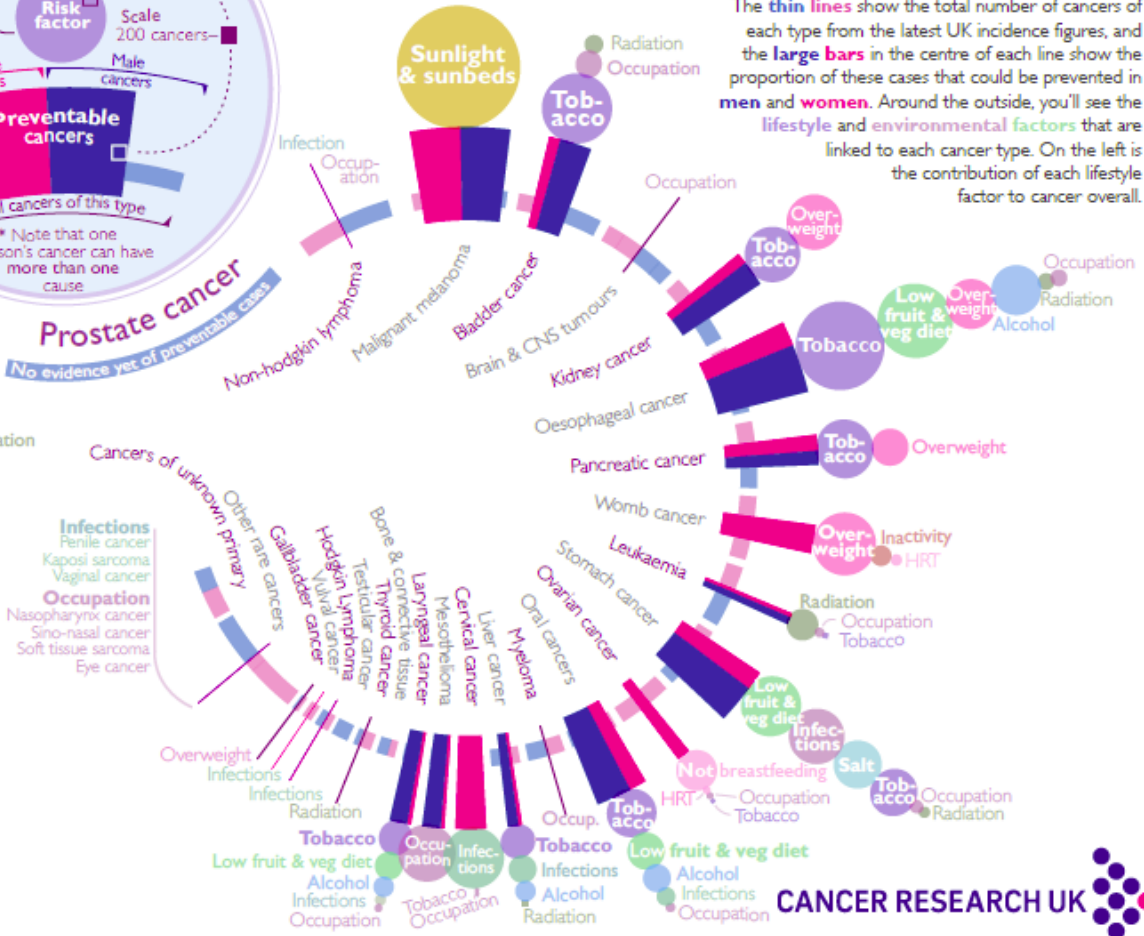


How many cancers can be prevented?

Although there are some things we can't control about our cancer risk, decades of research have clearly shown that by living a **healthy life**, people can reduce the risk of developing the disease. But how many cancers in the UK are really caused by things we can change?

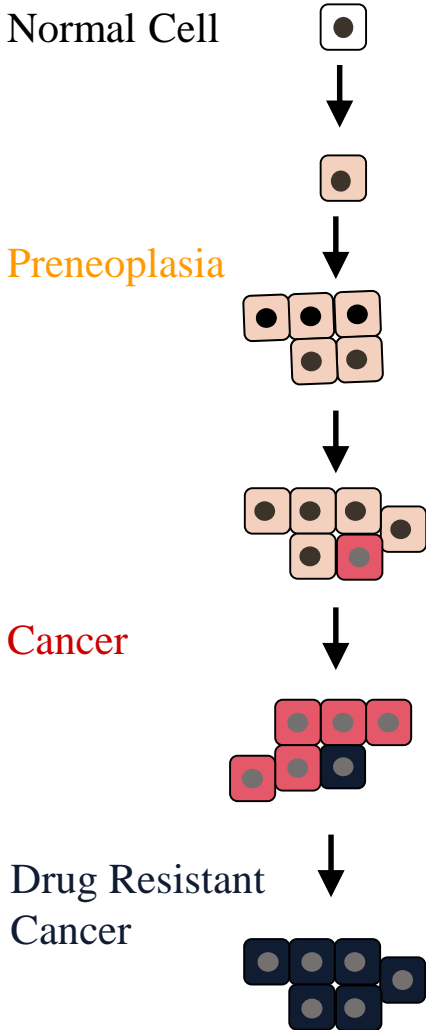
This diagram shows the results of new research funded by Cancer Research UK, which aims to show the number of cancer cases in the UK that could be prevented by known lifestyle and environmental factors, like being a **non-smoker**, keeping a **healthy weight**, drinking **less alcohol**, eating a healthy, **balanced diet**, and **avoiding** being exposed to certain infections or radiation.

The **thin lines** show the total number of cancers of each type from the latest UK incidence figures, and the **large bars** in the centre of each line show the proportion of these cases that could be prevented in **men and women**. Around the outside, you'll see the **lifestyle and environmental factors** that are linked to each cancer type. On the left is the contribution of each lifestyle factor to cancer overall.



Together we will beat cancer

Chemical Safety and Cancer Prevention



Associate Professors/Group Leaders



Bettina
Grasl-Kraupp



Wolfgang
Huber



Siegfried
Knasmüller



Gergely
Szakacs

Questions addressed....

What are the environmental factors contributing to cancer?

How can we use this knowledge to prevent cancer?

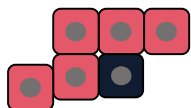
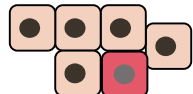
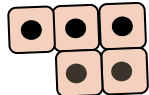
How can we prevent drug resistance?

Genotoxic Carcinogens



Siegfried
Knasmüller

Normal Cell



Preneoplasia

Cancer

Drug Resistant
Cancer

- **Prevention of nutritional effects: obesity**

- **Environmental control**

Misik et al. Environ Sci Pollut Res Int. 2015; Misik et al. Environ Res. 2014.

- **Occupational exposures: biomarkers, monitoring**

Bolognesi et al. Mutagenesis. 2015; Nersesyan et al. Mutat Res Rev 2014; Bonassi et al. Mutat Res. 2011; Thomas et al. Nat Protoc. 2009.

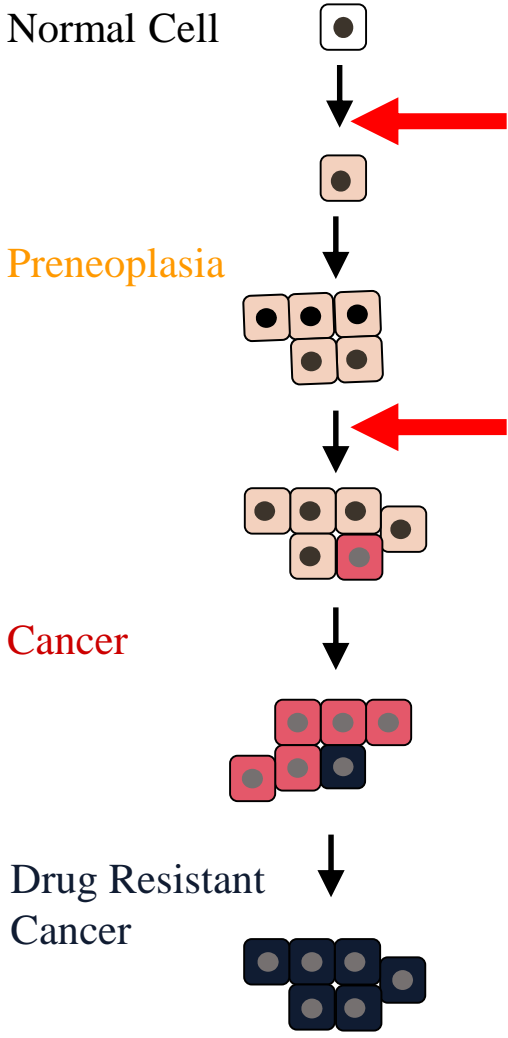
- **Newly developed chemicals**

Ferk et al. Arch Toxicol. 2016; Koller et al. Food Chem Toxicol. 2015; Koller et al. Arch Toxicol. 2013.



Bettina Grasl-Kraupp

Tumor promotion-hepatocarcinogenesis

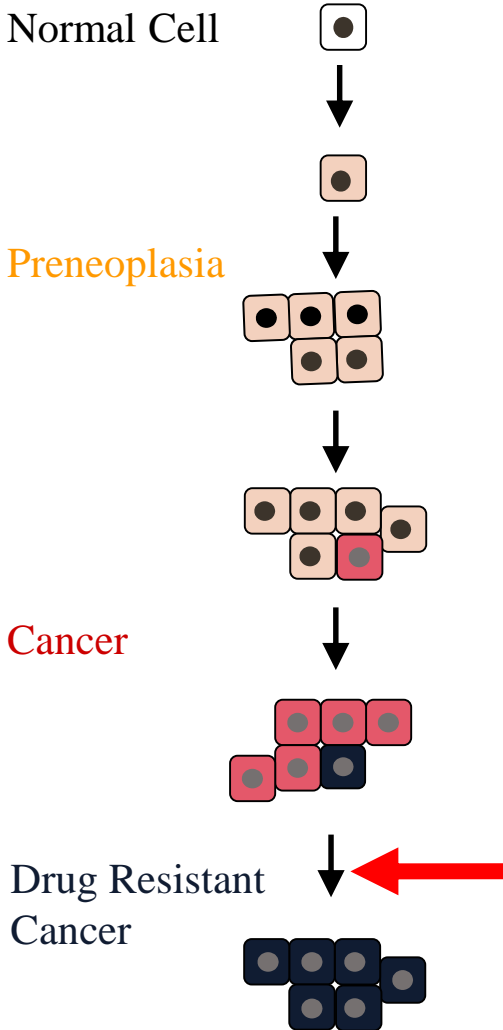


- **Peroxidized lipids in food**
Sagmeister et al. J. Hepatol 2008, Rohr-Udilova et al., Hepatology 2012, Böhm et al., J. Hepatol 2013
- **Secretome of mesenchymal liver cells**
Drucker et al., Carcinogenesis 2006; Klepeisz et al., PlosOne 2013
- **Secretion of HB-EGF from preneoplastic cells**
Sagmeister et al., J. Hepatol 2008; Nejabat et al., in preparation
- **Phox-activity in Kupffer cells**
Parzefall et al., Arch. Toxicol. 2015
- **Secretion of TNF α as anti-apoptosis factor**
Riegler et al., Carcinogenesis 2015

Chemoprevention of drug resistance



Gergely Szakacs



- **Role of efflux-based mechanisms in the drug resistance of cancer**

Szakacs et al., Nature Rev. Drug Disc 2004

- **Investigating the pathophysiological role of ABCB6**

Kiss et al. PlosOne 2012, Kiss et al. et al., Biochem J 2015

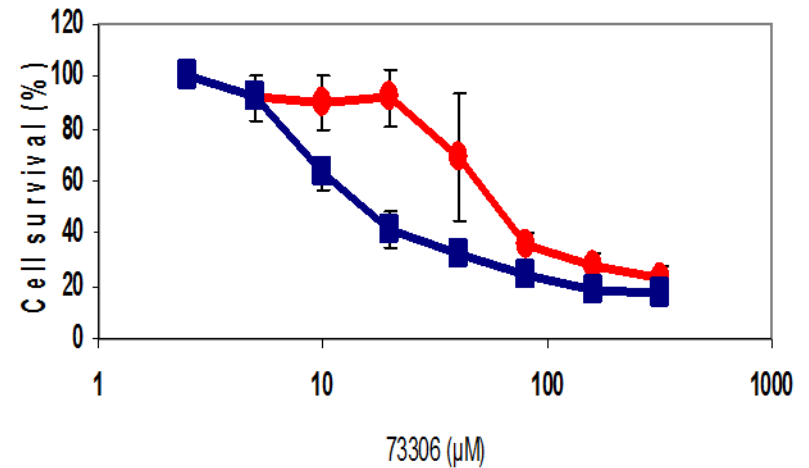
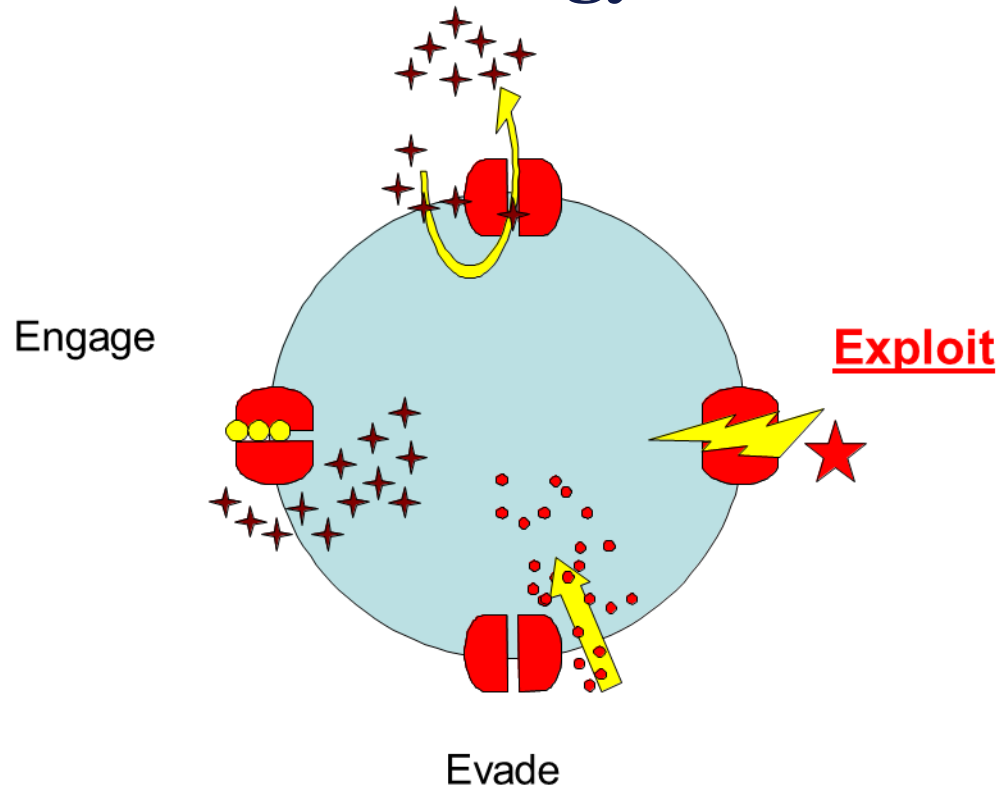
- **Investigating the mechanism of action of ABCB1**

Bársony et al., Scientific Reports 2016


- **Collateral sensitivity**

Szakács et. al., Chem Rev 2014, Pape et al., Eur J Med Chem 2016, Pape et al., J Inorg Biochem 2015

Targeting the Achilles' heel: a radically new strategy to eliminate MDR cells

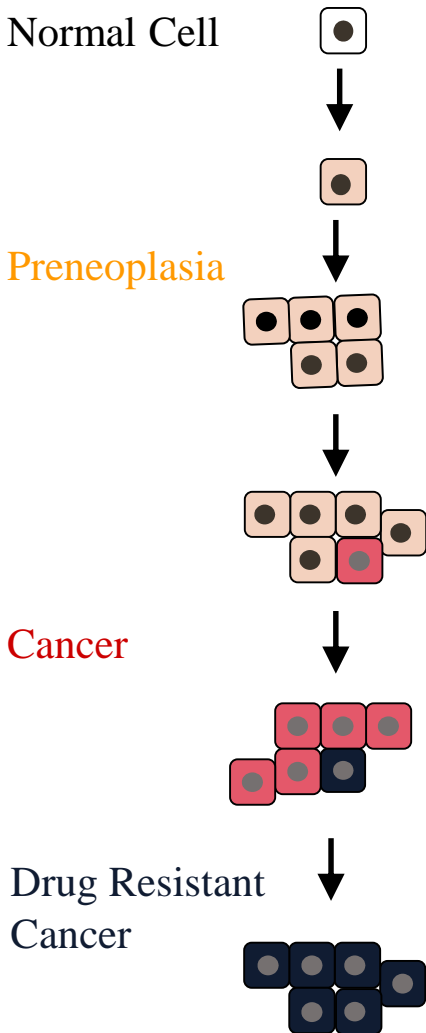


MDR-selective compounds exploit the paradoxical vulnerability of MDR cells

- 
- Szakács *et al.* *Nature Reviews Drug Discovery*. 2006; 5, 219–234
 - Szakács *et al.* *Drug Discov Today*. 2008;13(9-10):379-93.
 - Szakacs G *et al.* *Cancer Cell*. 2004;6(2):129-37.
 - Szakacs G *et al.*, *Chem Rev*. 2014 Jun 11;114(11):5753-74.

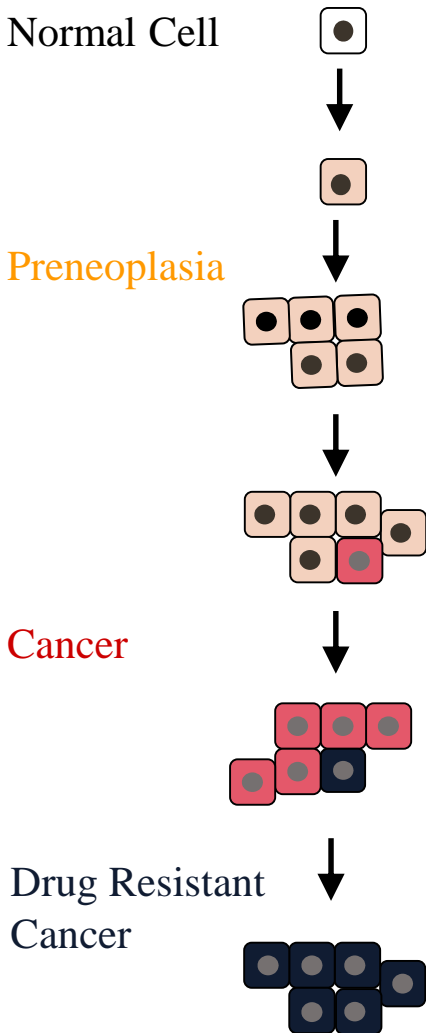


Chemical Safety and Cancer Prevention



•Study of chemical and physical factors contributing to cancer

Chemical Safety and Cancer Prevention



- Study of chemical and physical factors contributing to cancer

- Work with federal agencies

AUSTRIAN GOVERNMENT

Codex Alimentarius

FAO/WHO Codex-Alimentarius commission (WECO)

Scientific committee for genetic technology (WAFI)

Health committee for tobacco products and e-cigarette

EUROPEAN FOOD SAFETY AUTHORITY

Scientific Panel on food contaminants (CONTAM)

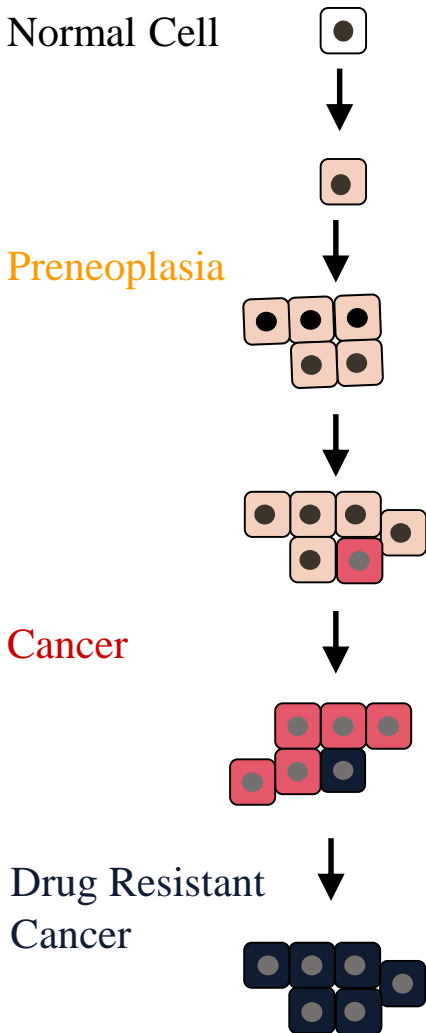
GERMAN AUTHORITY

National Institute for Risk Assessment Berlin:

BfR-Kommission für „Lebensmittelzusatzstoffe,

Aromastoffe und Verarbeitungshilfsstoffe“

Chemical Safety and Cancer Prevention



- Study of chemical and physical factors contributing to cancer
- Work with federal agencies
- Engage public stakeholders



The European Human Biomonitoring Initiative:
 a cross-sector Science-Policy initiative
 for a better regulated internal market

Understanding and tackling the possible human health problems related to chemical exposure whilst protecting industrial competitiveness

umweltbundesamt^U
 ENVIRONMENT AGENCY AUSTRIA

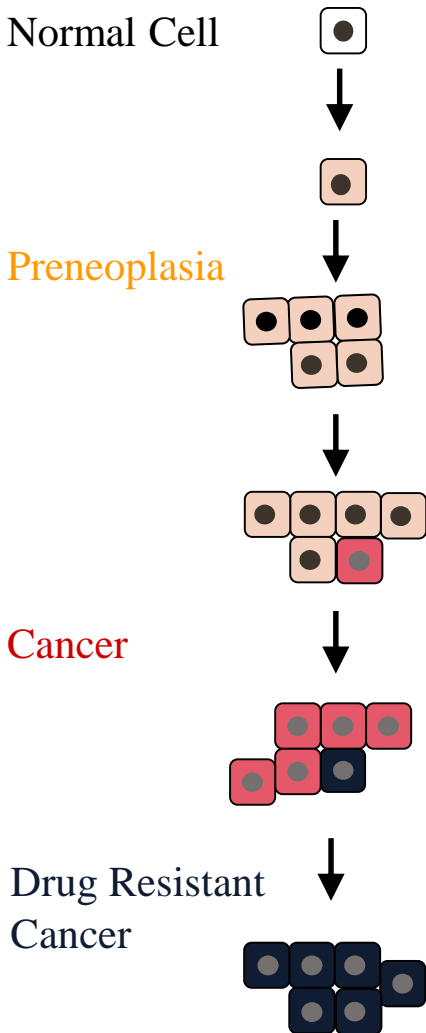
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 UNIVERSITÄT
 WIEN

Institute of
 Environmental Health,

Inst. of Cancer
 Research
 B. Grasl-Kraupp
 S. Knasmüller

Department of
 Epidemiology

Chemical Safety and Cancer Prevention



- Study of chemical and physical factors contributing to cancer
- Work with federal agencies
- Engage public stakeholders

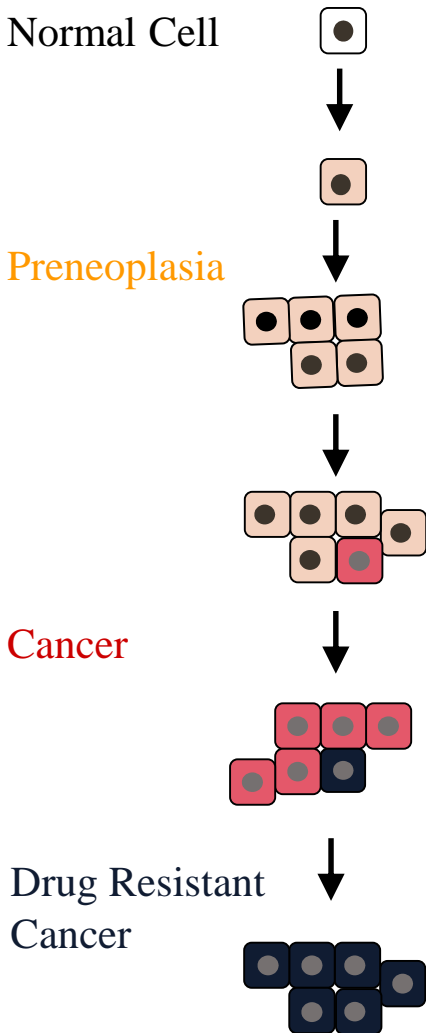
- Train interdisciplinary researchers

Postgraduate Course Toxicology, MUW IKF

- **Master of Sciences in Toxicology**
- **European Registered Toxicologist (ERT)**
- **Since 1993 -150 international attendees from Regulatory Authorities, Companies, and Universities.**



Chemical Safety and Cancer Prevention



- Study of chemical and physical factors contributing to cancer
- Work with federal agencies
- Engage public stakeholders
- Train transdisciplinary researchers
- Prioritize prevention
- Transform how research is conducted
- Translate and communicate science to society