Cancer risk assessment, prevention and long-term follow-up

- EUROCAN Platform WP2

WP leader: Chris Wild, IARC – represented by Zdenko Herceg
Outline

- Partnership
- Concepts: Exposome and « two ways translational research »
- Objectives (6)
- Deliverables (7)
- Projects:
  - Metabonomics
  - Epigenetics
- Coordination within and outside EUROCAN platform
## Partners

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Ranges in Biomarker Research

« Epidemiological range »

Disease genotype/phenotypic correlations (molecular pathology and classification)

Preclinical markers, precursors and early detection

Adaptive responses and effects of exposure

Exposures

Assessing baseline variations

EXPOSOME
Exposome

- Integrated sum of measurable factors that influence individual risk to develop cancer over lifetime

- Maternal and childhood exposures, effects of exposures and lifestyle throughout life and factors that modulate the responses of individuals

- Understanding the molecular diversity of cancer (genomics, transcriptomics, epigenomics, proteomics, and metabonomics).
Two-ways translational research

• To ensure the translation of emerging molecular knowledge to population as well as to clinical context
WP 2 Objectives (1-2)

1. Translational research on biomarkers of risk, early detection, prognosis and prediction of cancer
   - Use of large cohort studies (e.g. EPIC)
   - Blood samples/tumor tissues

2. Epignetics and metabonomics to identify preventable risk profiles
   - Preanalytical variables
   - Identify patterns for dietary/pharmacological modulation
WP 2 Objectives (2-4)

3. Improve evidence-based quality assurance in screening
   - Guidelines on digital imaging for BC screening

• Develop biomarker-based chemoprevention trials (EIO)
  - clinical selection of subjects with early disease
  - early detection/biomarkers of effect
WP 2 Objectives (5-6)

5. Integrate biobanks and cancer registries for evaluation of interventions
   - use of registries for long-term follow-up and for monitoring outcomes

6. Promote evidence-based prevention recommendations
   - Update and develop the European Code against Cancer
Deliverables

1. D2.1: Expert group meeting on “two way translational cancer research” and recommendation and guidelines for developing biomarkers for cancer prevention (month 18)

2. D2.2: Position paper on “Assessment of genome-wide research for understanding molecular pathways causal for cancer and amenable to drug-based intervention” (month 48).

3. D2.3: SOPs and guidelines on biobanking and pre-analytical processing for metabonomics (month 36).

4. D2.4: Expert group on “Research needs for evidence-based guidelines on cancer screening (month 24)

5. D2.5: Expert meeting and report on “European recommendations on biomarker-based chemoprevention trials” (month 48)

6. D2.6: Expert group meeting and recommendations on “Roadblocks and remedies for the use of cancer registration as instruments for long-term patients follow-up” (month 12)

7. D2.7: Consensus meeting on “Contribution of molecular epidemiology to evidence-based developments of the European Code against Cancer: (month 55)
Projects

1. Metabolomics: unravelling the associations between nutrition, lifestyles and cancer

2. Epigenetics: identifying epigenetic markers for early detection of cancer using large prospective cohort
European Prospective Investigation on Nutrition and Cancer (EPIC)

- EPIC was designed to investigate the relationships between diet, lifestyle and environmental factors and the cancer
- over half a million (520,000) people in 10 European countries recruited
- currently over 2,200 incident (newly diagnosed) lung cancer cases
Metabolomics to unravel new associations between nutrition, lifestyles and cancer

Augustin Scalbert, IARC

- **Biomarkers** to improve measurement of exposure to cancer risk factors
  - Measurement errors using dietary questionnaires
  - Missing food composition data (bioactives, contaminants)
- **Exposome** = thousands of compounds derived from the diet and other environmental exposures and found in biospecimens
- **Challenge** = assessment at the individual level of a large variety of environmental exposures
- **Metabolomics**
  - Discovery of new biomarkers of exposure
  - Quantitative measurement of biomarkers in metabolome-wide association studies

28,000 compounds in foods
Identification of biomarkers of dietary exposure in the EPIC cohort

- **Metabolomics to compare groups of subjects with different exposure levels**
  - European Prospective Investigation into Cancer and Nutrition (EPIC)
  - 1,000 subjects with urine/plasma samples and detailed information on dietary intake
  - High-resolution mass spectrometry
  - Comparison of metabolic profiles in low and high consumers of foods of interest
  - Identification of discriminating features

- **Database on the food metabolome**
  - Selection of foods/nutrients of interest
  - Food constituents, metabolism in the body to identify promising candidate biomarkers (specificity, sensitivity)
  - Spectral data used for the identification of biomarkers in metabolomic profiles

- **Development of analytical methods for measurement of biomarkers of exposure in large-scale cohort studies**
A general framework for the identification of biomarkers of dietary exposure

- Candidate biomarkers
  - Biomarker identification
    - Biofluid analysis
  - Metabolomics to compare groups with varying exposure
- Biomarker qualification
- Analytical development and validation
- Validated biomarker
- Food metabolome database
  - Food composition
  - Pharmacokinetics
  - Metabolism
- Candidate biomarkers
Epigenome as an interface between genome and environment
Identifying early epigenetic markers associated with cancer risk and their environmental determinants

Zdenko Herceg, IARC

- Goals - to identify epigenetic changes in breast and lung cancer and surrogate (blood) tissues and to identify the dietary/lifestyle determinants of these epigenetic changes in the context of a large prospective study.

- Takes advantage of large prospective cohort (European Prospective Investigation into Cancer and Nutrition, EPIC).

- Combined with powerful tools for epigenomic (DNA methylome) analysis of large series of biological samples and next generation sequencing as well as measurement of one-carbon metabolism metabolites.
Cumulative risk of lung cancer among never, former and current smokers

Cumulative risks up to age 79 were based on age-specific incidence rates estimated within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, separately for men and women, and among never, former, and current smokers, combined with odds ratio estimates of lung cancer by median serum levels of B_6 and methionine. High/high indicates having above-median levels of both vitamin B_6 and methionine and low/low indicates having below-median levels.

Johansson et al., JAMA 2010
Coordination within and outside EUROCAN Platform

- WP3, 10, 11, 12
- BBMRI (Biobanks)
- UICC (European Code)
- EACR, EUROCOURSE (Registries)
- Metabonomics: CRMN, ICL
- Large cohorts: EPIC (EU/NIH)
- ECGC (EU Screening)