# **ERACOL| Research lines University of Torino, Italy** Updated 2010-03-10

# **General information**

Institution:	University of Torino
City:	Turin
Country:	Italy

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1. research line 1:

Birth cohort studies

# 2. general description of the research line:

Birth cohort study in Italy: the NINFEA project

### 3. specific subtopics within the research line:

NINFEA is an ongoing internet-based multi-purpose birth cohort set up to investigate the effects of exposures acting during pre-natal and early post-natal life on infant, child and adult health. Women are recruited during pregnancy. To participate they register at the study website (<u>www.progettoninfea.it</u>) and complete a baseline on-line questionnaire. The study involves other two on-line questionnaires at 6 months and 18 months after delivery and passive and active follow-up of the children for at least 18 years. A sample of saliva from the mothers and the children is obtained from approximately 50% of the participants in the cohort. The saliva is frozen at - 80°C and stored in a biobank. Recruitment is ongoing. By February 2010, some 2600 pregnant women have participated in the study. Current research lines within the framework of the birth cohort include:

- Methodological studies on the validity and feasibility of internet-based studies
- Nested studies within the cohort: current focus is on determinants of growth and wheezing in the first years of life
- Collaboration in international projects involving birth cohort studies (see for example the European projects enrieco and chicos).
- 4. contact person for interested students/teaching staff:

Lorenzo Richiardi, Cancer Epidemiology Unit. Email: Lorenzo.richiardi@unito.it

# 5. Field of research (for example: epidemiology, public health, statistics, medicine):

epidemiology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 2:

Epigenetics

# 2. general description of the research line:

Studies of association between epigenetic patterns and cancer development and progression

### 3. specific subtopics within the research line:

Analysis of epigenetic patterns in different case cancer series

Prostate cancer

- Two cohorts of approximately 250 prostate cancer patients diagnosed in the 1980s and in the 1990s and followed-up for mortality until 2007. The study focuses on the methylation status in the tumor and in the non-tumor tissue in association with survival. Both hyper- and hypomethylation patterns will be investigated, as well as proteins involved in the methylation machinery
- Cervical cancer
- Population-based case-control study in Curitiba (Brazil). It involves approximately 300 cases with high grade histology [Cervical Intraepithelial Neoplasia (CIN) grade 2 and 3] and 300 controls both testing positive for human papillomavirus (HPV) infection. Cases and controls donated cervical and blood samples for investigation on the HLA-G gene methylation status and polymorphisms in relation with HPV persistence and neoplastic evolution.
- Brain Cancer
- Study of MGMT methylation as potential biomarker of prognostic and therapeutic significance. Analysis of the methylation status of MGMT gene in tumor tissue and in serum circulating DNA in relation with alkylating chemotherapy response and overall survival. Specific aim is to verify the utility of monitoring MGMT methylation in circulating DNA to predict chemotherapy response and prognosis. The study involved consecutive patients (120/year) with brain tumors recruited at the Neuro-Oncology Department in Turin. Patients donated a blood sample at time of diagnosis and subsequently every three months during clinical controls.

### 4. contact person for interested students/teaching staff:

Anna Gillio Tos, Cancer Epidemiology Unit. Email: gilliotos\_demarco@libero.it

### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Molecular epidemiology

# 6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

Undergraduate, master, doctorate, post-doctorate

# 1. research line 3:

Cervix Uteri screening

# 2. general description of the research line:

The CPO (Centre for cancer prevention of the Piedmont region is the co-ordination centre of the NTCC (New Technologies for Cervical Cancer) trial. The large, multicenter, population based randomized trial estimated the effect of HPV testing as a primary screening tewst for cervical cancer. The HPV test is more sensitive than conventional cytology for CIN2+ but less specific. Especially in young women the prevalence of HPV infections is high as well as the proportion of HPV infection which regress. The NTCC trial showed (Ronco G, Giorgi-Rossi P, Carozzi F, Confortini M, Palma PD, Del Mistro A, Ghiringhello B, Girlando S, Gillio-Tos A, De Marco L, Naldoni C, Pierotti P,Rizzolo R, Schincaglia P, Zorzi M, Zappa M, Segnan N, Cuzick J; the New Technologies for Cervical Cancer screening (NTCC) Working Group. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. Lancet Oncol. 2010 Mar;11(3):249-257) that in women younger than 35 years of age the higher relative sensitivity of HPV test causes an overtreatment of precursor lesion (CIN2+), but over 35 years HPV test prevents more invasive cancers than conventional cytology , being the specificity the same and the lead time longer than lead time of conventional cytology.

### 3. specific subtopics within the research line:

1. Implementation of pilot programs in the female population invited to cervical screening in Piedmont with HPV test .

According to the results of NTCC and other trials with HPV adopted as a primary screening test , the CCN (Centro Controllo Malattie of Italian Ministry of Health) funded a multicentre pilot screening program in Piedmont , Emilia and Trentino, lead by CPO, with HPV HC2 as test of screening.

The pilot screening study is a randomized trial: women over 35 years of age are randomized by birth year to HPV or conventional cytology. The objectives of the trial are to compare the compliance to HPV test and to cytology, the referral rate to colposcopy, the detection rate of precursor lesions and the costs of the two screening tests.

2. P16 protein as triage test in HPV screening versus cervical cytology. HPV positive women are referred to colposcopy if the cytology is positive. The predictive value of P16 for CIN2+ has been shown higher than conventional cytology as triage test (Carozzi F, Confortini M, Dalla Palma P, Del Mistro A, Gillio-Tos A, De Marco L, Giorgi-Rossi P, Pontenani G, Rosso S, Sani C, Sintoni C, Segnan N, Zorzi M, Cuzick J, Rizzolo R, Ronco G; New Technologies for Cervival Cancer Screening (NTCC) Working Group. Use of p16-INK4A overexpression to increase the specificity of human papillomavirus testing: a nested substudy of the NTCC randomised controlled trial. Lancet Oncol. 2008 Oct;9(10):937-45). The implementation in the screening program of this triaging approach deserves a careful evaluation in order to organize the population screening.

### 4. contact person for interested students/teaching staff:

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5. Field of research (for example: epidemiology, public health, statistics, medicine):

Cancer epidemiology and public health

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 4:

Lymphoma

# 2. general description of the research line:

Biological and molecular stratification in high grade B- and T-cell lymphoma

# 3. specific subtopics within the research line:

B-cell Non-Hodgkin lymphoma

A cohort of 97 Diffuse Large B-cell Lymphoma (DLBCL) in young patients (<61yrs) with poor prognosis and treated with 4 courses of dose-dense R-MegaCEOP14, followed by R-HDC and ASCT (2 R-MAD + BEAM and ASCT) (Recruitment period: 2002-2005). The study focuses on expression stratification of and clinical correlation using a panel of protein markers (i.e. CD20, CD3, CD10, CD138, Ki67, Bcl6, Bcl2, MUM1 and cyclinD1), FISH probes (c-myc, Bcl-2, p53 etc.) and qRT-PCR analyses (*LMO2*, *BCL6*, *FN1*, *CCND2*, *SCYA3*, and *BCL2*). The main objective is the define and validate a "routine clinical stratification approach" for the designed of "ad hoc tailored therapies".
Collaborative studies with centers in Europe and outside Europe (USA).

T-cell Non-Hodgkin lymphoma

- A cohort of 271 Peripheral T-cell Lymphoma, including PTCL-NOS (158), AILD (38), ALK+ ALCL (41) and ALK-ALCL (34) molecularly stratified lymphoma (GEP). The study focuses on high density genome wide-SNP based array analyses and on the bioinformatics integration of genomics transcriptional data. The main objective is the identification of biomarkers/molecular signatures for patient selection and stratification and the discovery of relevant pathogenetic defects among different subtypes.
- Collaborative studies on PTCL with Centers in Europe and American Countries (USA, Brasil etc.).

### 4. contact person for interested students/teaching staff:

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### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Molecular Oncology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

Master, doctorate, post-doctorate/teaching staff

# 1. research line 5:

Cervix Uteri screening

# 2. general description of the research line:

The CPO (Centre for cancer prevention of the Piedmont region is the co-ordination centre of the NTCC (New Technologies for Cervical Cancer) trial. The large, multicenter, population based randomized trial estimated the effect of HPV testing as a primary screening tewst for cervical cancer. The HPV test is more sensitive than conventional cytology for CIN2+ but less specific. Especially in young women the prevalence of HPV infections is high as well as the proportion of HPV infection which regress. The NTCC trial showed (Ronco G, Giorgi-Rossi P, Carozzi F, Confortini M, Palma PD, Del Mistro A, Ghiringhello B, Girlando S, Gillio-Tos A, De Marco L, Naldoni C, Pierotti P,Rizzolo R, Schincaglia P, Zorzi M, Zappa M, Segnan N, Cuzick J; the New Technologies for Cervical Cancer screening (NTCC) Working Group. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. Lancet Oncol. 2010 Mar;11(3):249-257) that in women younger than 35 years of age the higher relative sensitivity of HPV test causes an overtreatment of precursor lesion (CIN2+), but over 35 years HPV test prevents more invasive cancers than conventional cytology , being the specificity the same and the lead time longer than lead time of conventional cytology.

### 3. specific subtopics within the research line:

1. Implementation of pilot programs in the female population invited to cervical screening in Piedmont with HPV test .

According to the results of NTCC and other trials with HPV adopted as a primary screening test , the CCN (Centro Controllo Malattie of Italian Ministry of Health) funded a multicentre pilot screening program in Piedmont , Emilia and Trentino, lead by CPO, with HPV HC2 as test of screening.

The pilot screening study is a randomized trial: women over 35 years of age are randomized by birth year to HPV or conventional cytology. The objectives of the trial are to compare the compliance to HPV test and to cytology, the referral rate to colposcopy, the detection rate of precursor lesions and the costs of the two screening tests.

2. P16 protein as triage test in HPV screening versus cervical cytology. HPV positive women are referred to colposcopy if the cytology is positive. The predictive value of P16 for CIN2+ has been shown higher than conventional cytology as triage test (Carozzi F, Confortini M, Dalla Palma P, Del Mistro A, Gillio-Tos A, De Marco L, Giorgi-Rossi P, Pontenani G, Rosso S, Sani C, Sintoni C, Segnan N, Zorzi M, Cuzick J, Rizzolo R, Ronco G; New Technologies for Cervival Cancer Screening (NTCC) Working Group. Use of p16-INK4A overexpression to increase the specificity of human papillomavirus testing: a nested substudy of the NTCC randomised controlled trial. Lancet Oncol. 2008 Oct;9(10):937-45). The implementation in the screening program of this triaging approach deserves a careful evaluation in order to organize the population screening.

### 4. contact person for interested students/teaching staff:

Lorenzo Richiardi, Cancer Epidemiology Unit. Email: Lorenzo.richiardi@unito.it Guglielmo Ronco, Nereo Segnan

5. Field of research (for example: epidemiology, public health, statistics, medicine):

Cancer epidemiology and public health

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 6:

Male cancers

# 2. general description of the research line:

Studies on aetiological and prognostic factors in prostate and testicular cancer

# 3. specific subtopics within the research line:

Testicular cancer

• population-based case-control study in the province of Turin. It involves approximately 250 cases of testicular cancer diagnosed between 1997 and 2008 and 500 matched controls (Recruitment period: 2008- July 2010). Cases and controls completed a questionnaire focusing on puberty and exposures occurring during puberty, fertility and testicular health, and donated a sample of saliva from which DNA was extracted and stored at -80 °C.

• Collaborative studies on testicular cancer with centers in Europe and outside Europe.

Prostate cancer

- Two cohorts of approximately 250 prostate cancer patients diagnosed in the 1980s and in the 1990s and followed-up for mortality until 2007. The study focuses on the methylation patterns in the tumor and in the non-tumor tissue in association with survival.
- Series of approximately 150 prostate cancer patients with a negative prostate biopsy obtained at least three months before the diagnosis of prostate cancer. The study focuses on the methylation pattern in the prostate tissue before and after the diagnosis of the cancer.

# 4. contact person for interested students/teaching staff:

Lorenzo Richiardi, Cancer Epidemiology Unit. Email: Lorenzo.richiardi@unito.it

# 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Cancer epidemiology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 7:

Occupational cancer

# 2. general description of the research line:

Studies on mortality and cancer incidence among workers employed in certain industrial settings and Surveillance of mesothelioma incidence in the general population (residents in Piedmont, 4.2 million inhabitants)

# 3. specific subtopics within the research line:

Rubber industry

• Mortality study in a tyre factory with 9500 workers, follow-up 1962-2003. Study of incident cases of bladder cancer 1977-2003. Standard analyses of mortality and cancer incidence completed. A nested case-control study on bladder cancer is being carried out.

• Mortality study in a tyre factory with 3000 workers, follow-up 1972-2007. Study of incident cases of bladder cancer 2000-2007. Standard analyses of mortality and cancer incidence under way. A nested case-control study on bladder cancer is planned.

• Mortality study in a tyre factory with 4500 workers, follow-up is being planned. Factory opened in 1955.

• Factory-specific job exposure matrices will be developed.

Asbestos industry

- Two cohorts of 5000 workers employed in asbestos-cement factories, follow-up 1950-2008. Standard analyses of mortality and cancer incidence completed. Analyses of mesothelioma mortality and incidence according to time-related variables are being planned.
- Factory-specific job exposure matrices will be developed.

Registry of malignant mesotheliomas, Piedmont Region

- Surveillance: Publication of statistics on incidence, survival at the regional and national level
- Ad hoc studies: Population-based case-control studies on gene-environment interactions

### 4. contact person for interested students/teaching staff:

Dario Mirabelli, Cancer Epidemiology Unit. Email: dario.mirabelli@cpo.it

5. Field of research (for example: epidemiology, public health, statistics, medicine):

Cancer epidemiology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

## 1. research line 8:

Longitudinal research on social inequalities and health

### 2. general description of the research line:

Lifecourse study of the influence of working careers on morbidity/mortality and of health conditions on social mobility and premature retirement

### 3. specific subtopics within the research line:

The study is conducted on a longitudinal dataset including the whole population resident in Turin at 1971, 1981, 1991 and 2001 censuses, linked at the individual level with archives of hospital admissions and drug prescriptions, and with population registries (cancer, diabetes, miocardial infarction). Main objectives are:

- monitoring socioeconomic inequalities in cause-specific mortality, morbidity (cardiovascular diseases, depression, cancer, diabetes) and health service utilisation;

- evaluating the independent and mutual effects of neighbourhood socioeconomic deprivation and of individual socioeconomic conditions on cause-specific mortality;

- analysing the distribution of mortality over time, trying to disentangle: the effect of individual socioeconomic conditions, the effect of neighbourhood socioeconomic deprivation and the effect of the different degree of segregation by socioeconomic conditions over time;

- assessing the relationship among morbidity before census 2001, employment status of the subjects at 2001 and the occurrence of new morbidity after 2001, in order to assess the effect of health status as a determinant and as a consequence of continuing work or retiring;

- comparing strength and direction of the associations observed between social and health careers in Italy with those assessed in the United Kingdom and in Finland, in the light of the different welfare typologies operating in these countries, in order to evaluate the impact of the work and pension policies on health and retirement.

### 4. contact person for interested students/teaching staff:

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5. Field of research (for example: epidemiology, public health, statistics, medicine):

Social epidemiology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 9:

Childhood cancer

# 2. general description of the research line:

Descriptive studies on childhood cancer in Italy and on the risk of acute promyelocitic leukaemia in Latino children as compared to other ethnic phenotypes

### 3. specific subtopics within the research line:

- Geographic comaprison of incidence rates by tumour type (ACCIS classification) in Italy, period 2003-2007. Data source 19 population-based registries covering 45% of the country.
- Time trends of childhood and adolescent cancer incidence in Italy; data source: populationbased registries with continuing data from 1988 to 2007.
- Comparison of survival probability by cancer type in children (age 0-14 years), adolescents (15-19) and young adults (20-29). Data from the central archive of Italian cancer registries.
- APL is a rare sub-type of acute myeloid leukaemia. In adult Americans higher rates have been observed in Hispanic compared to other races. Higher rates have also been reported in clinical and population-based series in Southern Europe as compared to Nordic countries, but comprehensive analyses of the geographic distribution in children have not been carried out.

Descriptive study of the incidence of APL in migrants in the Americas, comparing rates in population-based registries in Latin America and the US by race (Hispanic *vs.* Non-Hispanic) Data sources: registries published in Cancer Incidence in Five Continents (www-dep.iarc.fr) and the SEER database (seer.cancer.gov).

#### 4. contact person for interested students/teaching staff:

Paola Pisani, Cancer Epidemiology Unit, email: paola.pisani@unito.it

### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Cancer Epidemiology

# 6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 10:

Cardiovascular and cerebrovascular diseases

# 2. general description of the research line:

Environmental and genetic risk factors for cardiovascular diseases in the EPICOR cohort

### 3. specific subtopics within the research line:

EPICOR is a collaborative prospective investigation on the causes of cardiovascular diseases in Italian population-based cohorts recruited in the period 1993-1998, as the Italian section of the European Prospective Study on Nutrition and Cancer (EPIC). The total number of individuals who volunteered to participate in the study was 47,749 (15,171 men, 32,578 80 women). Five centres contributed to the total cohort: two in Northern Italy (Varese = 12,083 and Turin = 10,604), one in Central Italy (Florence = 13,597), and two in Southern Italy (Ragusa = 6,403 and Naples = 5,062). Highly standardized procedures were used, during recruitment and follow-up, across centres.

Promising genetic polymorphisms from Genome Wide Association (GWA) studies on cardiovascular disease will be replicated in the Italian cohort and epigenomic analysis will be carried out in order to identify new susceptibility genes. Gene-diet interaction will also be investigated in relation to population health.

4. contact person for interested students/teaching staff:

Giuseppe Matullo Email: Giuseppe.matullo@unito.it

5. Field of research (for example: epidemiology, public health, statistics, medicine):

Molecular and Genetic Epidemiology

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 11:

Social inequalities in health

### 2. general description of the research line:

Multicentre project on mechanisms of social inequalities in health and healthcare and on policies and interventions to fight them

### 3. specific subtopics within the research line:

Following the recent Communication of the European Commission on "Solidarity in health: reducing health inequalities in the EU", an EU expert group is developing a Health Inequalities Joint Action aiming at developing knowledge for action on health inequalities; supporting the engagement of Member States, regions and other stakeholders in action to tackle socio-economic health inequalities; sharing learning between Member States and other actors; supporting the development of effective action to tackle socio-economic health inequalities at the European policies level.

In this framework the Regional Epidemiology Unit ASL TO3 is building up a national network of collaborating centres, carrying out activities in different fields:

- evaluation of the impact on health of social policies (EU *Health in All Policies* approach), with an assessment of the differential impact by socioeconomic position;
- evaluation of the impact on socioeconomic inequalities in health of primary and secondary prevention policies (healthy lifestyles and cancer screening), including the estimation of Global Burden of Disease indicators for socioeconomic determinants;
- implementation and evaluation of equity audit models, for the monitoring of social inequalities in some of the main healthcare pathways (breast cancer, stroke) and in the introduction of new technologies (equity oriented Health Technology Assessment).

### 4. contact person for interested students/teaching staff:

Giuseppe Costa, University of Turin and Regional Epidemiology Unit ASL TO3 email: giuseppe.costa@epi.piemonte.it

#### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Social epidemiology, policy analysis

# 6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 12:

Clinical research network

# 2. general description of the research line:

How to support clinical research and help to facilitate the conduct of trials and other well-designed studies within the National Health Service (SSN).

### 3. specific subtopics within the research line:

Since 2003, the Center for Clinical Trials has been developed within the Clinical Epidemiology group, located at the Cancer Epidemiology Unit. The Center supports a regional network of clinical professionals, sites, and organizations for independent research, mainly in Oncology and Heamatology. At present about 100 clinical trials protocols (phase I, II, III) were reviewed. The Center contribution regarded:

- consultancy on protocol design and methodology, monitoring support, sample size calculation and statistical analysis;
- provision of a web based tool for collecting data and managing the process of patient enrollment and randomization (<u>www.epiclin.cpo.it</u>).

Main research fields in the next future will concern:

- definition of priority areas in which clinical studies are more needed;
- identification of standardized criteria to evaluate clinical research.

### 4. contact person for interested students/teaching staff:

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### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Clinical epidemiology

# 6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 13:

Bladder Cancer

### 2. general description of the research line:

Studies on aetiological and prognostic factors in bladder cancer

### 3. specific subtopics within the research line:

We are conducting a hospital-based case-control investigation at S. Giovanni Battista hospital in Turin, where about one third of the incident BC in the Turin metropolitan area are treated. Cases are histologically confirmed incident bladder cancer patients, while controls are patients with no neoplastic or smoking-related diseases. Until January 2010 we recruited approximately 600 cases and 600 controls. Each case and control filled in a questionnaire on history of tobacco smoking, occupational history, 24-hours medication use recall and food habits, and provided a blood and urine sample. We plan different research lines for the next three years that include study of genetic and environmental determinants of incidence and survival of bladder cancer. The Turin bladder case control study is involved in international collaborative studies (the NCI International Consortium of Bladder Cancer).

Promising genetic polymorphisms from Genome Wide Association (GWA) studies on bladder cancer will be replicated in the Turin case control study and epigenomic analysis will be carried out in order to identify new susceptibility genes and new genes involved in survival.

# 4. contact person for interested students/teaching staff:

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5. Field of research (for example: epidemiology, public health, statistics, medicine):

Molecular epidemiology.

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 14:

Clinical practice guidelines

# 2. general description of the research line:

Evaluation of the impact of clinical practice guidelines on quality of care and healthcare costs

# 3. specific subtopics within the research line:

- Within the Piedmont Regional Cancer Care Network clinical practice guidelines have been elaborated and implemented as tools for improving the quality of care. During the last ten years specific guidelines have been published for breast cancer, colorectal cancer, lung cancer and soft tissue sarcoma.
- Several cancer-specific indicators were identified for monitoring the guidelines impact on the appropriateness of care, outcomes, and healthcare costs. Main tools for monitoring clinical practice were:
  - administrative health data linked at individual level to identify patients' patterns of care;
  - ad hoc studies collecting patients' data from individual clinical records.

The first source allows population based studies and can provide useful information on whether key services are over- or underused but are limited in clinical details. The latter is more costly but provide more accurate information.

- Recently a clinical practice guideline on prostate cancer have been published. In the first instance the following aspects are going to be assessed:
  - compliance to key recommendations;
  - effect on appropriateness of care;
  - impact on resource consumption.

All these aspects will be analyzed with the appropriate tools described above. In particular, a study comparing the pre- and post- guideline implementation clinical practice will be conducted at Regional level, by collecting data from clinical records in the Cancer Care Network hospitals. Administrative data will be used to compare resource consumption across different time periods.

#### 4. contact person for interested students/teaching staff:

Cancer Epidemiology Unit

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### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Health Service Research

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 15:

Evidence Based Medicine

# 2. general description of the research line:

How to product and implement EBM Guidelines and Health Technology Assessment

# 3. specific subtopics within the research line:

The Cancer Epidemiology Unit – Center for Oncological Prevention (CPO) has contributed to the production of several evidence based (EBM) clinical practice guidelines, both at Regional and Hospital levels. Recently, the relevance of the EBM approach in medical decision making has been recognized at Regional level through the implementation of a pilot Health Technology Assessment group. HTA reports are in progress for major technologies, with particular attention to local needs and appropriateness of utilization.

Among the instruments for developing recommendations, GRADE approach is actually the most recommended. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group has developed a common, sensible and transparent approach to grading quality of evidence and strength of recommendations (www.gradeworkinggroup.org). The GRADE method is intended to be applied within different contests of regional HTA production such as:

- bisphosphonates in bone metastasis
- PET
- new cancer drugs

### 4. contact person for interested students/teaching staff:

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### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

Clinical epidemiology

# 6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

1. research line 16:

Genetics of transplants

# 2. general description of the research line:

Studies on genetics factors influencing graft outcome

### 3. specific subtopics within the research line:

- HLA molecules play a key role in the genetics of transplant, but other relevant polymorphic genes (the products of which are involved in immune response) might be important. We intend to analyse recipients of Lung (n: 150) and liver (N:1500) for several genetics characteristics.
- For lung transplantation, genetic variants of donors and recipients are correlated with rejection (underlining high reactivity) or infection (low reactivity)
- For liver transplantation, since half of recipients are HCV-infected, genetic backgrounds of transplanted patients and their donors are correlated with HCV re-infection after liver transplant and with graft outcome.

### 4. contact person for interested students/teaching staff:

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### 5. Field of research (for example: epidemiology, public health, statistics, medicine):

immunogenetics

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

Undergraduate, master, doctorate, post-doctorate

1. research line 17:

Genetics of transplants

### 2. general description of the research line:

Anti-HLA immunization

### 3. specific subtopics within the research line:

- A relevant question in HLA immunization, not yet well understood, is why only a fraction of all subject challenging allogeneic stimuli produce antibodies. Until now, the humoral response has been evaluated with classical complement-dependent cytotoxicity (CDC) methods only. As the new technique could better define all types of antibody response, we are now able to consider why the anti-HLA response might be elicited only in a subgroup of patients. We can expect that two different orders of reasons might explain this phenomenon. The first is in relationship with the immunogenicity of the epitope challenge: the same HLA antigen could be immunogenic only in those patients having certain HLA genotypes. Alternatively, the ability to grow an antibody response could be due to the particular genetic background of each exposed individual.
- At this purposes we intend to analyse at least 100 immunized patients before and after transplantation. The immunogenetic challenges (and particularly the previous HLA mismatches) will be compared with the humoral response and categories of HLA produced antibodies. When a humoral response is detected, a correlation between HLA genotype of patients and type of antibody produced will be done. We can hypothesize that certain mismatch might evoke a humoral response only in patients with particular HLA genotypes. Moreover, polymorphism in the HLA region, or in other genetic regions relevant for immune response, may influence the humoral response. For this reason we aim to correlate antibody response with HLA-A, B, C, DR and DQ alleles, as their relevance in allogeneic response. Moreover, polymorphisms in HLA-G, IL-10, IL2, IL4, IL2R, IFNG, TNFA will be typed and correlated with the humoral response, since it is well known that the individual reactivity also depends on genotypes at this loci.
- The ability to recognize the antigenic HLA mismatches that could be more immunogenic, or the immunological condition of high or low humoral response, could have an important impact on the selection of candidates for a certain donor

# 4. contact person for interested students/teaching staff:

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5. Field of research (for example: epidemiology, public health, statistics, medicine):

immunogenetics

6. for which levels the research line is applicable (undergraduate, master, doctorate, post-doctorate/teaching staff)

Undergraduate, master, doctorate, post-doctorate