UNIVERSITÀ DEL PIEMONTE ORIENTALE

SCUOLA DI ALTA FORMAZIONE

Phd program in Medical Sciences & Biotechnology

(XXIX Cycle)

Second year report

Study on the evolution over time of the risk of disease among former asbestos exposed and genetic risk factors for malignant pleural mesothelioma

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2014-2015

Index

Background

The International Agency for Research on Cancer has recently confirmed that inhalation of airborne asbestos fibers (amphibole and chrysotile) is associated to the onset of mesothelioma (pleura, peritoneum, pericardium and tunica vaginalis testis), lung, larynx and ovary cancer. Limited evidence of a causal association is also reported for the onset of cancer of the pharynx, stomach cancer and colorectal cancer (IARC, 2012). Consequently, a number of members of the scientific community have repeatedly called for a universal ban on the use of all types of asbestos as a mandatory measure to protect public health (Kanarek et al. 2011). Debate exists as to the different effect of the different asbestos types and on the effect of asbestos after cessation of exposure. Hodgson and Darnton (2000) stated that per unit fibre exposure mesothelioma risk from amphiboles exposure is far greater than risk from chrysotile exposure. The recent literature confirms that chrysotile causes MM, although with a lower potency than amphiboles (Magnani et al. 2015).

A limited number of studies exists on cohorts of workers exposed to chrysotile (Hodgson and Darnton 2010).

Mortality of workers was studied by Piolatto et al. (1990) and Pira et al. (2009) and the mesothelioma incidence in the cohort was studied by Mirabelli D et al. (2008).

The cohort of the Balangero mine in Italy, active from 1917 to 1990, is one of the few cohorts of workers exposed to chrysotile which could be observed for a long time. Results on chrysotile are very important because it is still used widely in industrial premises in the world.

The role of cumulative and duration asbestos exposure in determining malignant mesothelioma is reported in several case-control studies (Howell et al. 1999; Iwatsubo et al. 1998; Lacourt et al. 2014). The observation of workers exposed to asbestos is relevant for public health in order to study the evolution of the risk of cancer due to asbestos exposure and of the risk after the end of exposure. Epidemiological studies reported a significant risk of mesothelioma also for people exposed to asbestos in non-occupational settings, mainly because of cohabitation

with occupationally exposed subjects or residence near an asbestos-cement plant (Marinaccio et al. 2015). A recent study (Ferrante et al. 2015) underlines the contribution of environmental and familial/domestic asbestos exposures to the occurrence of PMM in the population of Casale Monferrato, where the most important Italian asbestos cement plant "Eternit" was operational until 1986. This study underlines the increased risk of PMM in relation to asbestos in place in the living environment even at low levels of exposure. Continuing epidemiological surveillance and investigation into the specific routes and circumstances of exposures contributing to MM occurrence in this population is, therefore, important.

In Italy the standardized incidence rate of pleural malignant mesothelioma (PMM) estimated by the Italian Registry of Malignant Mesothelioma (ReNam) in 2008 was 3.6 cases per 100,000 persons year in men and 1.3 in women and the corresponding rates for peritoneal MM were 0.24 and 0.12 (Marinaccio et al. 2012).

Asbestos exposure is the main cause of MM. However, only 5%–17% of individuals heavily exposed to asbestos develop MM, suggesting a genetic component in the etiology of the disease, which is also supported by reports of familial clustering and candidate-gene association studies (Matullo et al. 2013).

Asbestos fibers cause MM through genetic/cellular damage of the lung cells and chronic inflammation (Matsuzaki et al. 2012). Some studies carried out in Italy and Finland suggested a possible association between PMM and polymorphisms of genes active in the repair of DNA damaged by oxydative stress (Dianzani et al. 2006; Neri et al. 2008; Gemignani et al. 2009; Betti et al. 2011). We also performed a GWAS study on 392 pleural MM cases and 379 controls from Casale Monferrato, Turin, Genoa and La Spezia (Matullo et al. 2013). A validation study was performed in collaboration with an Australian group (Cadby et al. 2013). MM familiar clustering was observed and the dominant mutations in *BAP1* gene were associated to a new cancer prone syndrome. Germ-line *BAP1* mutations have been described in families with high incidence of mesothelioma and in 25% of sporadic mesotheliomas, but its role in mineral-fibre carcinogenesis has not been established (Røe et al. 2015).

Objective

My activity is part of the "asbestos" project, funded by the Italian Minister of Health and coordinated by the Italian Superior Health Institute (ISS), that represents the first implementation of the National Plan for Asbestos (www.salute.gov.it). This project involves four research units including the Italian Superior Health Institute (ISS) in Rome, the University of Eastern Piedmont in Novara, the University of Turin and "Regina Elena" Cancer Institute in Rome.

The general objective of the "Asbestos" project is to provide answers to the open issues concerning epidemiology, diagnosis and treatment of asbestos-related diseases. In particular the activities are focused on: the risk related to environmental exposure after the asbestos ban, methods for health and epidemiological surveillance, innovative methods of diagnostics and treatment of the diseases related to exposure to asbestos.

Our unit is in charge of the research regarding increased knowledge about the risk of mesothelioma and other cancers among subjects occupationally exposed to asbestos: the risk after the cessation of exposure and long latency in a pool of Italian asbestos-exposed cohorts, the risk among the "Balangero" mine worker cohort, the biggest open air chrysotile asbestos mine in Europe, and the evaluation of individual factors that could be relevant in detecting the individual susceptibility to asbestos exposure. In particular, during this last year, I was involved in the first part of the project regarding the preliminary statistical analyses concerning cancer mortality and specifically for asbestos-related causes of the pool of Italian asbestos-exposed cohorts.

Methods

The main part of the project regards the analysis of a pool of Italian cohorts of asbestos exposed subjects employed in plants located in different Italian regions that have already been the subject of epidemiological study such as Piemonte, Lombardia, Emilia Romagna, Marche, Veneto, Toscana, Lazio, Campania, Puglia. The study included 43 cohorts that are being updated up to 2010 or later. The main production sectors are: asbestos cement, construction and maintenance of rolling stock, shipbuilding. We collected information on the exposure level of the plant but information about each worker's personal asbestos exposure is not available. The analysis of data includes 55537 individuals.

The statistical analysis is based on the person-years method. Subjects in the cohorts contributed person-years of observation from the beginning of exposure until their most recent date of observation. Vital status was ascertained through the Registrar's Offices; the same office provided the cause of death for decedents.

We computed standardized mortality ratios (SMRs; i.e. the ratio of observed to expected deaths using indirect standardization) for the major causes of death. For SMR analyses, the number of deaths expected in the cohort was estimated from age- and sex-specific mortality rates of the participating Italian regions, provided by the National Institute of Statistics - ISTAT (Rome, Italy). Analyses were restricted to person-years and events occurring after 1965, because reference rates were available only for 1970–2012. For the 1965–1969, we applied the rates for 1970–1974. The rates for 2010–2012 were applied to 2013-2014.

Confidence intervals (95%CI) for SMRs were derived, assuming a Poisson distribution for the number of observed events. Statistical analyses were carried out using OCMAP-PLUS, release 3.10 (University of Pittsburgh, Pittsburgh, PA, USA) (Marsh et al. 2002) and SAS, release 8.2 (SAS Institute Inc., Cary, NC, USA).

A pooled analysis is performed in order to obtain information on the variation in the risk of malignant mesothelioma (MM) (mortality and incidence) and the risk of death from other malignancies. In order to obtain a quantitative estimation of the exposure

level to asbestos of the subjects of the cohorts, an index that takes into account the fraction of exposed to asbestos, direct or indirect use of asbestos and exposure level was computed. Information about these aspects has been provided for each cohort.

The second part of the project regards the cohort of miners and millers of "Balangero", the largest chrysotile mine in Western Europe active from 1917 to 1990. The cohort was established by Rubino et al. (1979) and studied further by Piolatto et al. (1990) and Pira et al (2009). The Unit of Cancer Epidemiology of Turin re-established the cohort of employees using the factory rosters available in the State Archives of Turin. The cohort included 1804 subjects (1766 men) and during this second year the follow-up of the subjects in order to ascertain the vital status has been completed. The worker's job classification is in progress. The analysis will be based on computation of standardized mortality ratios (SMR), standardized incidence ratios (SIR) and Poisson regression models. For SMR analyses, the number of deaths expected in the cohort will be estimated on the basis of mortality rates in Piedmont, provided by the National Institute of Statistics (ISTAT). SIR analyses will be computed for malignant mesothelioma (MM) using the incidence rates provided by the Mesothelioma Registry of Piedmont (Mirabelli et al. 2007).

In this second year, with reference to the third research project, a gene-environment interaction analysis was performed including asbestos exposure and fifteen Single Nucleotide Polymorphisms (SNPs) previously identified through a genome-wide association study on Italian subjects based on 392 cases and 379 controls. Cases and controls are from four towns in Northern Italy: Casale Monferrato and Turin in the Piedmont Region, and Genoa and La Spezia in the Liguria Region (Matullo et al. 2013). Interaction was analyzed in respect to both additive and multiplicative models based on the ORs obtained by logistic regression. Deviation from an additive model was explored as the Relative Excess Risk due to Interaction (RERI) and the Synergy Index (SI)(Rothman KJGS, 1998).

Preliminary results

Pooled cohorts study currently includes 55,537 subjects, of which 15,062 have worked in the production of cement - asbestos. The dataset includes 49,107 men and 6,430 women. At the end of follow-up, the 54.2% of the subjects were alive, 42.6% had died, and 3.2% were lost to follow-up or had moved abroad. The cause of death was known for 93% of deceased subjects. Considering the follow up period after 1965, the cohorts contributed altogether 1,533,000 person-years for men and 209,137 for women.

Both genders showed increased mortality for all causes ($p<0.001$), all malignancies ($p<0.01$), pleural and peritoneal malignancies (both $p<0.01$) and lung cancer ($p<0.01$). In women, ovarian malignancies were more frequent than expected ($p<0.05$).

No statistically significant increase was found for laryngeal cancer. Asbestosis was the underlying cause of death for about 400 men and 50 women. The number of deaths due to cardiovascular diseases was lower than expected in both genders, which is indicative of the healthy work effect.

As regards the "Balangero" cohort study, the search for causes of death begun last year has been concluded. The information on the tasks of the employees are going to be completed through the documentation preserved in the State Archives of Turin. Analyses will follow.

As regards the genetic study, during the first year, BAP1 mutations were studied among five MM families showing germline BAP1 mutations only in one family and no mutation carriers observed in the 103 sporadic patients. The 95% confidence interval of the prevalence of BAP1 mutations was 0-3.58% using the Poisson distribution (Breslow and Day 1980). The data has been published in the article by Betti et al. (2015). The research conducted during this last year is related to the genome-wide association study regarding about 370,000 SNPs. The gene-asbestos interaction analysis, studied among the fifteen Single Nucleotide Polymorphisms (SNPs) previously identified through the genome-wide study, suggests that gene-

asbestos interaction may play an additional role on MM susceptibility, given that asbestos exposure appears as the main risk factor (Tunesi et al. 2015).

Conclusions and perspectives

As regards the pooled cohort study, we are going to plan the SMR analyses by latency (time since first exposure) and duration of exposure corresponding to the total duration of employment in the factory. The analyses by production sectors and by cumulative exposure, detected through the quantitative index of the exposure level, will be computed. We are also going to plan to compute the standardized incidence ratio (SIR) for MM detecting cases using a record linkage to the National Mesothelioma Registry (ReNaM) (Marinaccio et al. 2012).

During the next year, we are planning on performing the statistical analyses of the mortality and incidence among the workers of the "Balangero" cohort considering the different exposure patterns.

Epigenetic studies will also be conducted. In this context, several studies have demonstrated that epigenetics is an important contributor of MM development playing, a determining role in response to treatment as well (Vandermeers F et al. 2013). Understanding epigenetic regulation and biological pathways involved in the PMM could possibly contribute to develop new immunotherapies/chemopreventive treatments.

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Phd activity: first and second year

Scientific articles: 2014-2015

1. Ferrante D, Mirabelli D, Tunesi S, Terracini B, Magnani C. *Pleural mesothelioma and occupational and non-occupational asbestos exposure: a case-control study with quantitative risk assessment*. Occup Environ Med. 2015 [Epub ahead of print]

2. Tunesi S, Ferrante D, Mirabelli D, Andorno S, Betti M, Fiorito G, Guarrera S, Casalone E, Neri M, Ugolini D, Bonassi S, Matullo G, Dianzani I, Magnani C. *Gene-asbestos interaction in malignant pleural mesothelioma susceptibility*. Carcinogenesis. 2015 [Epub ahead of print]

3. Padoan M, Ferrante D, Pretti G, Magnani C. *Studio delle caratteristiche diagnostiche, della qualità dell'assistenza sanitaria e degli interventi chirurgici, nelle donne residenti nelle ASL di Novara e Verbano Cusio-Ossola ricoverate per carcinoma della mammella*. Ig Sanita Pubbl. 2015;71:179-94

4. Ripoll Gallard A, Meneghetti G, Ragazzoni L, Kroumova V, Ferrante D, Ingrassia PL, Ruzza P, Dell'Era A, Boniolo E, Koraqe G, Faggiano F, Della Corte F. *Multiple withdrawals from single-use vials: A study on sterility*. Int J Pharm. 2015; 485:160-163

5. Betti M, Casalone E, Ferrante D, Romanelli A, Grosso F, Guarrera S, Righi L, Vatrano S, Pelosi G, Libener R, Mirabelli D, Boldorini R, Casadio C, Papotti M, Matullo G, Magnani C, Dianzani I.
   Inference on germline BAP1 mutations and asbestos exposure from the analysis of familial and sporadic mesothelioma in a high-risk area. Genes Chromosomes Cancer. 2015;54:51-62

6. Oddone E, Ferrante D, Cena T, Tunesi S, Amendola P, Magnani C
   Studio di mortalità in una fabbrica per la produzione di manufatti in cemento-amianto in provincia di Pavia. Med Lav. 2014; 105:15-29

7. Reid A, de Klerk NH, Magnani C, Ferrante D, Berry G, Musk AW, Merler E. *Mesothelioma risk after 40 years since first exposure to asbestos: a pooled analysis.* Thorax 2014; 69:843-50

8. Terracini B, Mirabelli D, Magnani C, Ferrante D, Barone-Adesi F, Bertolotti M. *A critique to a review on the relationship between asbestos exposure and the risk of mesothelioma.* Eur J Cancer Prev. 2014; 23:492-4

Conference: abstract

1. VIII National Congress SISMEC, Italy, Turin, 16-19 September 2015

   "Case-control study in Casale Monferrato area: quantitative risk assessment of pleural malignant mesothelioma" (oral presentation)
   Ferrante D , Mirabelli D, Tunesi S, Terracini B, Magnani C

   "Gene-asbestos interaction in pleural mesothelioma" (oral presentation)
   Tunesi S, Ferrante D, Mirabelli D, Andorno S, Betti M, Fiorito G, Guarrera S, Casalone E, Neri M, Ugolini D, Bonassi S, Matullo G, Dianzani I , Magnani C

2. XXXVIII Congress of the Italian Epidemiological association (AIE), Italy, Napoli, 5-7 November 2014

   "Long-term effect of the domestic exposure to asbestos in the Cohort of Wives of Asbestos Workers in Casale Monferrato, Italy" (oral presentation)
   Ferrante D, Mirabelli D, Terracini B, Magnani C

   "The risk of asbestos-related disease after cessation of exposure" (oral presentation)
   Magnani C, Ancona L, Cena T, Chellini E, Cuccaro F, Ferrante D, Legittimo P, Luberto F, Marinaccio A, Mattioli S, Menegozzo S, Merler E, Mirabelli D, Musti M, Oddone O, Pettinari S, Pirastu R, Scarnato C, Silvestri S and the project working group

3. International Conference on Monitoring and Surveillance of Asbestos-Related Diseases, 11-13 February 2014, Helsinki, Finland

   "Prevalence of germline BAP1 mutations in sporadic pleural mesothelioma from a high risk area" (poster)
   Magnani C, Betti M, Casalone E, Ferrante D, Guarrera S, Libener R, Botta M, Piccolini E, Mirabelli D, Matullo G, Dianzani I,

Conference and Seminar participation

1. Convegno IRCAD, *"Il lupus eritematoso sistemico"*, Novara, 22 November 2014

2. Conference SISMEC 2014 *"Large scale population-based surveys on respiratory health in Italy and Europe"*, Verona, 23-24 October 2014

3. Seminar "Molecular Epidemiological Studies of Colorectal Cancer", Dr. Marc Gunter, Faculty of Medicine, School of Public Health, Imperial College, London, Torino, 6 June 2014

4. Conference *"Emerging role of extracellular vesicles in pathophysiology: from cellular mediators to biomarkers"*, Department of Health Science, University of Eastern Piedmont, Italy, Novara, 12 May 2014

Seminar and courses participation, University of Eastern Piedmont, Novara

3 september 2015
Seminar "Cell based models for studying molecular mechanism of Facioscapulohumeral Muscolar Dystrophy" and "Toward animal model for Facioscapulohumeral Muscolar Dystrophy", Prof. Bosnakovski Darko, University "Goce Delcev" Stip, Macedonia

28 July 2015
Seminar "Le cellule staminali nel danno renale acuto e nel trapianto di rene", dr. Vincenzo Cantaluppi, University of Eastern Piedmont, Department of Traslational Medicine, Novara

15 July 2015
Seminar "High-tech product preservation and operator protection: two apparently opposite requirements in different fields of medicine and biotechnology: the emerging glove box approach, Dr.Ing. Marco Fadda, COMECER Group

9 July 2015
Miniworkshop on "Biotechnology for dermatology", dr. Gwenaël Rolin and Thomas Lihoreau, Department of Dermatology, Clinical Investigation Center, Besançon University Hospital, France

10 June 2015
Seminar "Basis of scientific research", Prof. Nicoletta Filigheddu, University of Eastern Piedmont, Department of Traslational Medicine, Novara

5 June 2015
Seminar "Recent Developments in (cutaneous) human polyomavirus research", prof. Feltkamp Mariet, Leiden University Medical Center, Leiden, The Netherlands

14 May 2015
Seminar “Conflicting interests and scientific communication”, dr. Kathleen Ruff, RightOnCanada Founder & Senior Advisor to the Rideau Institute

7 May 2015
Seminar “An integrated approach to the diagnosis and treatment of ovarian cancer”, Prof. McDonald John, Georgia Tech University, Georgia (Atlanta, US)

21 April 2015
Seminar “Actin-based mechanisms in the control of gene expression and cell fate”, Prof. Piergiorgio Percipalle, Karolinska Institute

9 April 2015
Seminar “Signal control in iNKT cell development and function”, dr. Xiaoping Zhong, Duke University

11 March 2015
Seminar “Proof of principle for cell therapy: from autologous transplantation of tissue specific progenitors to gene corrected patient specific injured pluripotent stem cells”, Prof. Bosnakovski Darko, University “Goce Delcev” Stip, Macedonia

27 January 2015
Seminar “Myeloid cells as therapeutic target in cancer”, Prof Sica Antonio, DiSCAFF, UPO, Novara

21 January 2015
Seminar “Targeting the liver to cure myocarditis: a lesson from a model of STAT3-dependent auto-immune myocarditis”, Prof. Poli Valeria, Molecular Biotechnology Center, University of Turin, Turin

20 January 2015
Seminar “Different molecular mechanisms regulate hepatocyte differentiation during the transitions between epithelial and mesenchymal states”, Dr. Alonzi Tonino, Istituto Nazionale per le Malattie Infantili “L.Spallanzani” IRCCS, Rome

19 January 2015
Seminar “Anticancer strategy targeting cancer cell metabolism in ovarian cancer”, Prof. Yong-Sang Song, Cancer Research Institute, Seoul National University

5 December 2014
Seminar “Focus on the liver: from basics of NAFLD to hot topics in HBV & HCV infections”, Prof. Safadi Rifaat, Hadassah Medical Organization, Hadassah Hebrew, University Medical Center, Jerusalem

4 December 2014
Seminar “Defining a mechanism for β-HPV induced SCC in organ transplant recipients – a collaboration in progress”, Prof. Patel Girish, European Cancer Stem Cell Research Institute, Cardiff (UK)

1 December 2014
Seminar “Beta human papillomavirus infection and skin cancer in the immunocompromised host”, dr. Lanfredini Simone, phd student

28 November 2014
Seminar “Humoral responses to HCV infection and clinical outcomes”, prof. Arvind Patel, MRC Centre for Virus research, University of Glasgow (UK)

27 November 2014
Seminar “Nuove sfide ed opportunità dell’epidemiologia molecolare per lo studio dei tumori”, Prof. Laura Baglietto, Inserm – Centre for Research in Epidemiology and population health, Paris

25 November 2014
Seminar “La scoperta del bosone di Higgs”, dr Roberta Arcidiacono, Department of Pharmaceutical Sciences, and dr. Marta Ruspa, University of Eastern Piedmont, Department of Health Science, Novara

21 November 2014
Seminar “Stem cell in the regeneration and repair of the tissues and organs”, prof. Prat Maria, University of Eastern Piedmont, Department of Health Science, Novara

20 November 2014
First European workshop on Tolerogenic vaccination in autoimmune diseases, University of Eastern Piedmont, Novara

17 November 2014
Seminar “Optical coherence tomography, from bench to bedside: shining the light during percutaneous vascular intervention”, dr. Secco Gioel Gabrio, phd student

14 November 2014
Seminar “Tissue engineering: the state of the art”, dr Boccafoschi Francesca, University of Eastern Piedmont, Department of Health Science, Novara

3 November 2014
Seminar “The intracellular DNA Sensor IFI16 Gene acts as restriction factor for human papillomavirus replication through epigenetic modifications of the viral promoters”, dr. Lo Cigno Irene, phd student

28 October 2014
Seminar “Natural compounds as modulators of epigenetic events”, Prof. Marc Diederich, Seoul National University, Republic of Korea

20 October 2014
Seminar “The Krüppel-like factor 2 transcription factor is a novel tumor suppressor gene recurrently mutated in Splenic Marginal Zone Lymphoma” dr. Rosella Famà, phd student

1 October 2014
Seminar “Clonal evolution and clinical relevance of subclonal mutations in chronic lymphocytic leukemia” dr. Carmela Ciardullo, phd student

8-22 September 2014
Course “The borghese sessions”, Prof. Steven R. Ellis”, Department of Biochemistry and Molecular Biology, University of Louisville, Kentucky

21 July 2014
Seminar “A functional link between ARX and KDM5C genes linked to neurophenotypes defines a crucial epigenetic disease path” dr. Maria Giuseppina Miano, Institute of Genetics and Biophysics ABT, CNR - Napoli

15 July 2014
Course “Applicazioni Terapia Genica” prof. Antonia Follenzi, University of Eastern Piedmont, Department of Health Science, Novara

30 June 2014
Course “The C-value paradox, junk DNA and ENCODE”, dr. Diego Cotella, University of Eastern Piedmont, Department of Health Science, Novara

27 June 2014
Seminar “Has nature done the experiment for us? Evolutionary insights into infection susceptibility and autoimmunity”, Prof. Manuela Sironi, University of Milan

26 June 2014
Seminar “Disarming mutant P53 in Cancer”, Prof. Gianni Del Sal, Department of Life Sciences, University of Trieste

12 June 2014
Seminar “Metformin rewires the signaling network of breast cancer cells and changes their sensitivity to growth and apoptotic stimuli”, Prof. Gianni Cesareni, Department of Biology, University of Roma Tor Vergata

11 June 2014
Seminar “Ribosome alteration in cancer: effect or cause?”, Prof. Fabrizio Loreni, Department of Biology, University of Rome Tor Vergata

9 June 2014
Seminar “Assessment of cervical cancer control in Randa and Bhutan”, Dr. Iacopo Baussano, University of Eastern Piedmont, Department of Traslational Medicine, Novara

23 May 2014
Seminar “Methods for the analysis of the exposure-time-response relationship in epidemiology” Dr. Francesco Barone-Adesi, Division of Population Health Sciences and Education St George’s, University of London

21 May 2014
Seminar “CERN, 60 anni “accelerando” per l’uomo” tenuto dal Prof. Ugo Amaldi, Fondazione TERA – CERN di Ginevra, “Ricerca all’UPO”, Prof. Cesare Emanuel, University of Eastern Piedmont

5 May 2014
Seminar “Atmosheric pressure plasma sources and processes for biomedical and surface treatment applications”, Prof. Vittorio Colombo and Dr. Matteo Gherardi, Department of Industrial Engineering, University of Bologna

25 March 2014
Course “Horizon 2020, European Framework Programme for Research and Innovation (2014-2020)” , Ing. Maria Bulgheroni, Ab.Acus, Milano

19 March 2014
Seminar “Role of Phosphoinositides-3-kinase C2-alpha, a Class II PI 3-kinase, in development and cancer“, Prof. Emilio Hirsch, Department of Molecular and Cellular Biology and Molecular Genetics, University of Torino and “Medical Biotechnology day”

19 February 2014
Seminar “Epigenetic modifications that control stem cell differentiation”, Prof. Salvatore Oliviero, Department of Life Sciences and System Biology, University of Torino