University of Eastern Piedmont

Phd program in Sciences & Medical Biotechnology

(XXIX Cycle)

First 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

Phd student: Dr. Daniela Ferrante

Tutor: Prof. Corrado Magnani

2013-2014

Index

Background	***Pag 3***
Objective	***Pag 5***
Methods	***Pag 6***
Preliminary results	***Pag 7***
Reference	***Pag 9***
Phd activity	***Pag 13***

Background

Asbestos is a generic term used to identify a number of well-known silicate minerals that are capable of producing thin and flexible fibers when crushed. There are different types of asbestos: serpentine mineral chrysotile (also known as 'white asbestos'), and the five amphibole minerals – actinolite, amosite (also known as 'brown asbestos'), anthophyllite, crocidolite (also known as 'blue asbestos') and tremolite (Case et al. 2011).

The carcinogenity of asbestos is established (IARC 2012) and there are significant variations in risk among and within the industries using asbestos suggesting that this could be explained by variations in the distribution of asbestos fibres sizes in addition to differences in the types of asbestos (Loomis et al. 2010; Hodgson & Darnton 2000).

A total of 95% of world asbestos production has been chrysotile, largely in the past from Canada, but also from mines in several other countries around the world (Kanarek et al. 2011). In comparison to amphiboles, chrysotile fibers are generally finer with high flexibility and good heat resistance (www.asbestos.com).

Chrysotile asbestos is less potent than amphibole forms of asbestos (IARC 2012) but the issue of its potency relative to amphiboles for inducing malignant mesothelioma (MM) remains unresolved (Magnani et al. 2013).

By 2011 there are numerous occupational epidemiology and registry and case studies clearly linking all types of asbestos, including chrysotile, to pleural and peritoneal mesothelioma. Chrysotile is the only type of asbestos being used in many countries so it is of public health importance to stop its use (Kanarek et al. 2011).

A controversy is whether contamination with tremolite fibre, rather than chrysotile could be entirely responsible for causing mesothelioma (Mirabelli et al. 2008).

Fewer studies were conducted to investigate cancer risks in exclusive chrysotile asbestos workers. In particular in China, one of the the world's largest producers of asbestos, a huge amount of chrysotile has been mined and produced. In a cohort of 1539 male workers from a exclusive chrysotile mine, a clear exposure-response relationship between asbestos exposure and lung cancer and non malignant respiratory diseases was found (Wang et al. 2013).

Chrysotile from Balangero mine in Italy, active from 1917 to 1985, is tremolite-free and contains trace of balangeroite (0.2%-0.5% of the total mass of samples of

chrysotile), a non asbestos fibrous mineral similar in shape to amphiboles (Piolatto et al. 1990). In light of current knowledge, balangeroite cannot be considered a carcinogen, nor it can be implied to cause mesotheliomas instead of chrysotile (Mirabelli et al. 2008). The occurrence of mesotheliomas in individuals with exposure to Balangero chrysotile is important because no tremolite has been detected in it (Mirabelli et al. 2008).

Biopersistence in the lung is lower for chrysotile and for short fibers (Pinto et al. 2013).

The possible reduction of the risk of asbestos-related diseases, particularly malignant mesothelioma (MM) after cessation of exposure is still matter of debate (Pinto et al. 2013).

Asbestos clearance is a possible biological explanation as it occurs for nondurable carcinogens (Barone-Adesi et al. 2008). Some studies evaluated asbestos fibres clearance in human lungs, observing a reduction in asbestos lung burden with time since exposure cessation, that was associated to fibre type (Magnani et al. 2013).

Within the Eternit workers cohort the rate of pleural MM increased up to 40 years following first exposure and plateaued thereafter, whereas peritoneal MM showed a continuing increase (Barone-Adesi et al. 2008). The overall rate of MM appeared to level off after 50 years following first exposure in the Wittenoom workers in pleural and peritoneal MM (Reid et al. 2014). Some studies suggest a different fate for the fibres reaching the pleural and the peritoneum (Barone-Adesi et al. 2008).

It is essential to extend, verify and strengthen the epidemiological observations on the reduction of the risk of cancer after exposure has ceased, which are still limited to a few cohort studies.

The genetic risk factor may play an additional role in the development of mesothelioma. The collection of biological samples allows to investigate the role of genetic background in asbestos-related carcinogenesis and define the risk profile of people with a high exposure to asbestos.

Only 5%-17% of individuals heavily exposed to asbestos develop MM (Matullo et al. 2013), suggesting a genetic component in the etiology of the disease which is also supported by reports of familial clustering (Ugolini et al. 2008; Ascoli et al. 2007), candidate-gene association studies (Neri et al. 2008; Betti et al. 2011) and genome-wide studies (Matullo et al. 2013; Cadby et al. 2013).

Among the top SNPs identified in the study by Matullo et al., there were several genes previously reported to be involved in MM or other cancer types as well as chromosomal regions reported to be altered in MM. In the Australian sample (Cadby et al. 2013), regional analyses showed significant signals in 5 of the chromosomal regions where the Italian top SNPs are located (Matullo et al. 2013).

Recent reports have described germline BAP1 mutations in families predisposed to MM, uveal melanoma as well as atypical melanocytic tumors and renal cancer carcinoma. BAP1 is an oncosuppressor gene implicated in several cellular processes such as cell proliferation, DNA repair response and chromatin dynamics (Zauderer et al. 2013).

The germline genome studies do not show an alternative role of genes in relation to asbestos exposure in the development of mesothelioma but gene variants can increase the effects of asbestos exposure. The identification of genes can increase our understanding of the etiology and pathogenesis of MM and may open new perspectives for the control and treatment of this disease (Ugolini et al. 2008).

Objective

Our 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).

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 sanitary and epidemiological surveillance, innovative methods of diagnostics and treatment of the diseases related to exposure to asbestos.

The 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.

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 through 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.

Methods

The first study includes a pool of Italian cohorts of asbestos exposed subjects in different Italian regions that have already been the subject of epidemiological study such as Piemonte, Lombardia, Emilia Romagna, Marche, Veneto, Trentino, Friuli, Toscana, Lazio, Campania, Puglia and Sicilia.

These cohorts are being updated up at 2010 or later. The production sectors are: asbestos cement, construction and maintenance rolling stock, shipbuilding. We collect information on the exposure level of the plant because information about each worker's asbestos exposure is not available. The analysis of data will include about 50,000 individuals.

The vital status and the cause of death for deceased subjects are under investigation.

A pooled analysis will be performed in order to obtain information on the variation in the risk of MM (mortality and incidence) and the risk of death from other malignancies after a very long latency (over 40 years) and after cessation of exposure.

The statistical analysis will be computed using the standardized mortality ratio (SMR), the standardized incidence ratio (SIR) and Poisson regression models. Mortality will be compared with the corresponding mortality rates by region and the MM incidence will be detected using the National Mesothelioma Registry (ReNaM) (Marinaccio et al. 2012).

The second part of the project regards the cohort of miners and millers of "Balangero" 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 includes 1794 subjects and the follow-up and worker's job classification are in progress. The analyses 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 last year, with reference to the third research project, the role of dominant mutations in the BAP1 gene was studied. The aim was to evaluate the role of germline BAP1 mutations in familial predisposition to MM and in patients with sporadic cases who live in a highly asbestos-polluted environment.

In order to study the contribution of BAP1 mutations in familial MM aggregations, five families with multiple MM cases were studied. Furthermore, the prevalence of BAP1 mutation in 103 sporadic MM cases selected from the list of cases included in a population-based case control study among resident in the Local Health Authority of Casale Monferrato was evaluated (Betti et al. 2011).

Preliminary results

During this first year, I was involved in all the three parts of the project.

The “Eternit” cohort of Casale Monferrato (Magnani et al. 2008) and the cohort of their wives indirectly exposed to asbestos from contact and washing of work clothes of their husbands (Ferrante et al. 2007) were updated to 2013. In particular, the latter cohort is the largest cohort study of family members of asbestos relevant for the number of subjects and duration of follow-up. Both cohorts are included in the pooled cohort study.

"Eternit" was one of the major plant for the production of corrugated and plain sheets, tubes and high-pressure pipes in asbestos-cement in Italy active between 1907-1986 (Magnani et al. 2008). The vital status was updated at 2013: 3,443 blue-collar workers (2,663 men and 780 women) of the “Eternit” cohort and 1779 workers’ wives were followed for more than 40 years.

The preliminary results show a statistically significant increased mortality ($p<0.01$) for all cancers, pleural and peritoneal cancer in both sexes, lung cancer in men, uterine and rectal cancer in women and non malignant respiratory diseases in both sexes. A statistically significant increase of mortality ($p<0.01$) for all cancer, respiratory system cancer and in particular for pleural cancer has been found among the wives’ cohort. The incident cases of MM will be searched in the Mesothelioma Registry of Piedmont.

As regards the “Balangero” cohort, during these last months, I have been involved in finding the causes of death of some cohort members also through the ISTAT source.
As regards the third part of the project, the analysis of BAP1 mutations among five MM families showed germline BAP1 mutations only in one family. For that family, the study showed another tumor-type associated with BAP1, the rare mucoepidermoide carcinoma. No mutation carriers were 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 show that BAP1 mutations are very rare in sporadic patients with MM and are not an explanation for epidemics of the disease in the area (Betti et al. 2014).

Reference

Ascoli V, Cavone D, Merler E, Barbieri PG, Romeo L, Nardi F, Musti M. Mesothelioma in blood related subjects: report of 11 clusters among 1954 Italy cases and review of the literature. Am J Ind Med. 2007; 50:357-69

Barone-Adesi F, Ferrante D, Bertolotti M, Todesco A, Mirabelli D, Terracini B, Magnani C. Long-term mortality from pleural and peritoneal cancer after exposure to asbestos: Possible role of asbestos clearance. Int J Cancer. 2008;123:912-6

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. 2014 Sep 18. doi: 10.1002/gcc.22218. [Epub ahead of print]

Betti M, Ferrante D, Padoan M, Guarrera S, Giordano M, Aspesi A, Mirabelli D, Casadio C, Ardissone F, Ruffini E, Betta PG, Libener R, Guaschino R, Matullo G, Piccolini E, Magnani C, Dianzani I. XRCC1 and ERCC1 variants modify malignant mesothelioma risk: a case-control study. Mutat Res. 2011; 708:11-20

Breslow NE, Day NE. Statistical methods in cancer research. Volume I - The analysis of case-control studies. IARC Sci Publ. 1980; 32:5-338

Cadby G, Mukherjee S, Musk AW, Reid A, Garlepp M, Dick I, Robinson C, Hui J, Fiorito G, Guarrera S, Beilby J, Melton PE, Moses EK, Ugolini D, Mirabelli D, Bonassi S, Magnani C, Dianzani I, Matullo G, Robinson B, Creaney J, Palmer LJ. A genome-wide association study for malignant mesothelioma risk. Lung Cancer. 2013; 82:1-8

Case BW, Abraham JL, Meeker G, Pooley FD, Pinkerton KE. Applying Definitions of “Asbestos” to Environmental and “Low-Dose” Exposure Levels and Health

Effects, Particularly Malignant Mesothelioma. J Toxicol Environ Health B Crit Rev. 2011; 14: 3–39

Ferrante D, Bertolotti M, Todesco A, Mirabelli D, Terracini B, Magnani C. Cancer Mortality and Incidence of Mesothelioma in a Cohort of Wives of Asbestos Workers in Casale Monferrato, Italy. Environ Health Perspect. 2007; 115:1401-5

Hodgson JT, Darnton A. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. Ann Occup Hyg 2000;44:565-601.

IARC Monogr Eval Carcinog Risks Hum. Arsenic, metals, fibres, and dusts. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2012;100(Pt C):11-465

Kanarek MS. Mesothelioma from chrysotile asbestos: update. Ann Epidemiol. 2011; 21:688-97

Loomis D, Dement J, Richardson D, Wolf S. Asbestos fibre dimensions and lung cancer mortality among workers exposed to chrysotile. Occup Environ Med. 2010; 67:580-4

Magnani C, Ferrante D, Barone-Adesi F, Bertolotti M, Todesco A, Mirabelli D, Terracini B.Cancer risk after cessation of asbestos exposure: a cohort study of Italian asbestos cement workers. Occup Environ Med. 2008; 65:164-70

Magnani C, Fubini B, Mirabelli D, Bertazzi PA, Bianchi C, Chellini E, Gennaro V, Marinaccio A, Menegozzo M, Merler E, Merletti F, Musti M, Pira E, Romanelli A, Terracini B, Zona A. Pleural mesothelioma: epidemiological and public health issues. Report from the Second Italian Consensus Conference on Pleural Mesothelioma. Med Lav. 2013; 104:191-202

Marinaccio A, Binazzi A, Branchi C, Corfiati M, Di Marzio D, Scarselli A, Iavicoli S, Verardo M, Mirabelli D, Gennaro V, Mensi C, et al. "Quarto Rapporto. Il Registro Nazionale dei Mesoteliomi". Ed. INAIL, Roma Ottobre 2012

Matullo G, Guarrera S, Betti M, Fiorito G, Ferrante D, Voglino F, Cadby G, Di Gaetano C, Rosa F, Russo A, Hirvonen A, Casalone E, Tunesi S, Padoan M, Giordano M, Aspesi A, Casadio C, Ardissone F, Ruffini E, Betta PG, Libener R, Guaschino R, Piccolini E, Neri M, Musk AW, de Klerk NH, Hui J, Beilby J, James AL, Creaney J, Robinson BW, Mukherjee S, Palmer LJ, Mirabelli D, Ugolini D, Bonassi S, Magnani C, Dianzani I. Genetic variants associated with increased risk of malignant pleural mesothelioma: a genome-wide association study. PLoS One. 2013; 8:e61253

Mirabelli D, Calisti R, Barone-Adesi F, Fornero E, Merletti F, Magnani C. Excess of mesotheliomas after exposure to chrysotile in Balangero, Italy. Occup Environ Med. 2008; 65:815-9

Mirabelli D, Stura A, Gangemi M, Bertolotti M, Maule MM, Magnani C. Incidence of malignant mesothelioma in Piedmont, 1990-2001. Epidemiol Prev. 2007; 31:132-8

Neri M, Ugolini D, Dianzani I, Gemignani F, Landi S, Cesario A, Magnani C, Mutti L, Puntoni R, Bonassi S. Genetic susceptibility to malignant pleural mesothelioma and other asbestos-associated diseases. Mutat Res. 2008; 659:126-36

Pinto C, Novello S, Torri V, Ardizzoni A, Betta PG, Bertazzi PA, Casalini GA, Fava C, Fubini B, Magnani C, Mirabelli D, Papotti M, Ricardi U, Rocco G, Pastorino U, Tassi G, Trodella L, Zompatori M, Scagliotti G. Second Italian consensus conference on malignant pleural mesothelioma: state of the art and recommendations. Cancer Treat Rev. 2013; 39:328-39

Piolatto G, Negri E, La Vecchia C, Pira E, Decarli A, Peto J. An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. Br J Ind Med. 1990; 47:810-4

Pira E, Pelucchi C, Piolatto PG, Negri E, Bilei T, La Vecchia C. Mortality from cancer and other causes in the Balangero cohort of chrysotile asbestos miners. Occup Environ Med. 2009;66:805-9

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

Rubino GF, Piolatto G, Newhouse ML, Scansetti G, Aresini GA, Murray R. Mortality of chrysotile asbestos workers at the Balangero Mine, Northern Italy. Br J Ind Med.1979; 36:187-94

Ugolini D, Neri M, Ceppi M, Cesario A, Dianzani I, Filiberti R, Gemignani F, Landi S, Magnani C, Mutti L, Puntoni R, Bonassi S. Genetic susceptibility to malignant mesothelioma and exposure to asbestos: the influence of the familial factor. Mutat Res. 2008; 658:162-71

Wang X, Yano E, Lin S, Yu IT, Lan Y, Tse LA, Qiu H, Christiani DC. Cancer mortality in Chinese chrysotile asbestos miners: exposure-response relationships. PLoS One 2013; 8:e71899

Zauderer MG, Bott M, McMillan R, Sima CS, Rusch V, Krug LM, Ladanyi M. Clinical characteristics of patients with malignant pleural mesothelioma harboring somatic BAP1 mutations. J Thorac Oncol. 2013;8:1430-3

Internet site:
http://www.asbestos.com
http://www.salute.gov.it/imgs/C_17_pubblicazioni_1945_allegato.pdf

First year Phd activity

Articles – year 2014

1. 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. 2014 Sep 18. doi: 10.1002/gcc.22218. [Epub ahead of print]

2. 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

3. 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

4. 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 presentations

1. 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" (accepted for oral presentation)
   Ferrante D, Mirabelli D, Terracini B, Magnani C

   "The risk of asbestos-related disease after cessation of exposure"
   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 (accepted for oral presentation)

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

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

3. 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

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