

PATHOLOGY AND LABORATORY MEDICINE DEPARTMENT



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UNITS

ANATOMIC PATHOLOGY 1

Maria Luisa Carcangiu

ANATOMIC PATHOLOGY 2 AND 3

Giuseppe Pelosi

EXPERIMENTAL MOLECULAR PATHOLOGY LABORATORY

(part of Anatomic Pathology 3)

Silvana Pilotti

SIMT - IMMUNOHEMATOLOGY AND TRANSFUSION MEDICINE

Fernando Ravagnani

LABORATORY MEDICINE

Daniele Morelli

The mission of the Department is to provide accurate diagnoses and information of prognostic and therapeutic value to clinicians. The activities of Surgical Pathology, Diagnostic Molecular Pathology, Cytopathology, and Autopsy Pathology are carried out in the three Anatomic Pathology Units, while biological tests/microbiological investigations and blood collection, screening, processing, storage, and distribution are carried out at the Laboratory Medicine Unit and SIMT-Hematological Transfusion Service, respectively.

The activities are performed using conventional and state-of-the-art techniques, and all the laboratories are quality certified (ISO9001; 2000, confirmed in 2008 until 2011).

The Pathology Department is also involved in two Institutional activities:

Human frozen tumor tissue bank (see Shared Research Resources page 150) The frozen tumor tissue bank of INT is a systematic collection that looks much like a project-driven collection, but is not restricted to a specific organ or disease type.

Telepathology In order to acquire uniform high quality in pathologic diagnostics and to rapidly spread knowledge related to cancer research, a Virtual Pathology group is being developed in Italy. It is composed of pathologists working in the seven Italian Cancer Institutes within the national ACC project. The programs of the ACC Virtual Pathology Institution include consensus sessions, quality control, educational activities, second opinion, and research.

ANATOMIC PATHOLOGY UNITS 1, 2 & 3

HEADS

Maria Luisa Carcangiu, MD: Anatomic Pathology Unit 1
Giuseppe Pelosi, MD: Anatomic Pathology Units 2 & 3
Silvana Pilotti, MD: Experimental Molecular Pathology Laboratory (part of Anatomic Pathology 3)

STAFF MEMBERS

Marta Barisella, MD, Antonello D. Cabras, MD, Paola Collini, MD, Maurizio Colecchia, MD, Alessandra Fabbri, MD, Flavia Melotti, MD, Massimo Milione, MD, Biagio Paolini, MD, Alessandro Pellegrinelli, MD, Pasquale Quattrone, MD, Gabrina Tragni, MD, Barbara Valeri, MD, Antonella Aiello, Biol Sci D, Annunziata Gloghini, Biol Sci D, Federica Perrone, Biol Sci D, Carla Riva, Biol Sci D (Coordinator of Cytopathology), Mario Ruggeri, Biol Sci D, Elena Tamborini, Biol Sci D, Adele Testi, Biol Sci D

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Claudia Bertan, Biol Sci D, Silvia Brich, Biol Sci D, Elisa Ciulla, Biol Sci student (since October 2010), Elena Conca, Biol Sci D, Barbara Cortelazzi, Biol Sci D, Genny Jaccollè, Biol Sci D (until October 2010), Andrea Lampis, Biol Sci D, Valentina Mauro, Biol Sci D, Eva Tarantino, Biol Sci D

In 2010, the clinical activity of Anatomic Pathology Units 1, 2 & 3, devoted to provide accurate, exhaustive and timely diagnoses, included more than 20,000 histological and more than 20,000 cytological pathology reports, all carried out according to internationally shared classification schemes. An autopsy service is also available for precisely identifying causes of death in patients admitted to the hospital. The spectrum of the diverse tumor types has comprises skin tumors (including melanomas), lymphoproliferative disorders, male genitourinary tract tumors, non-neuroendocrine gastrointestinal tumors, thoracic and mediastinal lesions, endocrine tumors (including thyroid, adrenal glands, gastroenteropancreatic tract and lung), soft tissue tumors, head and neck tumors, pediatric malignancies, gynecologic and breast tumors, and malignancies from unknown primary sites. Most diagnoses in 2010 were rendered within 7 days of admission. The details of histological diagnoses on surgical pathology specimens included cases seen in consultation for second opinion, frozen section examinations, sentinel lymph nodes, and biopsy samples, as well as cytological diagnoses on fine needle aspiration biopsies or extravaginal cytology samples and PAP tests, half of which came from screening programs as a part of routine preventive healthcare for gynecological cancers.

DIAGNOSTIC ACTIVITY OF ANATOMIC PATHOLOGY UNITS 1,2 & 3 IN 2010

Type of Report	Number
Histological (total 21,387)	
Surgical pathology specimens	11,467
Biopsy samples	7,114
Frozen section examinations	2,544
Sentinel lymph nodes	657
Consultation for second opinion	2,797
Cytological (total 21,890)	
Fine needle aspiration biopsy or extravaginal cytology samples	3,266
Conventional PAP tests	9,452
PAP tests from screening programs	9,172

Most pathological reports were supplied with extensive pheno-genotyping for diagnosis, indicating predictive and/or prognostic factors and personalization of the best care according to criteria of so-called therapeutic pathology. About 50,000 immunohistochemical reactions, over 5,000 special stains, and 2898 genetic reports were carried out in 2010 for characterization of malignancies, with particular reference to lymphoproliferative disorders and pediatric, thoracic, soft tissue, neuroendocrine, head and neck, breast and gynecologic tumors, including the immunohistochemical evaluation of estrogen and progesterone receptors and Her-2/neu in breast cancer, the assessment of the status of several genes for tailored therapy (such as, Her-2/neu, EGFR, CD117, PDGFRA/B, VEGFR, ALK or TP53) or characterization of malignancies from unknown primary sites.

There is also a Laboratory of Molecular Pathology hosted under Anatomic pathology Unit 3, whose aim is extensive molecular testing both at diagnostic and experimental levels.

DIAGNOSTIC ACTIVITY OF THE MOLECULAR PATHOLOGY LABORATORY IN 2010

Type of Analysis	Number
Mutational analysis (EGFR, K-ras, PDGFRA/B, c-kit, TP53, RET, beta-catenin, and BRAF)	701
FISH	776
CISH	318
Clonality tests	115
Cytogenetic assessments	249
Total	2,159

The experimental activity of the Molecular Pathology Laboratory has focused on: a) characterization of tumor profiles for identifying therapeutic targets; b) identification of the basis of response/resistance to target therapies by using pre- and post-treatment tumor patient samples; and c) validation of the consistency and reproducibility of molecular markers in clinical settings. Specifically, the following projects are in progress: a) characterization of the activation profile of RTKs and their signalling (MAPK, AKT, mTOR) in diverse naïve tumors and sarcomas, including peritoneal mesothelioma, chordoma, and myxoid liposarcoma, also with mice xenograft models; b) biological basis of response/resistance to target treatments in solitary fibrous tumor and dermatofibrosarcoma protuberans-derived fibrosarcoma; c) demonstration of impaired response to neoadjuvant cisplatin and fluorouracil chemotherapy in TP53 mutated squamous cell carcinoma of the oral cavity. Furthermore, we have reported on a significant association between Her-2/neu gene amplification and beclin1 gene loss in breast cancer samples.

Keywords: diagnosis, tumor grading, staging, therapeutic pathology, immunohistochemistry, cytology, molecular assay



2010 RELEVANT NOTES

Collaborations

Marta Barisella: Italian Sarcoma Group (ISG)

Maurizio Colecchia: Italian Society of Urology (SIU); Hospital Urologist Association (AURO); Project on "Sorveglianza attiva del carcinoma della prostata", Italian Society of Urology (SIURO); Italian Group of Uro-pathology (SIAPEC, Italy) (Coordinator)

Paola Collini: Italian Group of Oncologic Pediatric Pathology (GIPOP); Pediatric Oncology International Society (SIOP); Italian Sarcoma Group (ISG)

Alessandro Pellegrinelli: Integrative genomic analysis of human intrahepatic cholangiocarcinoma (PI: Llovet JM, Barcelona, Spain; Senior advisor: Mazzaferro V; Project Coordinator: Sia D, Spain)

Giuseppe Pelosi: Italian Group of Pleuropulmonary pathology (GIPP); Pathologist Panel Member of the International Academy for the Study of Lung Cancer (IASLC); International Association of Cytology (IAC) Member (MIAC), USA; Pulmonary Pathology Society (PPS) Member, USA

Silvana Pilotti: Sabrina Priel, Molecular Simulation Engineering Laboratory, DI3, University of Trieste; Maurizio D'Incalci, Oncology Department, Istituto di Ricerche Farmacologiche Mario Negri, Milan.

Annunziata Gloghini: Amedeo Avogadro East Piemonte University (G. Gaidano, D. Capello); CRO – Aviano (A. Carbone, V. De Re, D. Aldinucci); Oncology Institute of Southern Switzerland (IOSI) (F. Bertoni); Conway Institute for Biomolecular and Biomedical Research, Conway Institute for Biomolecular and Biomedical Research, University College Dublin (G. Elia)

Elena Tamborini: G. Kroemer and Zitvogel, INSERM Paris (expression of SNPs in GIST); J Trent, MD Anderson, Houston Texas (gene copy number evaluation in GIST)

Publications

Lynch syndrome—related endometrial carcinomas show a high frequency of nonendometrioid types and of high FIGO grade endometrioid types. *Int J Surg Pathol.* 2010;18:21-6.

Teratoma With Somatic-Type Malignant Components in Germ Cell Tumors of the Testis: A Clinicopathologic Analysis of 40 Cases With Outcome Correlation. *Int J Surg Pathol.* 2010 Dec 6. [Epub ahead of print]

Mammalian target of rapamycin signaling activation patterns in neuroendocrine tumors of the lung. *Endocr Relat Cancer.* 2010;17:977-87.

Paraneoplastic antigen Ma2 autoantibodies as specific blood biomarkers for detection of early recurrence of small intestine neuroendocrine tumors. *PLoS One.* 2010;5(12):e16010.

Functional mapping of receptor tyrosine kinases in myxoid liposarcoma. *Clin Cancer Res.* 2010;16:3581-93.

B-cell lymphomas with features intermediate between distinct pathologic entities. From pathogenesis to pathology. *Human Pathol.* 2010; 41:621-31

Analysis of receptor tyrosine kinases (RTKs) and downstream pathways in chordomas. *Neuro Oncol.* 2010;12:776-89

Contributions

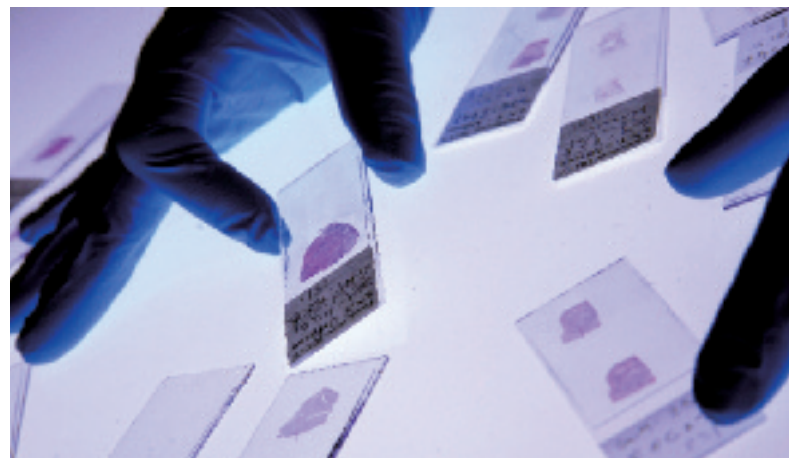
Antonello D. Cabras for: Peritoneal Tumors (primary lesions and metastases) and Lymphoproliferative disorders, Santa Chiara Hospital, Trento

Maria Luisa Carcangiu: Editorial Board, International Journal of Gynecological Pathology

Maruzio Colecchia: Guidelines on urinary bladder (Puppo et al, *BJU Int.* 2010;106:168-79) and penis tumors (edited by the Italian Society of Urology); Editorial Board, *Pathologica*

Giuseppe Pelosi: Associate Editor, International Journal of Surgical Pathology; Editorial Board, *Virchows Archiv*; Editorial Board, *Pathologica*

Annunziata Gloghini: Recommendations on minimal requirements, reporting criteria, and methods on Her-2/neu assessment in breast cancer (AIOM-SIAPEC cooperative group on molecular therapy of tumors (<http://www.aiom.it/Attivit%EO+Scientifica/Documenti+AIOM/Position+paper/Raccomdandazioni+per+la+determinazione+dello+stato+di+HER2+nel+c arcinoma+mammario/1,4296,0>))



SIMT, IMMUNOHEMATOLOGY AND TRANSFUSION MEDICINE

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Pedretti, Carmela Santolla

Involved in blood collection, screening, processing, storage, and distribution of blood components and laboratory activities. Immunohematology, serological and molecular virology, HLA typing of patients and related/unrelated donors, and therapeutic apheresis are also performed. Clinical work and laboratory testing are always in accordance with European and American technologies and standards. Therapeutic apheresis is focused on peripheral blood stem cell harvesting for autologous and allogeneic stem cell transplantation. The Apheresis Group has recently implemented the procedure of extracorporeal photopheresis (ECP), which is mainly used for the treatment of dermatologic diseases, autoimmune diseases, lymphoma, and treatment of acute and chronic graft versus host disease (GVHD). In 2010, we also implemented the production of platelet gel, a blood component used for local application with an important role in wound healing. Three patients have been successfully treated. In collaboration with the Virology Department at the University of Milan, a study on occult infection with HBV in donor blood samples is ongoing. A preliminary analysis shows very interesting data.

Keywords: immunohematology, transfusion medicine, virology

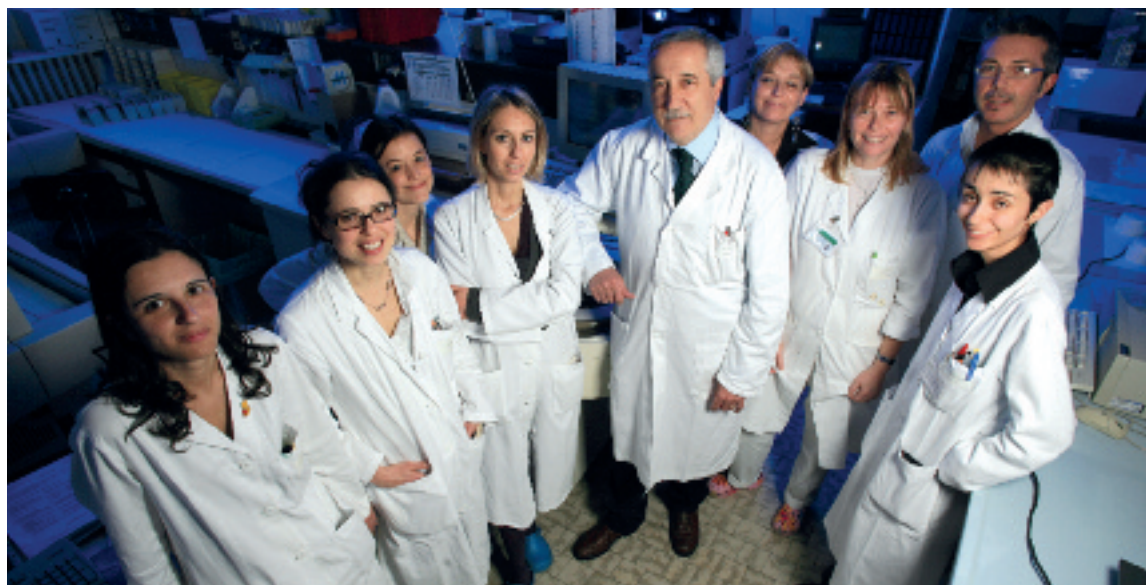
2010 RELEVANT NOTES

Collaborations

European Institute of Oncology, L. Sacco Hospital, Fondazione IRCCS Istituto Neurologico Besta, University of Milan, Virology Department

Publications

Single-nucleotide polymorphism inside microRNA target sites influence tumor susceptibility. *Cancer Res.* 2010;70(7):2789-98



LABORATORY MEDICINE

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Nicola Salvatore, Federica Sozzani

ADMINISTRATIVE

Santa Zingone

Laboratory Medicine performs biological tests and microbiological investigations that contribute to the diagnosis, prognosis, and monitoring of oncologic patients submitted to conventional and experimental therapies. In 2010, about 1,700,000 examinations were performed, an increase of almost 5% over the previous year. The reliability of the results is guaranteed by maintaining high quality standards, which are constantly monitored by national and international External Quality Assessment (EQA). Much attention has been paid to the choice of appropriate technologies and to the continuous improvement of technical and scientific knowledge of the medical and scientific staff. Moreover, the Unit tests new technologies and analytical methodologies and transfers scientific know-how relative to the clinical laboratory to professionals and students. The Unit is also involved in evaluation of the diagnostic potential of new tests and technologies and in the search for innovative organizational solutions. The Unit is engaged in support activity for several clinical trials conducted at the INT and is involved in the project "Personalized Treatment of Sarcomas".

Keywords: clinical chemistry, hematology, microbiology



2010 RELEVANT NOTES

Publications

Colorectal cancer detection by means of optical fluoroscopy. A study on 494 subjects. *Front Biosci (Elite Ed)*. 2010;2:694-700.

