Building blocks of the GIPU, Italian Group of Ultrastructural Pathology

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Summary
The Italian Group of Ultrastructural Pathology, GIPU, is a scientific organization committed to promote the art and science of Electron Microscopy (EM) in the pathology field in Italy, sharing its professional work with a public audience.

The history of the GIPU goes back to 1990 when a founder group set up the Italian Group of Ultrastructural Diagnostic (GIDU) in Milan. The central focus of annual meetings was on EM, transmission and scanning one, about interesting cases in which it was instrumental in diagnosis. In the 1990s, ultrastructure was still the gold standard for cell/tissue morphology, biology, biochemistry, diagnostic pathology, and played an important role in tailored medicine. So, especially transmission EM, could play a critical role in the diagnosis of various diseases as in human as in animals. Best topics of the annual scientific meetings of the group were kidney, muscle, heart, and liver pathology, infertility, neuropathology, respiratory diseases, skin diseases, storage diseases, tumor pathology, infectious diseases, parasitology, veterinary pathology and more. Nowadays, EM is a method whose importance for diagnosis and pathology is well established: it is still essential in several pathologies, helpful in others, and welcome implemented in eclectic research pathology. Omission of EM likely makes the studies suboptimal and wasteful.

So, from 2007 the name of the group has been changed to the Italian Group of Ultrastructural Pathology (GIPU) to favor broader applications of EM also to pathology research field. During last decades, GIDU/GIPU has interconnected with international (Society for Ultrastructural Pathology) and european (European Society of Pathology and Joint Meeting with the European Electron Microscopy Working Group) scientific society, according its statute.

By 1991, GIPU has had 40 members: membership in this Group is still open and welcome to all pathologists, PhD, electron microscopy technologists, pathology trainees, and researchers interested in pathology and electron microscopy.
The target audience included surgical pathologists, trainees, ultrastructural pathologists and technicians/scientists who engage in diagnostic EM either as episodic practitioners or supporting colleagues.

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GIDU aimed to make a strong contribution to these discussions by setting up a comprehensive program where electron microscopists could meet and discuss their work creating, also, a useful network.

Moreover, these annual meetings have hosted dynamic detours as:
• “What is it?” challenge, a contest with symbolic prizes about recognition of diagnostic EM images;
• “EM and art, the differences resemble”, a curious and comparative gallery of EM pictures which looks like to artistic paintings or sculptures;
• “The limit of resolution”, a humanistic and philosophical digression with a parallelism between the limit of resolution and the EM resolution’s power.

GIDU’s annual meetings have been taken up in different Italian cities, from north to south, giving equal opportunities to anyone to attend. One special effort of the group was to support young people’s participation, promoting their integration with senior specialists.

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From 1999 GIDU has participated in annual meetings of the Italian Society of Anatomy and Pathology and Diagnostic Cytology (SIAPEC) through an oral session in which a panel of invited speakers discussed on a topic of interest to the scientific community.

EM is, nowadays, a method whose importance for diagnosis and pathology is well established: it is still essential in several pathologies (i.e. kidney disease and storage disease), helpful in others (muscle and heart pathology), and welcome implemented in eclectic research pathology (i.e. nanoparticles, exosomes). Omission of EM likely makes the studies suboptimal and wasteful.

So, from 2007 the name of the group has been changed to the Italian Group of Ultrastructural Pathology (GIPU) to favor broader applications of EM to pathology research. GIDU first and GIPU later has a logo, it is made of electrons spin which turn around the name of the group (Fig. 1), representing a stylized EM.

EM is considered to be within its purview, as well are other special technologies that may come to impact upon or interplay with the use of this tool in diagnostic applications.

The crucial role that EM plays in diagnostic renal pathology is undisputed. It can be essential in recognition of findings not identifiable by light microscopic evaluation as very early membranous disease, early amyloid, or an abnormal basement membrane in normal looking glomeruli by light microscopy, or it can be very useful in distinguishing a renal sample of a patient with proteinuria between transplant glomerulopathy, and recurrent or de novo glomerulonephritis in order to correctly manage these patients and predict survival of the graft.

Moreover, it has a key role in excluding or localizing the presence of immune deposits and in detecting their morphologic nature. Certainly, a correct interpretation of a renal biopsy is based on a careful correlation of light, immunofluorescence and ultrastructural findings.

EM remains a powerful and even essential tool in modern diagnostic neuropathology. It is fundamental in unusual or atypical variants of meningioma, ependymoma, and schwannoma or oligodendroglioma-like tumors composed of small “clear” cells, and small “blue cell” tumors of childhood. It can provide diagnoses for poorly differentiated tumors that lack specific histological or immunohistochemical features, and can provide information on site of origin for metastatic adenocarcinomas.

EM is useful, also, in the diagnosis of peripheral nerve sheath tumors and gastrointestinal autonomic nerve tumors or in the evaluation of certain congenital, inherited and metabolic diseases – including ceroid lipofuscinoses – CADASIL, and of toxic and drug-induced peripheral neuropathies.

In the molecular era, modern enzyme analyses and genetic tests have not eliminated EM as a need for diagnosis of lysosomal and peroxisomal disorders, especially in those rare metabolic diseases with incomplete, atypical, or non-diagnostic clinical and metabolic findings which leave the clinician and the pathologist at a loss as to where to begin a workup.
EM remains a useful and even essential tool for the diagnosis of certain congenital and acquired myopathies. In those cases in which pathologic features and some histopathological features are inconclusive, EM has, instead, a key role. An example may be its decisive action in congenital, myofibrillar, metabolic or vacuole-associated myopathies, sporadic inclusion body myositis or some mitochondrial myopathies.

Unfortunately, nowadays, the method remains poorly known by the pathologists and it is often not part of the standard medical curriculum. GIPU has recently conducted a survey among Italian pathologists to clarify the use of EM in diagnostic pathology and to carry out a census of transmission and scanning EM used in Italy. 70% of respondents stated the utility of ultrastructural diagnosis for kidney and tumor pathology, neuromuscular disorders, myocardial, respiratory and storage diseases. Moreover, results indicated the use of remote electron microscopy with interactive instrumental control and an advisable future centralization of instruments in EM regional units.

Further factors like the lack of proper facilities and experience to perform ultrastructural diagnosis have to be addressed. EMs combined with molecular technologies create a powerful new approach which GIPU wants to foster and promote. It will also focus on the possible diagnostic role of new microscopy methods that are reshaping the way we perform and perceive microscopy, as well as broader applications to pathology research that ultimately constitute the engine for innovation of activities.

While the pioneers of the technique struggled with ill-suited instruments, state of the art cryo microscopes are now readily available and an increasing number of groups are producing excellent high-resolution structural data of macromolecular complexes, of cellular organelles, or the morphology of whole cells. Instrumentation developers, however, are offering yet more novel electron optical devices, such as energy filters and monochromators, aberration correctors or physical phase plates.

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GIPU would like to express its sincere appreciation and profound gratitude to all scientists who get EM in pathology growing with scientific incentives, inputs and professional expertise during last decades.

References