Integration of molecular pathology and a timely definition: Necessary for the future of pathology? The European / UEMS perspective

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Molecular Pathology

Introduction

• The future of modern medicine relies on two main aspects
  – Molecular medicine
  – Technical advances

• Molecular medicine implies personalised medicine and therapeutic pathology
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Introduction

• Development of new generation of drugs targeting specific genes and pathways combined with
• Biomarkers predicting the patient’s response to those drugs
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Introduction

• Discovery, validation and clinical application of novel biomarkers are cornerstones of medical advancement
• Central in this biomarker-related research is molecular pathology
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Introduction

• Integration of traditional and molecular pathology within a single laboratory management and delivery infrastructure is essential

• Translational research and diagnostics are one continuum rather than two distinct entities
Molecular Pathology Definition

- Emerging discipline within pathology focused on the study and diagnosis of disease through the examination of molecules within organs, tissues or body fluids.
- It shares some aspects of practice with anatomic and clinical pathology, molecular biology, biochemistry, proteomics and genetics.
Molecular Pathology

Definition

- It is sometimes considered a "crossover" discipline
- It is multi-disciplinary in nature and focuses mainly on the sub-microscopic aspects of disease
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Scope

• It encompasses
  – the development of molecular and genetic approaches to the diagnosis and classification of human tumours
  – the design and validation of predictive biomarkers for treatment response and disease progression
  – the examination of susceptibility of individuals of different genetic constitution to develop cancer and the environmental and lifestyle factors implicated in carcinogenesis
Molecular Pathology
Necessary competences

• Molecular Pathology is an integral part of the medical discipline of pathology because

• The pathologist is the only person able to select adequately altered tissues or cells for molecular pathological investigation
Molecular Pathology
Necessary competences

- A qualified pathologist has to
  - supervise the interpretation of in situ (tissue, cellular) molecular methods
  - consign the final diagnosis with a registered scientist eligible to perform molecular tests on human material and analyse the results
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• One of the fastest growing fields in medicine
• Molecular techniques (established and evolving) are used by a number of different specialties such as Pathology, Microbiology, Clinical Genetics, Laboratory medicine/ Biomedicine
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- The results of these applications are used to initiate, optimize or individualize therapeutic and/or follow up procedures for large subsets of patients.
- The best application of results obtained by techniques of molecular biology is warranted by integrating them with other patient data obtained by more conventional diagnostic procedures.
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- The type of analysis usually depends on the previously gathered data and on the question(s) to be answered.
- Some of these questions can be effectively answered within one diagnostic field; others need a broad collaboration of different type of expert in the clinical setting typically personified in multidisciplinary boards.
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- In translational research
  - Take the human tissue sample through different levels of examination
  - These activities can be translated into specific techniques and technologies (by other scientists)
  - Only those able to integrate morphological, clinical and molecular findings in the disease are able to deliver the results in an optimal fashion
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• In analysis of tissues before molecular testing
  • High-quality microscopy is conditio sine qua non for a high-quality molecular diagnosis
  • It is essential to confirm that
    – the tissue is representative for the disease
    – there are sufficient malignant cells for analysis
    – preanalytical steps were adequate
    – there is no potential interfering pathology
    – there is no strong morphological heterogeneity to bias the analysis
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– In bioinformatics

• Pathology integration of clinical data, pathological data and biomarker analytical results
• Translation of high-throughput analysis to biomarkers with meaningful diagnostic or clinical relevance
• Translation of high throughput analysis to pathology reports
A bioinformatician's nightmare:

I am out of memory
Arrgghhh!
They are all in different formats

Do something!
Use Perl! Java!
...whatever!
But PARSE them!

SAME DATA
with
DIFFERENT FORMATS,
DIFFERENT BUILDŞ...
DIFFERENT VERSIONS!

http://biocomicals.blogspot.com
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• This situation is even more emphasized through the extremely quick development of new techniques e.g. Next Generation Sequencing, very often necessitating introduction of more and more sophisticated and therefore expensive equipment and tools
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• Molecular diagnostics
  – Should be incorporated in the training of new generations of pathologists as numerous tests are at the core of tissue diagnostics e.g.
    – Sarcoma and lymphoma translocation detection, MSI, clonality testing, ER, PR, Her2Neu protein expression, Her2Neu amplification, c-KIT and PDGFRA mutation analysis etc. etc.
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The future?

• UEMS Section of Pathology is presenting an initiative to ask the UEMS Council to create a Multidisciplinary Joint Committee on Molecular Pathology in order
  – to optimize the application
  – to coordinate the approach of this field in modern medicine
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The future?

• Pathology, being one of the core medical specialties devoted to understanding the basis of disease as well as to finding most appropriate ways to define and classify disorders in order to facilitate therapeutic procedures, is also having the responsibility to help optimise these processes
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Conclusions

• Only pathologists who are able to integrate morphological, clinical and molecular dimensions of disease can deliver the data in an optimal fashion

• Evaluation of tissue samples is best provided by pathologists, trained to interpret tissue morphology, who understand the molecular basis of disease and the molecular performance of the tests
Molecular Pathology
Conclusions

• Introduction of molecular techniques with therapeutic intention (NGS) is needed to enter the future of molecular diagnostics and oncology treatment

• This may be the best way to serve the patients of today but also those of tomorrow
Thank you for your attention