The Royal College of Pathologists
Pathology: the science behind the cure

Part 1 examination

Molecular Pathology: First paper

Tuesday 25 September 2018

Candidates must answer FOUR questions ONLY

Time allowed: Three hours

1. Review the range of methodologies that are available to clinical laboratories for the detection of oncogene fusions. For each method given, describe the underlying principle of detection, provide an example of a clinical application where the method would be suitable and highlight the relative strengths and weaknesses of each methodology.

2. NGS gene panel testing is increasingly used for routine clinical work-up of myeloid neoplasms. You have been tasked with the development of an NGS panel to detect small somatic variants (SNV and indel) for diagnosis, prognosis and treatment of broad myeloid neoplasm including acute myeloid leukaemia, myelodysplastic syndrome and myeloproliferative neoplasmas. Describe your rationale behind the design of the panel. How would you plan to validate and implement the assay?

3. The interpretation of somatic variants to determine clinical actionability plays an increasingly critical role in the delivery of molecular pathology services. Describe the key considerations required in undertaking somatic variant interpretation and the principles, tools and resources that are used.

4. Recent clinical trial data suggests that tumour mutation burden (TMB) is a predictive biomarker of response to immune check point inhibitors irrespective of the PD-L1 expression status as tested by immunohistochemistry. Discuss potential issues around the implementation of TMB in clinical practice and challenges in the context of non-small cell lung carcinoma molecular testing.

5. There are several clinical applications of ctDNA as liquid biopsy: prediction of prognosis, early diagnosis, monitoring of therapies and therapeutic stratification on progressive disease. These are all of high clinical interest but there are challenges regarding the specificity and sensitivity of the current assays employed to deliver these tests. Please discuss pre-analytical issues affecting the ctDNA samples in patients with advanced lung cancer progressing on EGFR TKIs and address this in the context of technologies used for ctDNA testing with particular emphasis on the benefits and limitations for delivery in clinical practice.

The Royal College of Pathologists
Pathology: the science behind the cure

Part 1 examination

Molecular Pathology: First paper

Tuesday 21 March 2017

Candidates must answer FOUR questions ONLY

Time allowed: Three hours

1. Describe how you would validate a new “in-house” locally developed diagnostic assay. What would you do in the absence of an EQA scheme for the new diagnostic service?

2. Describe two examples of how the molecular monitoring of acquired resistance / disease relapse, can aid patient management?

3. What is epigenetics? Give an example of epigenetics in tumour biology, and of its clinical diagnostic application. How would you test for an epigenetic change in routine clinical diagnostics?

4. How does the tissue fixation process of FFPE (formalin fixed paraffin embedded) samples impact on downstream molecular analysis? What measures can be taken to counteract their impact?

5. Bioinformatics is playing a growing role in Molecular Pathology of neoplasia. Describe the key steps undertaken by a bioinformatics pipeline analysing raw next generation sequencing data from an oncogene panel for clinically relevant mutations.

The Royal College of Pathologists
Pathology: the science behind the cure

Part 1 examination

Molecular Pathology: First paper

Tuesday 22 March 2016

Candidates must answer FOUR questions ONLY

Time allowed: Three hours

1. Describe how and why you would replace existing methodology with a “Next Generation Sequencing” (NGS) method in your laboratory.

2. How does your quality management system contribute to the quality of results obtained in the laboratory?

3. Describe two examples of how molecular pathology has transformed the diagnosis and/or management of neoplasms.

4. How does the handling and processing of tissue samples affect downstream molecular analysis?

5. In the context of a molecular pathology laboratory, what are incidental findings? How do they arise and why are they an issue? Describe an approach to managing these incidental findings.