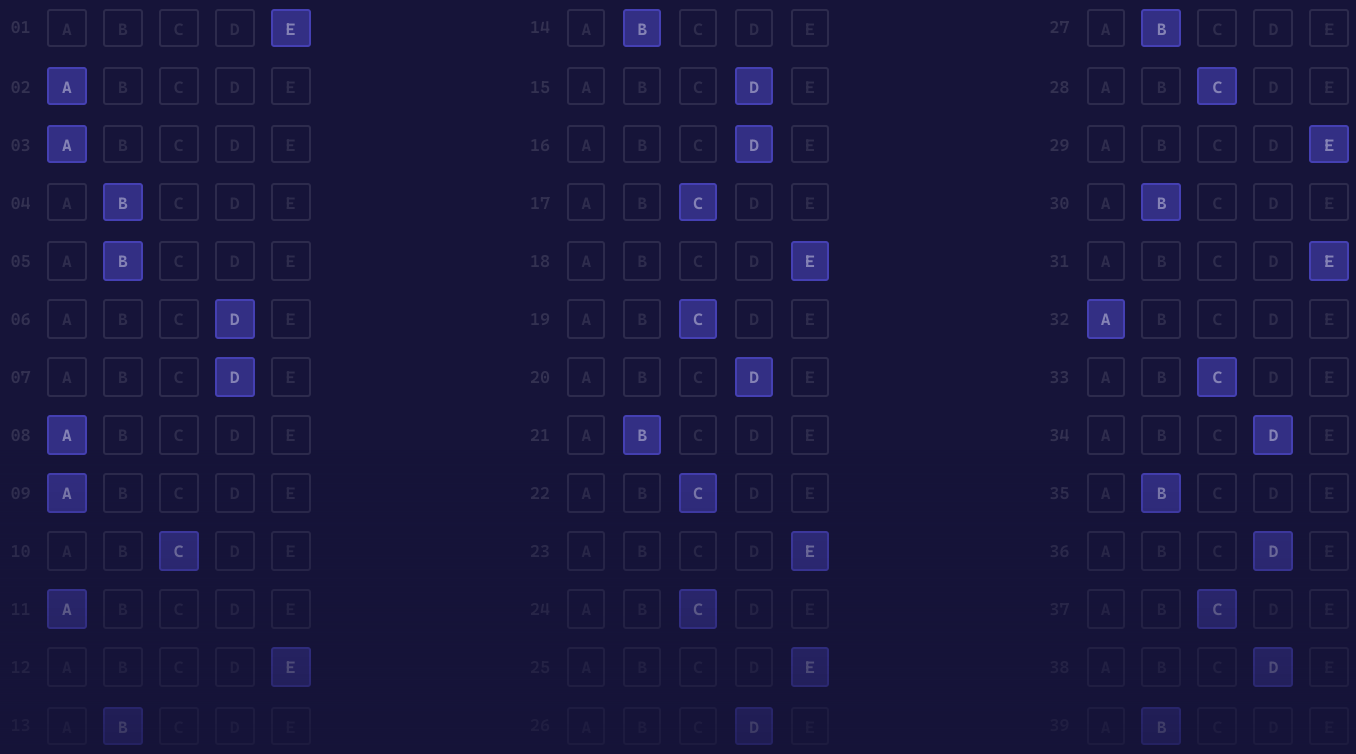
MOMETRIX
SMARTER PREP. BETTER RESULTS.



PRACTICE QUESTIONS

American Board of Medical Genetics And Genomics (ABMGG)

MG–LG

Laboratory Genetics & Genomics Examination

EDITION	QUESTIONS	FORMAT
Demo	9	Limited Edition PDF

WEB www.mometrix.net

SUPPORT support@mometrix.net

Before you begin

What this is

9 practice questions for American Board of Medical Genetics And Genomics (ABMGG) `MG-LG`, each with its answer key and an explanation. Answer a question before you read its key — the explanation is worth more once you have committed.

If something looks wrong

Send us three things and we will check it:

- the exam code, `MG-LG`
- the question number
- the email address on your order

Write to **support@mometrix.net**. We reply within one business day.

QUESTION 1 MULTIPLE CHOICE

A newborn screening result shows elevated C26:0-lysophosphatidylcholine (C26:0-LPC) on dried blood spot by tandem mass spectrometry. Which two of the following metabolic disorders are most consistent with this finding? (Choose two.)

A **X-linked adrenoleukodystrophy**

B Pompe disease (glycogen storage disease type II)

C Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency

D **Zellweger spectrum disorder (peroxisomal biogenesis disorder)**

E Phenylketonuria

ANSWER **A** · **D**

WHY C26:0-lysophosphatidylcholine is the established primary newborn screening biomarker for X-linked adrenoleukodystrophy (X-ALD), and is also elevated in peroxisomal biogenesis disorders (Zellweger spectrum), in which peroxisomal beta-oxidation is impaired. Pompe disease is detected by GAA enzyme activity/lysosomal enzyme panel; VLCAD is detected by acylcarnitine analysis (elevated C14:1); and PKU is detected by elevated phenylalanine.

QUESTION 2 MULTIPLE CHOICE

A patient with classic adult-onset spinocerebellar ataxia type 1 (SCA1) has a borderline allele size on standard PCR fragment analysis. Which two reflex methods are most appropriate to confirm the diagnosis and characterize the (CAG)n repeat expansion? (Choose two.)

A **Southern blot of genomic DNA**

B **Repeat-primed PCR**

C Karyotype

D Methylation-specific MLPA

E Sanger sequencing across the ATXN1 repeat

ANSWER **A** · **B**

WHY SCA1 is caused by a CAG trinucleotide expansion in ATXN1; normal alleles are <36 repeats and pathogenic alleles are typically >=39, with reduced penetrance in the 36-38 range. When standard fragment analysis is borderline or fails to amplify a large allele, repeat-primed PCR is used to detect the presence of expanded repeats, and Southern blot of genomic DNA is used to size large expansions precisely. Karyotype, methylation-specific MLPA, and Sanger across the repeat are not appropriate for sizing a CAG expansion at ATXN1.

QUESTION 3 SINGLE CHOICE

A peripheral blood karyotype is reported as 46,XX,add(5)(q35). Which statement best characterizes the result?

A A terminal deletion of 5q with documented breakpoints

B An unbalanced Robertsonian translocation involving chromosome 5

C **Additional material of unknown origin attached to 5q35; banding cannot identify the source**

D A balanced reciprocal translocation between 5q and an unknown partner

ANSWER C

WHY The 'add' designation indicates that additional chromosomal material of unknown origin is attached at the indicated band, and the source cannot be identified by G-banding alone. Reflex studies (FISH, CMA, or targeted assays) are required to characterize the origin of the additional material. It does not specify a deletion, a Robertsonian translocation, or a balanced rearrangement.

QUESTION 4 SINGLE CHOICE

According to the 2015 ACMG/AMP standards and guidelines, a truncating variant in a gene where loss of function is an established mechanism of disease, absent from population databases (PM2_Supporting), in a patient whose phenotype is highly specific for that gene (PP4), and for which a reputable source has reported the variant as pathogenic, should be classified as:

A Variant of uncertain significance (VUS)

B Likely benign

C **Likely pathogenic**

D Pathogenic

ANSWER C

WHY PVS1 (null variant in a gene where LOF causes disease) + PM2_Supporting (absent or extremely low frequency in controls) + PP4 (phenotype highly specific for a single gene) reaches Likely Pathogenic by combining one very strong, one supporting, and one supporting criterion; adding a reputable-source pathogenic report (PP5/PS3 depending on source criteria in 2018 ClinGen SVI updates) would typically push to Pathogenic, but on the 2015 framework as listed, the combination reaches Likely Pathogenic.

QUESTION 5 SINGLE CHOICE

In a clinical exome sequencing assay, a heterozygous nonsense variant in a gene associated with autosomal recessive disease is detected, and no second pathogenic allele is identified by exon-level read-depth analysis or by Sanger confirmation. What is the most appropriate next step?

A Report the variant as pathogenic and conclude the diagnosis

B Consider deletion/duplication analysis (e.g., exon-level microarray or MLPA) targeted to that gene to evaluate for a second, large deletion allele

C Assume the variant is benign and do not include it in the report

D Refuse to report the case until whole-genome sequencing is performed

ANSWER B

WHY For a single heterozygous pathogenic variant in an autosomal recessive gene, a second allele must be sought. Exome capture can miss large copy-number variants, and reflex deletion/duplication analysis targeted to that gene (MLPA, exon-level CMA, or gene-specific NGS CNV analysis) is the standard approach to identify a possible exonic deletion as the second allele.

QUESTION 6 SINGLE CHOICE

An asymptomatic infant has a newborn screen with elevated leucine, isoleucine, valine, and an elevated leucine-to-alanine ratio suggestive of maple syrup urine disease (MSUD). Which confirmatory test is most appropriate first?

A Plasma acylcarnitine profile

B Urine organic acids and plasma amino acids with quantitation of branched-chain amino acids

C Skin biopsy for electron microscopy

D Urine mucopolysaccharide screen

ANSWER B

WHY MSUD is a defect in branched-chain alpha-ketoacid dehydrogenase leading to accumulation of leucine, isoleucine, and valine, and elevation of allo-isoleucine. Diagnostic confirmation is by plasma amino acid analysis (demonstrating elevated branched-chain amino acids, often with elevated allo-isoleucine) and urine organic acids showing increased branched-chain ketoacids. Acylcarnitine, electron microscopy, and MPS screening do not address this differential.

QUESTION 7 SINGLE CHOICE

A bone marrow karyotype from a patient with suspected chronic myeloid leukemia (CML) shows 46,XX,t(9;22)(q34;q11.2). Which molecular finding is most consistent with this result?

A ETV6-RUNX1 fusion transcript

B BCR::ABL1 fusion transcript

C PML::RARA fusion transcript

D CBFB-MYH11 fusion transcript

ANSWER B

WHY The Philadelphia chromosome, t(9;22)(q34;q11.2), generates the BCR::ABL1 fusion characteristic of CML (and a subset of Ph+ ALL). ETV6-RUNX1 is associated with childhood B-ALL; PML::RARA with acute promyelocytic leukemia; and CBFB-MYH11 with AML M4Eo/inv(16).

QUESTION 8 SINGLE CHOICE

A 45-year-old man with progressive chorea, cognitive decline, and a family history consistent with autosomal dominant inheritance is suspected of having Huntington disease. Which laboratory test is the standard confirmatory diagnostic assay?

A **PCR-based sizing of the CAG trinucleotide repeat in HTT, with Southern blot if the allele fails to amplify**

B Sanger sequencing of the HTT coding region

C Methylation-specific MLPA at the HTT locus

D Whole-genome sequencing with default short-read chemistry

ANSWER A

WHY Huntington disease is caused by a CAG expansion in exon 1 of HTT; pathogenic alleles are >=36 repeats, with reduced penetrance at 36-39. Standard testing uses fluorescent fragment PCR to size the CAG repeat, with reflex Southern blot on genomic DNA for large expansions that fail to amplify. The HTT coding region is not expanded beyond the CAG tract, methylation is not the diagnostic feature, and standard short-read WGS does not size repeat expansions reliably.

QUESTION 9 SINGLE CHOICE

During validation of a new molecular assay, the laboratory performs the test on 100 known positive samples and 200 known negative samples. The assay correctly identifies 98 of the positives and 195 of the negatives. What is the calculated analytical specificity?

A 98 / (98 + 5) = 95.1%

B **195 / (195 + 5) = 97.5%**

C 195 / (195 + 2) = 98.99%

D 98 / 200 = 49%

ANSWER B

WHY Specificity = True Negatives / (True Negatives + False Positives). True Negatives = 195; False Positives = 200 - 195 = 5. Therefore specificity = 195/200 = 97.5%. Option A is sensitivity using the wrong denominator; option C describes a different calculation; option D is unrelated.