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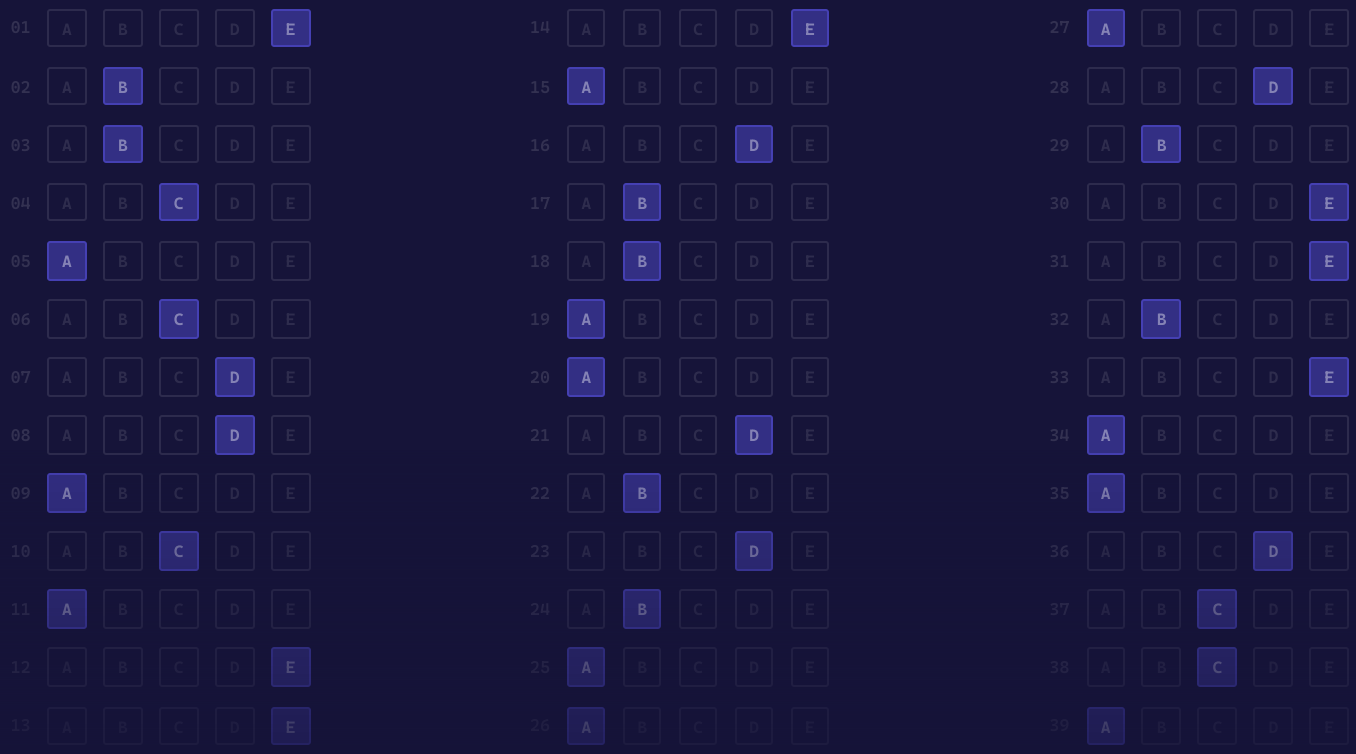

PRACTICE QUESTIONS

American Board of Medical Genetics And Genomics (ABMGG)

MG–MG

Clinical Molecular Genetics & Genomics Exam

EDITION	QUESTIONS	FORMAT
Demo	9	Limited Edition PDF

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Before you begin

What this is

9 practice questions for American Board of Medical Genetics And Genomics (ABMGG) `MG-MG`, 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-MG`
- the question number
- the email address on your order

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

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QUESTION 1 SINGLE CHOICE

Which of the following best describes the consequence of a nonsense mutation in the coding region of a gene?

A A silent substitution that does not alter the protein sequence

B A missense change that replaces one amino acid with another

C **A premature stop codon that typically leads to a truncated and often nonfunctional protein**

D An insertion of a single nucleotide that does not change the reading frame

E A duplication of a chromosomal segment containing the gene

ANSWER C

WHY A nonsense mutation converts a codon into a premature stop codon (UAA, UAG, or UGA). Translation is terminated prematurely, producing a truncated protein that is usually unstable or nonfunctional and is often degraded by nonsense-mediated decay. The other options describe different mutation classes (silent, missense, in-frame insertion, and duplication).

QUESTION 2 SINGLE CHOICE

In a standard polymerase chain reaction (PCR), which component provides the starting point for DNA synthesis by defining the boundaries of the amplified region?

A Thermostable DNA polymerase

B Deoxynucleotide triphosphates (dNTPs)

C **Oligonucleotide primers**

D Magnesium chloride as a cofactor

E Template DNA extracted from the patient

ANSWER C

WHY Short oligonucleotide primers complementary to the flanking regions of the target sequence anneal to the template and provide the 3' hydroxyl group required for DNA polymerase to initiate synthesis. The polymerase, dNTPs, magnesium, and template are all required, but only the primers determine where synthesis begins and ends.

QUESTION 3 SINGLE CHOICE

Which sequencing-by-synthesis method uses reversible terminators and fluorescently labeled nucleotides to allow millions of clusters to be read simultaneously on a flow cell?

A Classical chain-termination (Sanger) sequencing

B Pyrosequencing

C **Illumina sequencing**

D PacBio single-molecule real-time (SMRT) sequencing

E Nanopore sequencing

ANSWER C

WHY Illumina platforms perform sequencing-by-synthesis on a flow cell using reversible terminators, each nucleotide carrying a removable fluorophore and a 3' blocking group. After image acquisition, the terminator is cleaved and the cycle repeats. Sanger, pyrosequencing, PacBio SMRT, and nanopore all use fundamentally different detection chemistries.

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QUESTION 4 SINGLE CHOICE

A condition appears in every generation, affects males and females approximately equally, and can be transmitted from an affected father to both sons and daughters. Which inheritance pattern is most consistent with these findings?

A Autosomal recessive

B X-linked recessive

C X-linked dominant

D Autosomal dominant

E Mitochondrial (maternal)

ANSWER D

WHY Autosomal dominant traits classically show vertical transmission through every generation, equal sex distribution, and male-to-male transmission. X-linked recessive and dominant patterns show sex bias and typically lack male-to-male transmission, while autosomal recessive often appears in siblings but not in every generation, and mitochondrial inheritance is transmitted exclusively from mother to all offspring.

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QUESTION 5 SINGLE CHOICE

According to the American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP) framework, which combination of evidence best supports classifying a sequence variant as 'pathogenic'?

A **The variant is absent from population databases and occurs de novo in a patient with a consistent phenotype, with confirmation of paternity and maternity**

B The variant is common in population databases and has been observed in healthy adults

C The variant is a synonymous change with no predicted splice effect and is absent from databases

D The variant is located in a noncoding region with no functional evidence

E The variant is predicted in silico to be tolerated and is reported once in a population database

ANSWER **A**

WHY Strong or very strong evidence for pathogenicity includes null variants in genes where loss of function causes disease, established functional studies, or confirmed de novo occurrence with parental testing. Absence from population databases combined with a confirmed de novo event with a consistent phenotype is among the strongest criteria for classifying a variant as pathogenic. The other options describe evidence that would argue against pathogenicity or be insufficient to classify the variant.

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QUESTION 6 SINGLE CHOICE

Which molecular method is most appropriate as a first-tier screen to detect exon-level deletions and duplications across multiple genes when DNA sequencing alone will miss them?

A Sanger sequencing of the genes of interest

B Multiplex ligation-dependent probe amplification (MLPA)

C Standard PCR amplification of a single amplicon

D Northern blot analysis of mRNA

E Karyotype analysis at the 5 Mb resolution level

ANSWER **B**

WHY MLPA uses probe pairs that hybridize to adjacent sequences and are ligated; the ligated products are quantified by capillary electrophoresis, allowing detection of copy number changes at individual exons. Sanger sequencing cannot detect whole-exon deletions/duplications, single-amplicon PCR is too limited, Northern blot measures mRNA, and karyotype is far too low resolution to detect single-exon events.

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QUESTION 7 SINGLE CHOICE

A newborn is found to have hypotonia, upslanting palpebral fissures, a single transverse palmar crease, and a congenital heart defect. Karyotype analysis shows 47,XX,+21. Which cytogenetic mechanism most commonly accounts for this result?

A Robertsonian translocation between two acrocentric chromosomes

B Reciprocal translocation between two submetacentric chromosomes

C Paternal meiotic nondisjunction of chromosome 21, producing a gamete with two copies

D Postzygotic mitotic recombination leading to mosaicism

E Ring chromosome formation involving chromosome 21

ANSWER C

WHY Full trisomy 21 (Down syndrome) most commonly arises from maternal meiotic nondisjunction (~90% of cases), most often during meiosis I; paternal meiotic nondisjunction accounts for a smaller fraction. Robertsonian translocations account for a minority of cases and typically present with 46 chromosomes. The described karyotype with 47 chromosomes and a free extra chromosome 21 is consistent with meiotic nondisjunction, not a translocation, ring, or mosaic configuration.

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QUESTION 8 SINGLE CHOICE

In NGS data analysis, which step is most directly responsible for identifying differences between the sequenced reads and a reference genome?

A Base calling from raw signal intensities

B Read alignment to a reference sequence

C **Variant calling from aligned reads**

D Variant annotation against population databases

E Demultiplexing of pooled samples

ANSWER C

WHY Variant calling is the analytical step that compares aligned reads to the reference genome and identifies positions at which the sample differs, producing a VCF. Base calling generates the raw nucleotide calls, alignment places reads on the reference, annotation adds functional and population information, and demultiplexing separates pooled libraries.

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QUESTION 9 SINGLE CHOICE

A clinical laboratory is evaluating a missense variant in the BRCA2 gene that has not been previously reported. Population databases show the variant is absent from gnomAD. In silico tools (REVEL, AlphaMissense) yield concordant deleterious predictions. The patient's tumor shows loss of heterozygosity at the BRCA2 locus. According to ACMG/AMP criteria, which combination of evidence codes is most appropriately applied to reach a classification of Likely Pathogenic?

A PVS1 + PM2

B PM2_supporting + PP3 + PS3

C PM2_supporting + PP3 + PP1

D PS3 + PM1 + PP3

ANSWER C

WHY A missense variant without functional or segregation evidence cannot reach PS3 (functional study in the patient-derived variant with strong evidence) or PP1 (segregation). The strongest applicable evidence is PM2_supporting (absent/rare in population databases), PP3 (multiple concordant in silico predictions of deleteriousness), and PP1 would require segregation data. With PM2_supporting + PP3 the variant still does not meet Likely Pathogenic without additional evidence. The most defensible combination consistent with the data provided — relying on absence from gnomAD, deleterious in silico predictions, and loss of heterozygosity in the tumor as supporting tumor-related evidence — is PM2_supporting + PP3 plus an additional supporting criterion such as PP4 (specific patient phenotype) or PP1 when segregation is available. Option C best reflects typical application. Note that LOH alone is not a validated ACMG criterion but may be reported as tumor evidence alongside these codes.