

Festivus 2020: “Molecular” Biology (aka proteins)

Note to players: All tossups are composed of three sentences. Superpowers (20s), powers (15s), and 10s correspond roughly to each sentence. Sometimes, power will extend beyond the phrase “For 10 points” in the last sentence.

0. **This is tossup zero, so it’s kind of goofy and/or dumb. Each question in this set was inspired by randomly selecting one of these molecules, which always appear in articles written and illustrated by David Goodsell, a structural biologist known for his watercolors of microbes. An “Exploring the Structure” section with illustrations from Jmol or RasMol ends all of the articles about these molecules, which often reference similar molecules written about by the European Bioinformatics Institute. For 20 points, name these molecules which existed for 20 years as of January 2020, meaning there are 252 of them now.**

ANSWER: RCSB **PDB Molecules of the Month** [accept answers mentioning **Molecules of the Month** and one of the following: **Rutgers**, The **Scripps** Research Institute, **Protein Data Bank**, or **Research Collaboratory for Structural Bioinformatics**; prompt on **Molecules of the Month**; reject any answer mentioning “Bristol” or “Bristol University School of Chemistry” or “European Bioinformatics Institute”] (<https://pdb101.rcsb.org/motm/motm-about>)

1. **Two aryl ether bonds and a biaryl bond are formed in this drug by the three cytochrome P450 enzymes: OxyB (“oxy-B”), OxyA (“oxy-A”), and OxyC (“oxy-C”), acting in that order. (+) Teicoplanin is structurally and mechanistically similar to this drug with a hexapeptide aglycone whose action is inhibited by a D-alanine-D-lactate ligase. For 10 points, name this (*) glycopeptide antibiotic administered intravenously to treat life-threatening infections by Gram-positive bacteria like Clostridioides difficile and MRSA (“MER-suh”).**

ANSWER: **vancomycin** (<https://pdb101.rcsb.org/motm/192>)

2. **Two members of this family of transcription factors interact with ménage à trois-1, or MAT1, to enhance CDK-activating kinase activity. One member of this family of transcription factors binds to (emphasize) a different transcription factor with a (+) HMG DNA binding domain to form a complex that binds to the fibroblast growth factor 4 enhancer. For 10 points, name this family of transcription factors with POU (“pow”) domains that bind to the sequence (*) ATGCAAAT, whose third or fourth member is one of the Yamanaka factors.**

ANSWER: **Oct** [or **Octamer**-binding transcription factor; accept **POU** before mentioned] (The other transcription factor mentioned is Sox2. <https://pdb101.rcsb.org/motm/112>)

3. **Unlike other antifungals that bind to ergosterol or inhibit its biosynthesis, the antifungal agent sordarin acts by binding one of these proteins. (+) Diphthamide, which binds diphtheria toxin, is uniquely found in one of these proteins whose subtypes in prokaryotes include Tu, Ts, and G. For 10 points, (*) tRNAs are transported to empty ribosome sites by what proteins that act after initiation factors and before release factors in protein synthesis?**
ANSWER: **elongation factors** [or **EF**; or eukaryotic **elongation factors**; or **eEF**; reject “eIF”]; (<https://pdb101.rcsb.org/motm/81>)

4. **Mutations in a gene encoding one of these enzymes is linked to a disease associated with loss of anterior horn cells, X-linked infantile spinal muscular atrophy. These enzymes (+) adenylate their substrate at its C terminus, then form a thio-ester linkage between the substrate and a cysteine residue, and finally shift the substrate to the next enzyme in the pathway via a trans-thio-esterification reaction. For 10 points, name these enzymes that activate a (*) 76-residue, universal protein before transferring it to E2 enzymes.**
ANSWER: **E1** enzymes [or **ubiquitin-activating** enzymes or **Ub-activating** enzymes before “activate”] (<https://pdb101.rcsb.org/motm/60>)

5. **Some of these synthetic molecules used to fluorescently label RNA are appropriately named Mango, Corn, Broccoli, and Spinach for the colors they give off. Some of these synthetic molecules with therapeutic uses include (+) pegaptanib sodium, a VEGF (“vej-F”) antagonist used to treat neovascular age-related macular degeneration, and TBA, an anticoagulant that binds to exosite I of thrombin. For 10 points, (*) riboswitches contain a natural domain similar to what short, single-stranded nucleic acids designed to bind to a specific target?**
ANSWER: **aptamers** (TBA is Thrombin Binding Aptamer. <https://pdb101.rcsb.org/motm/229>)

6. **Most members of this protein family catalyze a reaction that generates a mixture of 2'- (“two-prime”) and 3'- (“three-prime”) O-acetyl-ADP-ribose, a secondary messenger critical to heterochromatin formation. Most members of this protein family catalyze a reaction that proceeds by first removing the (+) nicotinamide (“nee-kuh-TEE-nuh-mide”) ring from NAD, and then transferring an acetylated lysine to what’s left of NAD. For 10 points, name this family of (*) ADP-ribosyl transferases and histone deacetylases that were first discovered when the silent information regulator 2 protein slowed down aging in yeast.**
ANSWER: **sirtuins** [prompt on histone deacetylases] (<https://pdb101.rcsb.org/motm/213>)

7. **The Tokyo II (“two”) type of this protein incorrectly polymerizes because its DD domains are defective, but when it polymerizes correctly, intermolecular end-to-middle associations form between EA domains and DA domains. The (+) mushroom-shaped lesions that erupt out of colonic glands in pseudomembranous colitis contain pus, mucin, and this protein whose cleavage is induced by the drugs alteplase and streptokinase. For 10 points, name this protein whose (*) zymogen is cleaved by thrombin in the last step of the coagulation cascade.**

ANSWER: **fibrin** [or **Factor Ia** (“one-A”); accept **fibrinogen**]
(<https://pdb101.rcsb.org/motm/83>)

8. **Mutations in the MOCOS gene cause this enzyme to malfunction because its cofactor is no longer sulfated. Febuxostat inhibits this enzyme found in (+) cow milk that degrades 6-mercapto-purine, and, more generally, this enzyme uses either NAD+ (“N-A-D-plus”) or oxygen as its final electron acceptor in the last step of purine degradation. For 10 points, (*) allopurinol inhibits what enzyme that relies on a molybdenum-containing cofactor to add an oxygen atom to its substrate to form uric acid?**

ANSWER: **xanthine oxidoreductase** [or **xanthine oxidase**; or **xanthine dehydrogenase**; or **XO**; or **XAO**; or **XOR**; or **XDH**] (The first clue refers to hereditary xanthinuria type II.
<https://pdb101.rcsb.org/motm/117>)

9. **One of these proteins has three known target receptors: SLAMF1, nectin-4, and membrane cofactor protein, also called CD46. Egg-adaptive changes bias the results of (+) inhibition assays performed on a different one of these proteins that changes shape once it is inside an acidic endosome, releasing its fusion peptide that binds with the endosome membrane. For 10 points, head and stem domains make up the ectodomain of what (*) viral proteins whose namesake inhibition assays are performed on ferrets to subtype influenza viruses.**

ANSWER: **hemagglutinins** [accept influenza **hemagglutinins** or flu **hemagglutinins**; accept measles **hemagglutinins**] (<https://pdb101.rcsb.org/motm/76>)

Note to moderator: Read answer line carefully before reading the question

10. **Phasins are associated with the formation of granules of one of these compounds synthesized from HB-CoA (“H-B-koh-A”) by the enzyme PhaC (“fah-C”), also called polyhydroxybutyrate synthase. A beta-hydrolase in (+) *Ideonella sakaiensis* breaks down one of these compounds, while bacteria used to synthesize them include *Pseudomonas putida* and *Cupriavidus necator*. For 10 points, name these compounds, examples of which include the (*) environmentally friendly Biopol, as well as PMMA and polyvinyl chloride.**

ANSWER: biodegradable **plastic** [accept specific types of plastics before they are mentioned (be lenient, it’s Festivus), including: **bioplastics**, **thermoplastics**, **polyesters**, **PETs**, **polyurethanes** or **PU**s or **PUR**s, **polyethylenes** or **polythenes** or **PE**s, **polypropylenes** or **PP**s, **polyvinyl chlorides** or **PVC**s, **polyamides** or **PA**s, **polyhydroxyalkanoates** or **PHA**s, and **nylons**; accept **polyhydroxyalkanoic acid**s; prompt on **polymers**] (The beta-hydrolase is PETase. <https://pdb101.rcsb.org/motm/216>)

11. **The WRAD complex activates the SET1 (“set-one”) family of lysine methyl-transferases, which is recruited by one of these enzymes to deposit H3K4me3 marks on chromatin. These enzymes, whose mechanism is commonly studied using one of them in bacteriophage (+) T7, prematurely release from their substrate in abortive cycling. For 10 points, alpha-amanitin inhibits what enzymes that bind to (*) promoters during transcription to create a nucleic acid used in protein synthesis?**

ANSWER: **RNA polymerases** [or **RNAP**; or **RNA pol**; or **DNA-directed RNA polymerase**; reject “RNA-directed RNA polymerase” or “RdRP”] (<https://pdb101.rcsb.org/motm/40>)

12. **The most severe instance of a subtype of this genetic disorder, usually fatal before or shortly after birth because it causes hydrops fetalis, is named after Bart’s, an abbreviation of St. Bartholomew’s Hospital. Patients living with (+) ATR-16 syndrome have intellectual disabilities along with this autosomal recessive disorder that comes in two main subtypes caused by either mutations in *HBB* or mutations in *HBA1* and *HBA2*. For 10 points, name this inherited (*) blood disorder caused by defects in the genes that produce the alpha or beta chains of hemoglobin.**

ANSWER: **thalassemia** [accept alpha **thalassemia**; accept beta **thalassemia**; accept **thalassemia** major; accept **thalassemia** minor; prompt on **Hb Bart’s hydrops fetalis** with “that is a subtype of what genetic disorder?”; accept **HbH** or **Hemoglobin H-Constant Spring disease**] (<https://pdb101.rcsb.org/motm/41>)

13. **Some of these receptors whose prototypical agonist is ketazocine (“key-TAY-zoh-seen”) are concentrated in the primary cells of the nucleus raphe magnus, which receives descending signals from the periaqueductal grey area. The (+) antidiarrheal medication racecadotril, also called acetorphan, inhibits enzymes that break down endogenous ligands that bind to these receptors; those ligands are enkephalins. For 10 points, name these receptors with (*) mu, kappa, and delta subtypes that inhibit pain signals when they are bound by drugs similar to morphine.**

ANSWER: **opioid** receptors [accept more specific types of **opioid** receptors: **mu**, **kappa**, **delta**; accept **nociceptin receptors**; prompt on GPCRs or G-protein coupled receptors]
(<https://pdb101.rcsb.org/motm/217>)

14. **Ceftriaxone is beginning to replace the use of these drugs in synergistic treatments of infective endocarditis because these drugs have a high risk of inducing acute tubular necrosis in elderly patients. By stabilizing the (+) ribosomal ambiguity conformation, one of these drugs induces translational errors in two ways: allowing near-cognate tRNAs to bind to the A site and disrupting proofreading. For 10 points, (*) streptomycin is the most prominent of what sugars modified with a nitrogen-containing functional group that kill Gram-negative bacteria?**

ANSWER: **aminoglycosides** [accept **streptomycin** before mentioned]
(<https://pdb101.rcsb.org/motm/146>)

15. **The restriction factors TRIM5 (“trim-five”) and MxB prevent the disassembly of one of these structures with an unusual cone-like structure. To model these structures, (+) Donald Caspar and Aaron Klug introduced a quantity calculated as the square of the distance between two five-fold vertices called the triangulation number, or T. For 10 points, what structures composed of (*) 12 pentamers and 10 times T minus one heptamers that resemble an icosahedron enclose the genetic material of viruses?**

ANSWER: viral nucleoc**apsids** [prompt on icosahedrons before mentioned with “what biological structure is modeled as an icosahedron?”] (The first clue refers to the HIV capsid.
<https://pdb101.rcsb.org/motm/200> and <https://pdb101.rcsb.org/motm/163>)

16. **Three answers required. Upon excitation, a tripeptide of these three amino acids undergoes excited-state proton transfer, relaying a proton from a phenol hydroxyl to glutamate 222. When (+) threonine is substituted for one of these three amino acids that occupy residues 65 through 67, the tripeptide normally composed of them remains in an ionized state. For 10 points, the post-translational (*) cyclization followed by the dehydrogenation of a tripeptide composed of what three amino acids forms the fluorophore of GFP?**

ANSWER: **serine** AND
tyrosine AND
glycine (<https://pdb101.rcsb.org/motm/42>)

17. **The 24 heavy and light subunits that make up this protein are each folded into four-helix bundles with an up-down-down-up topology, and those subunits of this protein can form either three-fold channels lined with aspartate and glutamate or four-fold channels lined with leucine. (+) Blood concentration of this protein is measured in a test ordered alongside TIBC tests when CBC results show low hemoglobin and hematocrit. For 10 points, name this (*) hollow globular protein that has enough space to store up to 4,500 iron ions.**

ANSWER: **ferritin** (<https://pdb101.rcsb.org/motm/35>)

18. **Enzymes that add this functional group have a sole cofactor whose biosynthesis is inhibited by sulfa drugs because sulfa drugs block sepiapterin reductase, which acts after PTPS and GTP cyclohydrolase I ("one") in the biosynthesis of that cofactor. The (+) catalytic domain of enzymes that add this functional group contains an iron ion that stabilizes the cofactor tetrahydrobiopterin. For 10 points, name this functional group added to (*) phenylalanine to make tyrosine.**

ANSWER: **hydroxyl** [or **OH**; or **hydroxy**; reject "alcohol"] (<https://pdb101.rcsb.org/motm/61> and <http://pdb101.rcsb.org/motm/188>)

19. **Lanabecestat and verubecestat were promising experimental drugs to inhibit this protease, but development of both was stopped during Phase III trials. The sorting protein (+) Golgi-localized gamma-ear-containing ARF binding protein 1, or GGA 1, aids the transport of this protease to the cell membrane, where it trims neuregulin and voltage-gated sodium channels. For 10 points, name this (*) aspartic acid protease that creates a C99 fragment from amyloid precursor protein that is then cleaved by a similarly named protease to form amyloid plaques.**

ANSWER: **beta-secretase 1** [or **BACE1**; or **memapsin-2**; or **Asp2**] (The similarly named protease is gamma-secretase. <https://pdb101.rcsb.org/motm/115>)

20. **The small molecules cerulenin and C75 induce apoptosis in cancer cells by inhibiting an enzyme that synthesizes these molecules, and that enzyme that synthesizes these molecules regulates estrogen receptor-alpha signalling in breast cancer cells. In addition to inhibiting lipases, (+) orlistat inhibits a multifunctional enzyme in which these molecules are moved between different catalytic sites by the phospho-panto-theine group attached to an ACP domain. For 10 points, name these (*) lipids, three of which are attached to glycerol in triglycerides.**

ANSWER: **fatty acids** [or **FAs**; accept **palmitic acid**; prompt on **lipids**; reject “fats”]
(<https://pdb101.rcsb.org/motm/90>)

21. **Proteins with short C-terminal sequences called targeting peptides or cargo loading peptides are destined for these structures which are coded for by part of the IMEF operon central to iron metabolism in Firmicutes. Proteins homologous to the gp5 capsid protein of bacteriophage HK97 make up these structures, one of which from *Brevibacterium linens* naturally houses a dye-decolorizing peroxidase. For 15 points, name these (+) nanocompartments found in bacterial culture supernatants whose potential applications include targeted drug delivery.**

ANSWER: **encapsulins** [prompt on bacterial nanocages; prompt on bacterial nanocompartments before “nanocompartments”] (IMEF is Iron-Mineralizing Encapsulin-associated Firmicute.
<https://pdb101.rcsb.org/motm/165>)

22. **Necrolytic migratory erythema is characteristic of the presence of a rare neuroendocrine tumor that causes the hypersecretion of this hormone. This hormone, which is (+) cleaved from its precursor by prohormone convertase 2 binds to its receptor to kick off a signalling pathway with two effects: increased transcription of carnitine acyl transferase-1 and inhibition of malonyl-CoA (“malonyl-koh-AY”) formation. For 10 points, name this hormone secreted by (*) pancreatic alpha cells that raises the concentration of glucose in the blood.**

ANSWER: **glucagon** (The first line refers to glucagonoma. Amusingly glucagon’s precursor, proglucagon, has a precursor called proglucagon. <https://pdb101.rcsb.org/motm/184>)

23. **Upon administration of one of these drugs, a phenol quickly diffuses away, after which it releases monomers as zinc ions are released. A substitution of (+) asparagine for glycine at the twenty first position of the A chain and two arginine residues added to the C terminus of the B chain distinguishes one of these drugs called glargine from the analogous molecule in the body. For 10 points, name these drugs that are (*) injected subcutaneously once a day to treat diabetes.**

ANSWER: **long-acting insulin** analogs [prompt on **insulin** analogs with “what pharmacological property do these insulin analogs have?”] (The first clue is degludec. <https://pdb101.rcsb.org/motm/194>)

24. **The mutation H274Y endows these enzymes with resistance to a common drug that inhibits them. The so-called (+) 150-loop or 150-cavity is targeted by novel inhibitors of these enzymes, whose substrates are substituted with two fluorines to create DFSA drugs. For 10 points, name these (*) sialidases inhibited by zanamivir and oseltamivir that are referred to in flu virus designations along with hemagglutinin.**

ANSWER: influenza **neuraminidases** [or **sialidases** before mentioned] (DFSA is difluorosialic acid. <https://pdb101.rcsb.org/motm/113>)

25. **The genotype 3 of the disease caused by this virus is thought to cause steatosis via interactions with three proteins: microsomal triglyceride transfer protein, SREBP-1c, and PPAR-alpha. This virus is treated using (+) boceprevir, ombitasvir, sofosbuvir, and other direct acting antiviral agents that inhibit several proteins including NS3/4A protease and NS5B nucleoside polymerase. For 10 points, (*) H. J. Alter, M. Houghton, and C. M. Rice won the 2020 Nobel Prize in Physiology or Medicine for their study of what virus that causes liver disease?**

ANSWER: **Hepatitis C** virus [or **Hep C** virus; or **HCV**] (<http://pdb101.rcsb.org/motm/252>)

26. **Enzymes that bind to sites within this structural feature have an active site primary sequence motif of PD...D/EXK (“P-D-dot-dot-dot-D-slash-E-X-K”). A kink of approximately (+) 50 degrees at the central TA (“T-A”) step of the EcoRV (“eco-R-five”) recognition sequence occurs alongside compression of this structural feature and widening of a different structural feature after EcoRV (“eco-R-five”) binds. For 10 points, (*) DNA methyl-transferases prevent type II restriction enzymes from binding their recognition sequences in what structural feature that is 22 Angstroms wide?**

ANSWER: **major groove** (<https://pdb101.rcsb.org/motm/8>)

27. **The first of these enzymes to be found attached to a cell membrane regulates EGF receptor signalling in rhomboid *Drosophila* mutants. Deficiency in (+) Protein S and in a zymogen of one of these enzymes can cause neonatal purpura fulminans, and warfarin-induced skin necrosis can occur due to deficiency of that zymogen of one of these enzymes, Protein C. For 10 points, (*) subtilisin and trypsin are what enzymes that use a nucleophilic amino acid with a hydroxymethyl side chain to cleave peptide bonds?**

ANSWER: **serine proteases** [or **serine peptidases**; or **serine proteinases**; prompt on **proteases**, **peptidases**, or **proteinases**] (<https://pdb101.rcsb.org/motm/140>)

28. **When this amino acid is released by the AWC and AFD sensory neurons, it activates ion channels on the AIY neuron, thus increasing the frequency of turns during locomotion. (+) Macrocyclic lactone drugs and fipronil target ion channels that this amino acid binds to, and those chloride channels gated by this amino acid are targeted by ivermectin, a drug used to kill heartworms. For 10 points, name this amino acid synthesized from (*) alpha-ketoglutarate by alanine transaminase, whose own receptors include NMDA receptors.**

ANSWER: **glutamate** [or **Glu**] (<https://pdb101.rcsb.org/motm/191>)

29. **The C terminus of the M10 alpha helix of this enzyme's alpha subunit has been called the "switch region" because deleting the five residues KETTY from the end of that region greatly reduces this enzyme's binding affinity. The (+) Post-Albers model describes the mechanism of this enzyme that is inhibited by cardiac glycosides, whose blood concentration increases during chronic kidney disease. For 10 points, name this (*) P-type ATPase inhibited by digoxin that maintains neurons' resting potential by exchanging ions of two different alkali metals across the cell membrane.**

ANSWER: **sodium-potassium pump** [or **Na⁺/K⁺ pump**; or **Na⁺/K⁺-ATPase**; or **sodium-potassium ATPase**] (<https://pdb101.rcsb.org/motm/118>)

30. **Two stable homodimers associate to form the four helix bundle that holds this homotetramer together, but unlike most homotetramers, it is V-shaped and does not possess three mutually perpendicular twofold axes of symmetry. (+) ONPF and ITPG have opposite effects on this protein that regulates a functional genetic unit activated by the upstream binding of CAP-cAMP ("cap-camp"). For 10 points, name this protein that binds to an (*) operator sequence to suppress the synthesis of three metabolic enzymes, including beta-galactosidase.**

ANSWER: **lac repressor** [reject "*lac* operon"] (<https://pdb101.rcsb.org/motm/39>)

31. **The landmark BHAT trial conducted in the 1980s demonstrated the numerous positive effects of these drugs used to treat essential tremors and Romano–Ward syndrome, the latter of which presents with (+) torsades de pointes (“tor-SAHD de PWANNT”).** Glucagon is used to treat overdoses of calcium channel blockers and these drugs that possess intrinsic sympathomimetic activity when they act as partial agonists. For 10 points, name these drugs whose names all (*) end in “lol” used to treat a variety of heart problems by preventing norepinephrine and epinephrine from binding to their receptors.

ANSWER: **beta blockers** [or **beta-adrenergic receptor antagonists**; or **beta-AR antagonists**; or **class II antiarrhythmics**; prompt on **antiarrhythmics**] (<https://pdb101.rcsb.org/motm/58> and <http://pdb101.rcsb.org/motm/100>)

32. **Defects in an ATP-binding cassette transporter specific to this tissue are associated with the accumulation of lipofuscin in it during Stargardt’s disease. (+) Franceschetti’s sign is characteristic of Leber congenital amaurosis, a dystrophy of this tissue that is affected by other dystrophies caused by defective guanylate cyclases.** For 10 points, mutations in **LRAT, RDH5, and (*) Rpe65-isomerase** disrupt the visual cycle in what tissue that contains opsins in its photoreceptor cells?

ANSWER: **retina** [accept **retinal pigment epithelium**] (<https://pdb101.rcsb.org/motm/27>)

33. **Mutations in the AAAS gene prevent the protein aladin from successfully reaching this structure in a genetic disorder characterized by three features: achalasia, Addison disease, and alacrima. Hydrophobic, disordered (+) FG-repeat domains allow molecules to pass through this structure, and large molecules passing through this structure from the outside have a short localization sequence, which is classically rich in arginine and lysine.** For 10 points, (*) karyopherins transport molecules across what structure that contains pores assembled from Nups?

ANSWER: **nuclear envelope** [or **nuclear membrane**] (<https://pdb101.rcsb.org/motm/205> and <https://pdb101.rcsb.org/motm/85>)

34. **Mutations in an enzyme that acts on this molecule cause the accumulation of D-2-hydroxyglutarate, an oncometabolite characteristic of gliomas, particularly diffuse astrocytomas and oligodendroglial tumors. An enzyme that acts on this molecule has two active sites that bind to (+) NAD+ (“N-A-D-plus”) or NADP+ (“N-A-D-P-plus”) and a divalent metal ion, usually magnesium or manganese.** For 10 points, the main control points of the Krebs cycle are: (*) pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase, and a dehydrogenase that acts on what molecule produced from an aconitase-catalyzed isomerization?

ANSWER: **isocitrate** [or **isocitric acid**; reject “citric acid” or “citrate”] (<https://pdb101.rcsb.org/motm/129>)

35. **Natural examples of this relationship include the relationship between the *F. succinogenes* beta-glucanase and other bacterial beta-glucanases and the relationship between saposin and swaposin. First applied to protein (+) engineering by Goldenberg and Creighton to modify the structure of bovine pancreatic trypsin inhibitor, this relationship was discovered when comparing the structure of concanavalin A (“CON-can-uh-VAIL-in A”) to other lectins. For 10 points, when a protein’s (*) native termini are linked, and then cleaved at a different location to create a new protein, the original and new proteins have what relationship?**

ANSWER: **circular permutation** [accept word forms of **permutation**, like **permuted**; or **CP**] (<https://pdb101.rcsb.org/motm/124>)