Hi, thank you to whoever volunteered to read this. I tried to provide pronunciation guides. There are 16 “real” tossups and then 5“speedchecks (shorter tossups on things I couldn’t find enough clues for) at the end.

Note on pronunciation: unless a pronunciation guide is provided, all acronyms should be read letter by letter, like ABCD1 is “A-B-C-D-one”

1. Minicircles of the kinetoplastids **(“kin-et-oh-plas-tids”)** of trypanosomes **(“trip-an-oh-somes”)** encode thousands of these things. A 2015 Nature paper by Konnerman et al. showed that these things can be modified by introducing MS2 loops and co-expressing a D10A/H840 catalytically dead mutant protein in order to activate transcription. Libraries of these things include GeCKO **(“gecko”)** and Brunello. For these things to work, their targets must be adjacent to a sequence, usually NGG, which is called a PAM **(“pam”),** or protospacer adjacent motif. A major advance in the use of these things came from the discovery that they could be constructed by combining crRNA and tracrRNA **(“tracer-RNA”)** into a single molecule by Emanuelle Charpentier and Jennifer Doudna **(“Dowd-nuh”)**. For 10 points, name these short RNA molecules used by Cas9 to target specific DNA loci.
ANSWER: **sgRNA** or **guide RNA** or **gRNA** or CRISPR **guides**

2. Note: this answer to this tossup is a class of diseases. A 2017 Science paper by Aseem Ansari’s lab at UW Madison described the development of a polyamide-JQ1 synthetic transcription factor used to treat a disease in this class.The pathogenesis of these diseases is *analogous* to the process that leads to production of five different dipeptides from the C9orf72 **(“C-nine-orf-seventy two”)** gene. A form of muscular dystrophy caused by DMPK mutations belongs to this class of diseases. The symptoms of these diseases become increasingly severe from generation to generation, a phenomenon known as anticipation. The pathogenesis of these diseases is believed to result from strand slippage during DNA replication and they usually lead to expansion of polyglutamine tracts in proteins. For 10 points, name this class of diseases, like Fredrich’s ataxia and Huntington’s, whose pathogenesis usually involves the expansion of CAG repeats.
ANSWER: **trinucleotide repeat** or **TNT repeat** disorders

3. One form of this protein has a my·ris·tic acid group attached to the lysine at its B29 residue, which allows it to bind albumin and prolong its half life. Mutations in this protein’s receptor causes small stature, upturned nostrils, and other “elvish” features, a disorder called leprechaunism or Donohue syndrome. Another form of this protein is mixed with a compound derived from trout semen, protamine, in a formulation named for Hans Christian Hagedorn. Variants of this protein that are unable to hexamerize include Lispro and Aspart, which are known as its short-acting forms. Secretion of this protein is stimulated by meg·lit·in·ides and sulf·on·yl·ureas. This protein is cleaved from its 31-amino acid C-peptide during packaging in the Golgi. For 10 points, name this protein secreted by beta cells of the pancreas.
ANSWER: **Insulin**

4. Like neuroblastoma, this disease can be imaged with an Iodine-131-labeled MIBG scan. A common ectopic site for this disease is located at the base of the inferior mesenteric artery, known as the Organ of Zuckerkandl. Urine of patients with this disease has increased levels of metanephrines **("met-uh-neph-rin")** and vanillylmandelic **("van-ill-ill-man-del-ic")** acid, or VMA. The drugs phentolamine **("fen-toll-uh-amine")** or phenoxybenzamine **("phen-ox-ee-benz-amine")** are administered to patients before undergoing resection of these tumors. Patients with this disease experience episodic symptoms that can be remembered as the 5 P's, which includes heart palpitation, elevated blood pressure, and perspiration. These tumors arise from chromaffin cells. For 10 points, name these tumors of the adrenal medulla, which lead to overproduction of norepinephrine and epinephrine.
ANSWER: **pheochromocytoma**

5. Trimethylglycine **("tri-meth-ill-gly-cine")**, or betaine **("bet-ane")**, can be administered to reduce accumulation of this compound. An accumulation of this compound leads to a disease in which the lens is subluxated **("sub-lux-ated")** downward and inward. PLP can be administered to treat patients who have a deficiency of an enzyme that combines this molecule and serine to produce cystathionine **("cis-tuh-thigh-own")**. Patients with that enzyme deficiency are often described as having a "Marfanoid-habitus". A derivative of this molecule is produced as a byproduct during the conversion of norepinephrine to epinephrine and during DNA methylation. That byproduct is formed when a methyl group is donated from S-adenosyl methionine. For 10 points, name this non-standard amino acid, which is like a cysteine but with an extra methylene group.
ANSWER: **Homocysteine**

6. Hematologic disorders like multiple myeloma can have cells that histologically resemble the crumpled tissue paper macrophages characteristic of one of these diseases. It's not hemophilia, but Sangamo therapeutics has several ongoing clinical trials using zinc finger nucleases to treat several of these diseases. One of these diseases, which is characterized by destruction of myelin, is named for its histologic appearance due to accumulation of sulfatides. That disease, caused by a deficiency of arylsulfatase A, is metachromatic leukodystrophy. Derivatives of the molecule ceramide accumulate in these diseases. Enzyme replacement therapies exist for several of these diseases, like replacement of gluco·cerebro·sidase and alpha-galactosidase A for Gaucher disease and Fabry's disease, respectively. For 10 points, name this class of diseases, characterized by dysfunction of an organelle that serves as the cell's garbage disposal.
ANSWER: **lysosomal storage disorders** or **LSDs**

7. Autoantibodies against a protein that catalyzes the production of these molecules are characteristic of a class of small-vessel vasculitides **("vasc-yule-it-eye-dees")** that includes microscopic polyangiitis **("poly-anj-eye-tis")** and Churg-Strauss syndrome. That autoantibody is p-ANCA. Phorbol myristate **("for-ball miss-trate")** acetate, or PMA, is added to a blood sample to detect the production of these molecules by observing conversion of di·hydro·rhodamine 123 to the fluorescent rhodamine 123. Another test for the production of these molecules looks for the appearance of a deep blue color when cells are incubated with nitroblue tetrazolium. Inability to produce these molecules is characteristic of chronic granulomatous **("gran-yule-oh-mat-ous")** disease, whose sufferers are very susceptible to infection by catalase-positive organisms. After being engulfed into a phago·lysosome, pathogens are degraded by these molecules which are produced by enzymes like myeloperoxidase and NADPH oxidase. For 10 points, the neutrophil respiratory burst involves the generation of what class of reactive radical species such as superoxide..
ANSWER: **Reactive oxygen species** or **ROS** [prompt on "radicals"]

8. Deficiency of an enzyme that hydrolyzes terminal residues of this molecule causes Sly syndrome. Patients homozygous for the "*28 **("star-twenty eight")** variant" of a protein that catalyzes the addition of this molecule are at higher risk of side effects from irinotecan **("irr-ee-noh-tee-can")**. An enzyme that hydrolyzes a derivative of this molecule, MUG, into the fluorescent substrate 4-methyl-um·belli·ferone is used to evaluate transgene expression in plants as part of the GUS reporter system. Infants treated with chlor·am·phen·i·col develop cyanosis because of their inability to attach this molecule to it, a condition known as Gray Baby Syndrome. Deficiency of an enzyme that catalyzes the addition of this molecule leads to kernicterus **("kern-ick-ter-us")** and requires treatment with phototherapy in Crigler-Najjar syndrome. A derivative of this molecule bound to UDP is used as a substrate by p450 enzymes in phase II metabolism to increase the solubility of xenobiotics. This molecule is derivative of glucose with the OH at its 6th carbon oxidized to a carboxylic acid. For 10 points, name this sugar, which is conjugated onto bilirubin to allow it to be excreted in the urine.
ANSWER: **glucuronic acid**

9. A 2017 Nature paper from this scientist's lab describes a lncRNA screen that identifies EMICERI, a novel lncRNA that regulates vemurafenib resistance in melanoma. As a graduate student, this scientist and Ed Boyden were the lead authors on a 2005 paper demonstrating the first use of microbial opsin genes to regulate gene regulation, which started the field of optogenetics and was done during their time in Karl Deisseroth's **("diss-uh-roth")** lab. This scientist's lab developed a method that uses Cas13a **("cas-thirteen-A")** for rapid RNA or DNA detection to identify virus and bacterial strains, a technique termed SHERLOCK **("sherlock"**) . A fast-tracked patent filed based on this man's work has led to a lengthy legal dispute with UC Berkeley over the use of a certain tool in prokaryotes versus eukaryotes. For 10 points, name this Broad Institute scientist who is credited with pioneering the use of CRISPR along with Jennifer Doudna and Emannuelle Charpentier.
ANSWER: Feng **Zhang**

10. This drug can be used in chromatography to determine the degree of conjugation of various ketones by forming hydrazone adducts that can be detected by their bathochromic shift. The half-life of this drug is bimodal due to the prevalence of different CYP2C19 **("sip-two-C-nineteen")** isoforms leading to the existence of so-called "slow" and "fast acetylators" in the population. Use of this antibiotic can cause arthralgias, a rash and anti-histone antibodies, indicative of drug-induced lupus. Side-effects caused by treatment with this drug include pellagra, due to inhibited niacin synthesis, and peripheral neuropathy and sideroblastic anemia, because this drug closely resembles vitamin B6. This antibiotic can cause high anion gap metabolic acidosis. The active metabolite formed by this drug binds to the enoyl-acyl carrier protein reductase InhA **("I-N-H-A")**. That metabolite is formed when this drug is activated by the catalase-peroxidase KatG **("cat-G")**. For 10 points, name this drug, often used with rifampicin as a first-line tuberculosis treatment and abbreviated INH.
ANSWER: **Isoniazid** or **INH**

11. Journalist Natalie Angier documents her time in Bob Weinberg's lab at the Whitehead Institute and in another laboratory located at this institution in "Natural Obsessions." A fictionalized version of this research institution is where Brown University graduate Leonard Bankhead conducts yeast genetics research in Jeffrey Eugenides's "The Marriage Plot". At this institution, work that began with discovery of the Ac/Ds **("A-C-D-S")** locus led to the discovery of transposons by Barbara McClintock. This institution runs the preprint server bioRxiv. In January 2019, this institution severed ties with a former director who has repeatedly expressed abhorrent views on race and intelligence, James Watson. For 10 points, name this independent research institution located on Long Island.
ANSWER: **Cold Spring Harbor Laboratory** or **CSHL**

12. Description acceptable. A March 2017 Science paper by Deepak Nijhawan's **("nye-juh-wans")** group at UTSW showed that sulfonamides induce cancer cell death by recruiting RBM39to the protein DCAF15 **("dee-calf-fifteen")**, which causes the addition of this modification to RBM39. A 2015 Nature paper by Benjamin Ebert's group at Dana-Farber showed that the anticancer activity of thalidomide derives from its ability to cause the addition of this modification to casein kinase 1 alpha. A family of these proteins that catalyzes the addition of this modification requires activation by NEDDylation **("ned-ill-ation")** to function. Hydroxylation of HIF1a **("hif-one-alpha")** during hypoxia prevents this modification from being added to it by von Hippel Landau. Securins have this modification added onto them by the anaphase promoting complex, triggering transition from metaphase to anaphase. This modification is added onto lysines of substrate proteins via an isopeptide bond and requires a cascade of 3 proteins called E1, E2 and E3s. For 10 points, name this modification that marks proteins for degradation by the proteasome.
ANSWER: **Ubiquitination**

13. The rare deficiency of the 3rd isoform of this protein leads to Khaziri syndrome and a glycosylation deficiency syndrome in which patients are unable to convert polyprenol to dolichol. The most commonly-used inhibitors of this protein being to a class of molecules known as azasteroids. XY infants born lacking this enzyme have ambiguous external genitalia and male internal genitalia, because the molecule produced by this enzyme is required for male external genitalia development. Male pattern baldness and benign prostatic hyperplasia can be treated by an inhibitor of this enzyme, finasteride. For 10 points, name this enzyme that catalyzes the conversion of testosterone into dihydrotestosterone.
ANSWER: **5alpha-reductase**

14. A 2006 PNAS paper by T. Funke describes a mutant form of an enzyme in this pathway whose G100A active site mutation confers drug resistance, known as its "CP4" variant. The final product of the *amino-variant* of this pathway is used by polyketide synthases to produce ansamycins. Synthesis of the iron siderophore enterobactin begins with the conversion of one molecule in this pathway to 2,3-DHB. An intermediate in this pathway is cleaved by its namesake lyase into 4-hydroxybenzoate and pyruvate in the first step of ubiquinone synthesis in *E. coli*. Prephenic acid is an intermediate in this pathway formed from the claisen rearrangement of chorismate. An inhibitor of a viral enzyme that cleaves sialic acids on the surfaces of human cells is synthesized from the final product of this pathway and is known as Tamiflu or oseltamivir. This pathway is named for a molecule first derived from the Japanese star anise. The herbicide glyphosate, or Roundup, functions by inhibiting an enzyme in this pathway. For 10 points, name this pathway used by bacteria and plants to synthesize aromatic amino acids.
ANSWER: **shikimic acid** or **shikimate** pathway

15. Talarazole increases the bioavailability of this molecule by blocking its metabolism by inhibiting CYP26 isozymes. 80% of the body's store of this molecule is located in cells that inhabit the perisinusoidal space of Disse, known as stellate or Ito cells. A derivative of this molecule is used to treat patients who have a cancer characterized genetically by a 15;17 translocation and histologically by promyelocytes with Auer (**"Ow-er")** rods. That disease is acute promyelocytic leukemia or APML. This molecule's receptor binds upstream of the Hox gene cluster, which is why one of its derivatives, accutane, is highly teratogenic. For 10 points, what vitamin is linked via a Schiff base to the protein rhodopsin?
ANSWER: **vitamin A** [accept **retinal**, **retinoic acid**, **isotretinoin**]

16. Note: please emphasize "named similarly" in the first line. Mutations in a protein that is *named similarly* to this protein lead to the presence of a grossly black liver due to inability to export conjugated bilirubin which is known as Dubin-Johnson syndrome. An assay for the activity of this protein uses the MDCK, or Madin-Darby Canine Kidney cell line. Another assay for the activity of this protein uses an acetyl-methoxy derivative of fluorescein, called calcein-AM. Small molecules designed to inhibit this protein include elacridar and zosuquidar which can be administered to increase cellular concentrations of substrates of this protein like paclitaxel. The calcium channel blocker verapamil is an inhibitor of this protein, which normally serves to maintain the integrity of renal and intestinal epithelia and the blood-brain barrier by pumping out xenobiotics. For 10 points, name this ABC transporter which is frequently upregulated by cancer cells to acquire drug resistance.
ANSWER: or **MDR1** or **multi-drug resistance** protein 1 [accept **p-glycoprotein** or **ABCB1**]

Speedchecks

1. The two most common congenital causes of hypo·para·thyroidism are DiGeorge syndrome and a syndrome caused by deficiency of this gene. Additional symptoms of that syndrome include polyendocrinopathy, candidiasis **("can-did-eye-uh-sis")** and ectodermal dystrophy, leading to its name of APECED or APS-1. This gene allows ectopic gene expression of tissue-restricted antigens in mTECs **("em-tecks"**). For 10 points, name this gene that allows expression of epitopes from all over the body in the thymic medulla to allow for negative selection of T cells.
ANSWER: ***AIRE*** or ***Autoimmune Regulator***

2. This drug, misoprostol and mife·pris·tone can be used to induce abortion. A predecessor to this drug was shown to cause remission of acute lymphocytic leukemia in children by Sidney Farber. That drug, aminopterin **("amino-tear-in"**), was developed by Yellapragada Subbarow. It's not 5-FU, but this drug inhibits synthesis of dTMP by thymidylate synthase by blocking production of tetrahydrofolate. For 10 points, name this drug that inhibits dihydrofolate reductase
ANSWER: **Methotrexate** or **MTX**

3. Mutations of this protein in mice are characteristic of the 'Scrufy' mouse line, which is why this protein is sometimes called scurfin. A deficiency of this protein causes a syndrome characterized by polyendocrinopathy and enteropathy and has X-linked inheritance, leading to its name of IPEX **("eye-pecks"**) syndrome. For 10 points, name this transcription factor that regulates differentiation of regulatory T cells.
ANSWER: **Foxp3**

4. These drugs are contraindicated in the third trimester of pregnancy because of their ability to close the ductus arteriosus. The toxic metabolite NAPQI accumulates during overdoses of one of these drugs, which is treated with N-acetyl cysteine. One of these drugs combined with IVIg **("I-V-I-G")** is used to treat

a small of small-vessel vasculitis that frequently occurs in asian children called Kawasaki syndrome. For 10 points, name this class of drugs that function by inhibiting cyclooxygenase enzymes, such as aspirin.
ANSWER: **NSAIDs** or **Non-steroidal anti-inflammatory** [accept specific answers like aspirin or acetaminophen or indomethacin]

5. This protein is the chaperone for a protein whose H63D and C282Y mutations cause hemochromatosis, HFE. Patients on dialysis can develop carpal tunnel syndrome from deposition of this protein in a type of amyloidosis. For 10 points, name this protein that associates with the alpha chains of MHC Class I complexes.
ANSWER: **beta-2 microglobulin** or **B2M**