USE THE SCANTRON FOR QUESTIONS 1-45. Multiple choice/true-false/open answer: there is only one correct choice per question: 2 pts each

1. Which of the following is **NOT** one of the 3 major types stem cells?
    a. adult stem cells
    b. bone marrow cells
    c. embryonic stem cells
    d. induced pluripotent stem cells

2. Which of the following is **TRUE** regarding human embryonic stem cells?
    a. they are transient
    b. they exist in adults
    c. they cannot be reprogrammed to produce various cell types
    d. they reside in the intestinal crypt

3. Adult stem cell can be found in all of the following anatomic locations **EXCEPT**:
    a. skin
    b. heart
    c. lung
    d. gut

4. Cells that proliferate subsequent to stem cell differentiation are termed:
    a. transit amplifying cells
    b. transitionally proliferating cells
    c. pluripotent cells
    d. differentiated cells

5. Dolly the cloned sheep was produced by:
    a. inserting an embryonic egg cell nucleus into an enucleated adult sheep skin (body) cell
    b. inserting an adult skin (body) cell nucleus into an enucleated adult sheep egg cell
    c. fusing a female egg cell with a male sperm cell
    d. fusing a male sperm cell with an enucleated adult female skin (body) cell

6. Induced Pluripotent Stem Cells (iPSCs) are created by:
    a. inserting specific genes into adult somatic cells
    b. fusing adult somatic cells
    c. inserting embryonic nuclei into adult somatic cells
    d. fusing an adult cell nucleus with an embryonic cell

7. Adult stem cells that undergo somatic mutations may do all of the following EXCEPT:
    a. replicate / propagate
    b. give rise to mutant daughter cells
    c. undergo malignant transformation
    d. differentiate into normal cells

8. Cancer stem cells can be identified by which of the following:
    a. specific cell surface markers
    b. their genetic make-up
    c. their association with other kinds of cells
    d. their appearance

9. The two signaling pathways that promote cancer stem cell self renewal are:
    a. Hippo and Campus
    b. Wnt and Hedgehog
    c. MAPK and PI3K
    d. Akt and NFkB

10. In the absence of Wnt, all of the following are true for beta-catenin **EXCEPT**:
    a. it is serially phosphorylated
    b. it is ubiquitinated
    c. it is degraded in the protosome
    d. it is available to associate with TCF/LEF

11. Intestinal (colon) stem cells require which of the following to keep from differentiating?
    a. hepatocyte growth factor
    b. fibroblast growth factor
    c. epidermal growth factor
    d. keritinocyte growth factor

12. Which of the following is **FALSE** regarding the sequence of events after hedgehog binds Patched?
    a. Inhibition of Smoothened is relieved
    b. Sufu and PKA release Gli
    c. Gli target genes are transcribed
    d. Gli target genes are repressed

13. All of the following are true regarding the PML-RARα fusion protein **EXCEPT**:
    a. it induces the self-renewal of Acute Promyelociyic Leukemia (APL) cells
    b. it blocks differentiation
    c. it can be blocked by high pharmacological levels of retinoic acid (RA)
    d. it can be blocked by physiological levels of retinoic acid (RA)

14. The basement membrane can be breached by:
    a. collagens
    b. nidogens
    c. proteases
    d. laminins

15. Loss of the basement membrane is associated with:
    a. a high probability of developing distant metastases
    b. a low probability of developing distant metastases
    c. tumor withdrawal
    d. extravasation

16. Epithelial Mesenchymal Transition (EMT) requires all of the following **EXCEPT:**
    a. the breaking of adherens junctions
    b. the up-regulation of E-cadherin
    c. the down-regulation of N-cadherin
    d. vascularization

17. The process of intravasation requires all of the following **EXCEPT**:
    a. attachment of tumor cells to the exterior ('stromal') surface of a blood vessel
    b. attachment of tumor cells to the internal ('luminal') surface of a blood vessel
    c. secretion of proteases
    d. degradation of extracellular matrix (ECM)

18. Lymph nodes, lung, liver, brain and bone marrow are frequent sites of metastasis because:
    a. tumor cells have affinity for those sites
    b. these are the first places reached by tumor cells
    c. these are the sites of tiny capillaries
    d. none of these sites are frequent sites of metastasis

19. Extravasation requires all of the following **EXCEPT**:
    a. tissue parenchyma
    b. platelets
    c. proteases
    d. tumor cell proliferation

20. All of the following are true about Angiogenesis **EXCEPT:**
    a. it is the process of forming new blood vessels
    b. it is not essential for metastasis
    c. it occurs through 'sprouting'
    d. it occurs because tumors must be within the diffusion limit of oxygen to survive

21. Components of the Angiogenic Switch include all of the following **EXCEPT:**
    a. angiostatin
    b. E-cadherin
    c. VEGF
    d. anti- and pro-angiogenic factors

22. The VEGF Receptors are:
    a. steroid receptors
    b. cytokine receptors
    c. tyrosine kinase receptors
    d. G-protein coupled receptors

23. Under hypoxic conditions, which of the following is **FALSE?**
    a. prolyl-4-hydroxylase is activated
    b. HIFα is activated
    c. the VEGF gene is transcribed
    d. Angiogenesis is activated

24. Tumors can be vascularization by all of the following **EXCEPT**:
    a. Angiogenesis
    b. Vascoxia
    c. Vascular Mimicry
    d. Vasculogenesis

25. Which of the following tumor imaging modalities requires ionizing radiation?
    a. PET
    b. CT (CAT)
    c. MRI
    d. X-rays

26. Which of the following is **NOT** part of the pre-metastatic niche?
    a. white blood cells
    b. bone marrow cells
    c. exosomes
    d. tumor cells

27. An MMP inhibitor used to treat metastatic cancer is:
    a. vinblastin
    b. tamoxifen
    d. doxycycline
    e. cisplatin

28. Anti-angiogenic drugs used to treat metastatic cancer include all of the following **EXCEPT:**
    a. avastin (bevacizumab)
    b. sunitinib
    c. gefitinib
    d. cabozantinib

29. Which of the following regarding Adaptive Immunity is **FALSE?**
    a. it is mediated by neutrophils
    b. it requires the activity of Antigen Presenting Cells (APCs)
    c. it is characterized by immunological memory
    d. it helps kill cancer cells

30. Activated cytotoxic T-Cells kill cancers by all of the following mechanisms **EXCEPT**:
    a. responding to tumor antigens 'presented' by APCs and T-Helper Cells
    b. phagocytosis of cancer cells
    c. secrete peroforins that poke holes in tumor cell membranes
    d. secrete granzymes that digest and kill tumor cells

31. Tumor cells can 'evade' detection by the immune system through:
    a. killing immune cells
    b. staying in areas of the body where immune cells can't go
    c. pretending to be immune cells
    d. expressing checkpoint inhibitors on their cell membranes

32. Which ligand/receptor pair prevents T-cell activation?
    a. MHCI /MHC II
    b. PD-1/PDL-1
    c. EGF/EGFR
    d. VEGF/VEGFR

33. The T-cell receptor targeted by Ketruda or Opdivo is:
    a. MHCII
    b. EGFR
    c. PD-1
    d. VEGFR

34. The overall strategy for drug development includes all of the following EXCEPT:
    a. identifying a molecular target
    b. optimization and formulation
    c. pre-clinical studies
    d. innoculation

35. A 'lead compound' in drug development is the:
    a. optimized compound
    b. final version of the compound
    c. first active compound identified
    d. formulated compound

36. Pharmacokinetics is:
    a. what the body does to the drug
    b. what solubility characterizes the drug
    c. what the drug does to the body
    d. what the melting point is of the drug

37. Pharmacodynamics is:
    a. what the body does to the drug
    b. what solubility characterizes the drug
    c. what the drug does to the body
    d. what the melting point is of the drug

38. Which of the following is **TRUE** regarding a drug's Therapeutic Window?
    a. it is the dosage range that provides maximal results with minimal side effects
    b. it is the maximal dosage tolerable by the body
    c. it is the minimal effective dose
    d. it is the dose with the highest cytostatic and cytotoxic effects

39. All of the following are TRUE regarding Phase I Clinical Trials **EXCEPT:**
    a. they measure safety
    b. they typically enroll <100 participants
    c. they are intended to determine the minimal tolerable dose (MTD) of a drug
    d. they are intended to determine the maximal tolerable dose (MTD) of a drug

40. The typical Phase I study design is termed a:
    a. 3 + 3 design
    b. 2 + 2 design
    c. preliminary design
    d. experimental design

41. All of the following are true regarding of Phase II Clinical Trials **EXCEPT**:
    a. they test drug efficacy
    b. they determine the drug response in specific types of cancer
    c. they determine whether a drug can replace the standard of care
    d. they extend our knowledge of the drug's pharmacogenomics and pharmacokinetics profiles

42. Which of the following is **NOT** part of a blinded clinical trial design?
    a. patients are randomized into experimental drug and placebo groups
    b. the patient does not know if he/she is receiving the drug or placebo
    c. the patient knows if he/she is receiving the drug or placebo
    d. neither the patient nor clinician/researcher knows whether the patient is receiving the drug or placebo

43. The primary endpoint of a Phase II Clinical Trials is:
    a. tumor size reduction
    b. the drug tolerability at a specific dose
    c. a molecular correlate (biomarker)
    d. patient survival

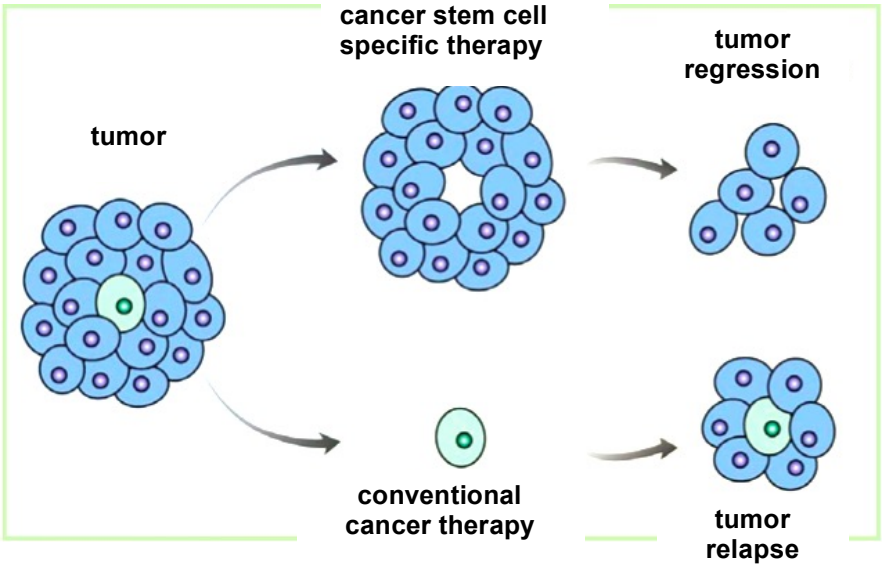
44. The 'gold standard' endpoint of a Phase III Clinical Trial is:
    a. increased progression-free survival
    b. increased overall survival
    c. disease stabilization
    d. tumor regression

45. A limiting factor in deciding whether a drug can replace standard of care is:
    a. limited accessibility
    b. high cost
    c. high percentages of Grade 3 or 4 adverse events
    d. the length of time it takes to gain FDA approval

ESSAY (10 pts): Choose **ONE of the following essays** to answer out of the two provided. Do not answer both, I will only grade the first one.

ESSAY ONE

Explain what's going on in this diagram:

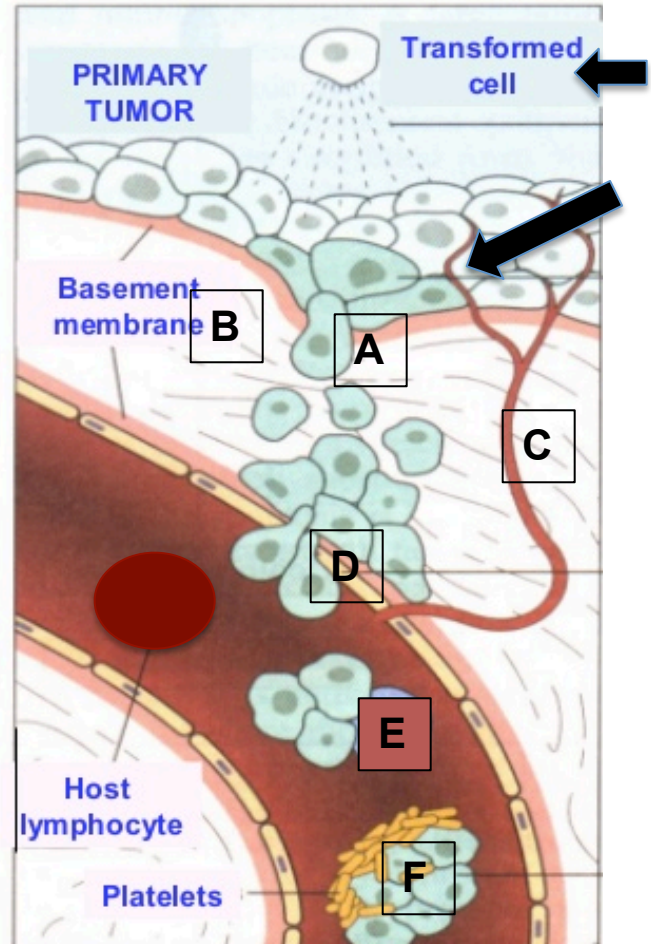


a. Which cell(s) is/are the cancer stem cell (s)? Describe some properties of these cells that make them unique.

b. What are the other non-stem cells? How did they originate?

c. How do the differences between cancer stem and cancer non-stem cells affect therapeutic strategies and efficiencies (refer to the figure to answer)?

ESSAY TWO



As shown, this initial TRANSFORMED CELL has grown into a sizable PRIMARY TUMOR. This tumor is now in the process of METASTASIS.

For each of the labeled areas - A, B, D, D, E and F - describe the composition (what is it) and what aspect of metastasis it represents (is this a specific step in metastasis? What are the cells doing in this step? How is this step contributing to the metastatic process?

BE SPECIFIC!