DIVIDE AND CONQUER

How to Win:

The player who has the highest number of cells wins the game. If there is a tie, the player with the highest number of ATPs wins the game. For a beginners game, the first player to divide their cell wins.

Physical Components:

- Cell boards (3x the number of players in the game, or 1x for a beginners game)
- Stack of enzyme cards
- Stack of event cards
- Stack of multiplier cards
- Small tokens
    - **Black**: Glucose
    - Red: Proteins
    - Yellow: Lipids
    - White: Amino Acids
    - Brown: Acetyl CoA
    - Orange: Pyruvate
- Poker chips: ATP (white - 1, blue - 5, red - 20, green - 50)

Setting Up the Game:

1. Each player starts with one cell board, on which are drawn cellular metabolic pathways (Figure 1).
2. Each player gets two enzyme cards on each of the pyruvate dehydrogenase and Citric Acid Cycle/Oxidative Phosphorylation boxes. Each player gets one enzyme card on every other rounded metabolic pathway box. (Figure 2)
3. Each player gets 10 ATPs at the start of the game.
4. Each player places 5 lipids in their membrane lipid stock and 5 proteins in their structural protein box. (Figure 3)
5. Common stocks of glucose, lipids, and proteins are placed between the players.
6. The oldest player (whose cells have undergone the most divisions) goes first. Play proceeds from this player in a clockwise fashion.

Figure 1

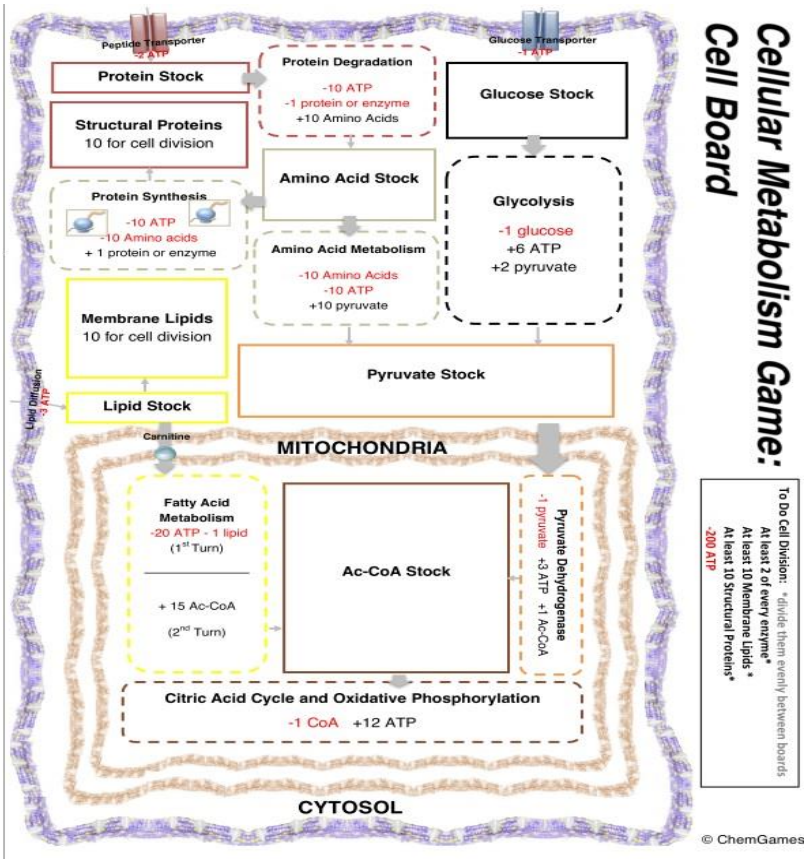


Figure 2

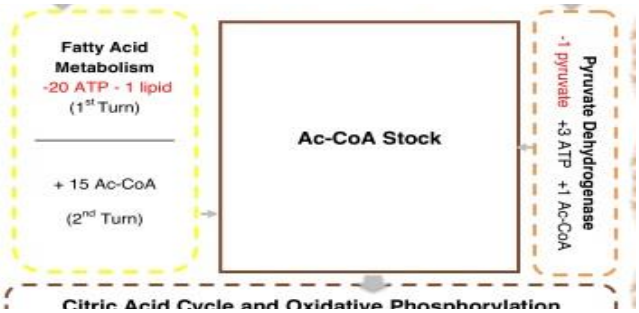
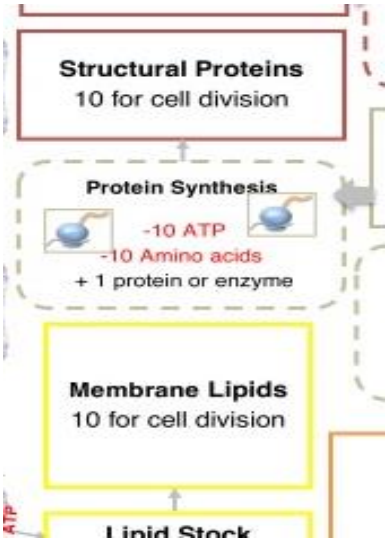


Figure 3



Gameplay - Turn Phases: Execute one turn for each of your cells!

1) **Turn over global event card:** All players are subject to the global event and take that action immediately.
2) **Reactivate enzymes and gain products:** You begin a turn by flipping over any occupied enzymes (except the enzyme for the lipid metabolic pathway, which is occupied for two turns). When an occupied enzyme is flipped over, the function of the enzyme, which is written in the rounded metabolic pathway box beneath it, is completed. Gain any molecules that are marked with a + sign in the box. *(For instance, if you put one glucose molecule into the glycolysis box last turn, you will gain 6 ATP and 2 pyruvates for glycolysis).*
   On your first turn, no enzymes are occupied, so you should not be able to perform this phase.
3) **Import food (glucose / lipids / protein):** You can choose to place a number of tokens for glucose, lipids or proteins inside your cell. However, each of the number of glucose tokens, lipid tokens or protein tokens inside a cell may never be higher than 10. Membrane lipids and structural proteins count towards that limit. The import of lipids, glucose, and protein costs energy (ATP). If you do not have enough ATP tokens to pay the cost of importing a molecule, you may not import it. *(If you had 5 ATP, you could not import 2 lipids, since that would cost 6 ATP. You could, however, import 1 lipid and 1 protein, or 2 proteins and 1 glucose, or any other combination of materials that would cost 5 ATP or less)*
4) **Use enzymes and pay starting materials:** Flip any number of activated enzymes into the occupied state. You must be able to pay the resources required by the metabolic

pathway box to flip the enzyme into the occupied state immediately. Return the tokens to the general stockpile. If you decide to make protein, you must dedicate it to a specific box at this point, but you cannot use it until your next turn.

5) **Division:** If you meet all the requirements written on the game board, you may divide your cell by paying 200 ATP. To do this, you must have on your cell board:
    a) 2 or more enzymes in every metabolic pathway box
    b) 10 structural proteins in the membrane protein box
    c) 10 membrane lipids in the membrane lipid box

    After you have paid the 200 ATP, take a new cell board and divide all of your enzymes and tokens evenly between both boards. If you have an odd number of metabolic tokens or enzymes in any box, you may choose which cell receives the additional enzyme or token. *(If you decided to make a membrane protein or enzyme in phase 4 this turn and it is the last requirement you would need to divide your cell, you may not divide your cell this turn, as the protein is not finished yet. You may divide next turn.)*

After All Players Take Turns: Draw one event card after a round of the game. This card will affect **all players** next turn.

Rules:

- If you decide to use an enzyme in a metabolic process, you must be able to pay the cost that turn. You do not receive the products until the next turn. You cannot pay for an enzyme in one turn with products from a metabolic process that you are using in the same turn. *(I.e. if you end your first turn by putting one glucose molecule into glycolysis, you may not also use pyruvate dehydrogenase in your first turn, even though glycolysis will generate the pyruvate necessary to use that enzyme. You may do so next turn.)*
- Enzymes are dedicated to their pathways. You may never transfer an enzyme from one metabolic pathway box to a different metabolic pathway box. You may, however, take an enzyme and turn it bioavailable protein by exchanging the enzyme card for a protein token and degrading the protein. You may not take a protein token and exchange it for an enzyme card.

- Membrane lipids can be obtained by transferring lipids from the lipid stockpile into the membrane lipid box. Structural proteins may not be obtained by transferring proteins from the protein stockpile into the structural protein box. They must be generated from amino acids. You may choose to use a protein from your structural protein box for protein degradation or use a lipid from your membrane lipid stock for fatty acid metabolism.
- Whenever you divide a cell, you may raise your fist and say loudly: “The cell is mine”. If you do so, you gain 5 ATP in each of your cells.

Definitions [Representation in Game]:

- Metabolic pathway: refers to a sequence of biochemical reactions catalyzed by enzymes [represented by rounded boxes and arrows on the board].
- Enzyme: refers to a protein catalyst that can accelerate a biochemical reaction by lowering the activation energy barrier [represented by enzyme cards; there are two states, available and occupied].
- ATP (Adenosine triphosphate): is equivalent to the "molecular unit of currency" of cellular processes [represented by poker chips].
- Lipids, Glucose, Protein: the three different sources of food for the cell. Lipids come from fat, Glucose is a sugar which comes from carbohydrates and protein is protein [represented by small yellow, black, and red tokens, respectively].
- Amino Acid: little molecules that proteins are made of [represented by small white token].
- Pyruvate: a molecule that is an intermediate for many metabolic pathways and can be turned into Ac-CoA [represented by small orange token].
- Ac-CoA (Acetyl Co-enzyme A): a molecule that is used to produce lots of ATP in mitochondria [represented by small brown token]

Alternate Modes of Gameplay and Expansions

1) With a large group of people and a game master/teacher:

- Players can team up into groups of two or three.
- Each turn, all players/teams **independently** and **simultaneously** determine which actions they will take and execute them. Possible actions are governed by the rules of the standard game.
- Two or three players/a single team can designate themselves as “judges” to ensure that all actions taken are legal according to the game rules, to manage the fact that all players act simultaneously.
- Each cell can import up to three of each of glucose, lipid, and protein per turn.
- After every round of play, the game master draws event cards that will globally affect the players (as in the standard game).

This mode of gameplay is designed for use in a classroom, where a teacher may want to use the game to introduce concepts from metabolism in a more structured fashion. It can also be used if a large group wants to play together.

2) Possible expansions to add more interactions to the game:

Signaling Proteins:
Players may produce proteins that increase or decrease the amount of a certain food resource (glucose, protein, lipid) that all players are allowed to take up.

Apoptosis:
Players may produce a protein which will cause one cell to die. For every other cell in the game, the owner of that cell flips a coin. If all coins flipped are heads, the cell that produced the protein dies. If only one coin is tails, the cell for which tails has been flipped dies. If several coins show tails, keep flipping until one coin has shown tails more often than any other coin. The cell for which that coin was flipped dies.

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