**Template MC Question**

LG06, Task 2

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| **Title** | **Avidity-mediated targeting** |
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| **Introduction/**  **Description** | **Avidity is the combinatory effect of multiple affinities between a substrate and its ligands. Cooperative binding occurs when molecules interact through multiple binding sites simultaneously. Platform building occurs when a molecule interacts with a point source where there is a high concentration of a molecular species that retains the binding partner.** |
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| **Question** | **Which of the following situations is an outlier?** |

Choice sheet - As the material will serve as a study aid, please put the correct answer randomly as one of the 4 choices.

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| **Choice 1** | **The change in predominant phosphatidylinositides from PI(3)P to PI(3,5)P2** |
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| **Choice 2** | **Ubiquinated EGFR is degraded instead of getting recycled.** |
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| **Choice 3** | **Clathrin – AP2 interaction leading to clathrin pit building.** |
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| **Choice 4** | **The recruitment of FYVE-domain containing myotubularin lipid phosphatases onto endosomes.** |

Feedback sheet – Please **label** the feedback to the choices as “CORRECT” or “INCORRECT”. Provide detailed feedback to explain why the choice was correct or incorrect.

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| **Feedback Choice 1** | **Incorrect: The change in predominant phosphatidylinositides are mediated by kinases which require local high density of interactions for targeting. This is an example of platform building.** |
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| **Feedback Choice 2** | **Correct. On the limiting membrane of the MVB, ubiquitinated EGFR interacts with Hrs and STAM1/2 complex, the main component of ESCRT-0. Hrs and STAMs recognize EGFR-Ub via their UBDs and retain the receptor in the limiting membrane of MVBs, thus preventing its recycling. The ubiquitinated EGFR is ultimately packaged into ILVs. The EGFR is both monoubiquitinated at multiple sites and polyubiquitinated via Lys63, providing interaction surfaces for multiple UBDs in the ESCRT components, thus increasing the avidity of weak ubiquitin–UBD interactions and the efficiency of sorting into ILVs. This interaction is receptor recognition and has nothing to do with platform building.** |
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| **Feedback Choice 3** | **Incorrect: The transient interactions between AP2 and clathrin retains clathrin at the surface of the membrane. This is an example of platform building.** |
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| **Feedback Choice 4** | **Incorrect. The FYVE-domain is a modular phosphoinositide binding domain and such proteins commonly contain several domains, such that multi-binding of phosphoinositides and membrane effector proteins can synergize to enhance the affinity. This is an example of platform building.** |