

Learning group 07

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Title	Membrane organization
Introduction/ Description	Endosomal membrane composition changes throughout the maturation from early to late endosome. Rab proteins are important for membrane identity during this process. Rab5 is a key player in membrane organization.
Question	Imagine an experiment where a point mutation is introduced to the <i>Rab5</i> gene that causes bound GTP to be refractory to hydrolyzation, resulting in a permanent GTP association without the possibility to hydrolyze to a GDP state. What are the consequences for the endosomal system?

Choice 1	The ordered transition from early to late endosome is not possible, which leads to an accumulation of early endosomes with large stable patches of Rab5.
Choice 2	The GTP-bound form of Rab5 accumulates on the membrane of the early endosome. This enhances the recruitment of HOPS complex and promotes Rab conversion.
Choice 3	The endosomal process is halted at the stage of early endosomes. Infection by Semiliki Forest Virus, which depends on low pH for uncoating, is therefore impaired.

Feedback Choice 1	CORRECT: GTP bound Rab5 recruits HOPS complex which stabilizes Rab7GTP in wild type cells. This represses Rab5 leading to a rapid disassembly and loss of Rab5 from the endosome membrane. In the mutant, GTP bound Rab5 can not dissociate from the membrane and Rab conversion cannot be completed in an ordered fashion.
Feedback Choice 2	INCORRECT: GTP-bound Rab5 accumulates on the endosome membrane. This leads to an increased recruitment of HOPS complexes. However, Rab5 cannot hydrolyze and dissociate from the membrane. This leads to the stable accumulation of Rab5 on the membrane that is unable to progress in maturation.
Feedback Choice 3	INCORRECT: The Semiliki Forest Virus uncoates in the early endosome, triggered by a decrease in pH of the early endosome. It is therefore expected to still be able to infect the cell, since many features of the early endosome including pH are still similar to an unperturbed wildtype endosome.