<Barresi13e, Further Development_c04_08>

Endosome Internalization: Morphogen Gradients Can Be Created by Literally Passing from One Cell to Another

The type and number of receptors that a cell displays at its cell surface represent its potential for response. Endocytosis is one mechanism used to eliminate a receptor at the membrane. Recent studies are revealing that internalization of ligand-receptor complexes into membrane-bound vesicles called endosomes is a common mechanism in paracrine signaling. When Wnt binds to its receptors, the β-catenin destruction complex binds to the receptor, and the entire complex (including the receptor and its bound Wnt) is internalized in endosomes (Figure 1; Taelman et al. 2010; Niehrs 2012). This process removes the complex, targets it for degradation, and enables the survival of β-catenin. The internalization of the signaling complex appears to be critical for the accumulation of β-catenin, and proteins that aid in this endocytosis (such as R-spondins; see Figure 4.28) make the Wnt pathway more efficient (Ohkawara et al. 2011). Similarly, Hedgehog-Patched complexes and FGF-FGFR complexes are also internalized in endosomes and targeted for degradation, a process that is required for proper limb development (Briscoe and Thérond 2013; Handschuh et al. 2014; Hsia et al. 2015).

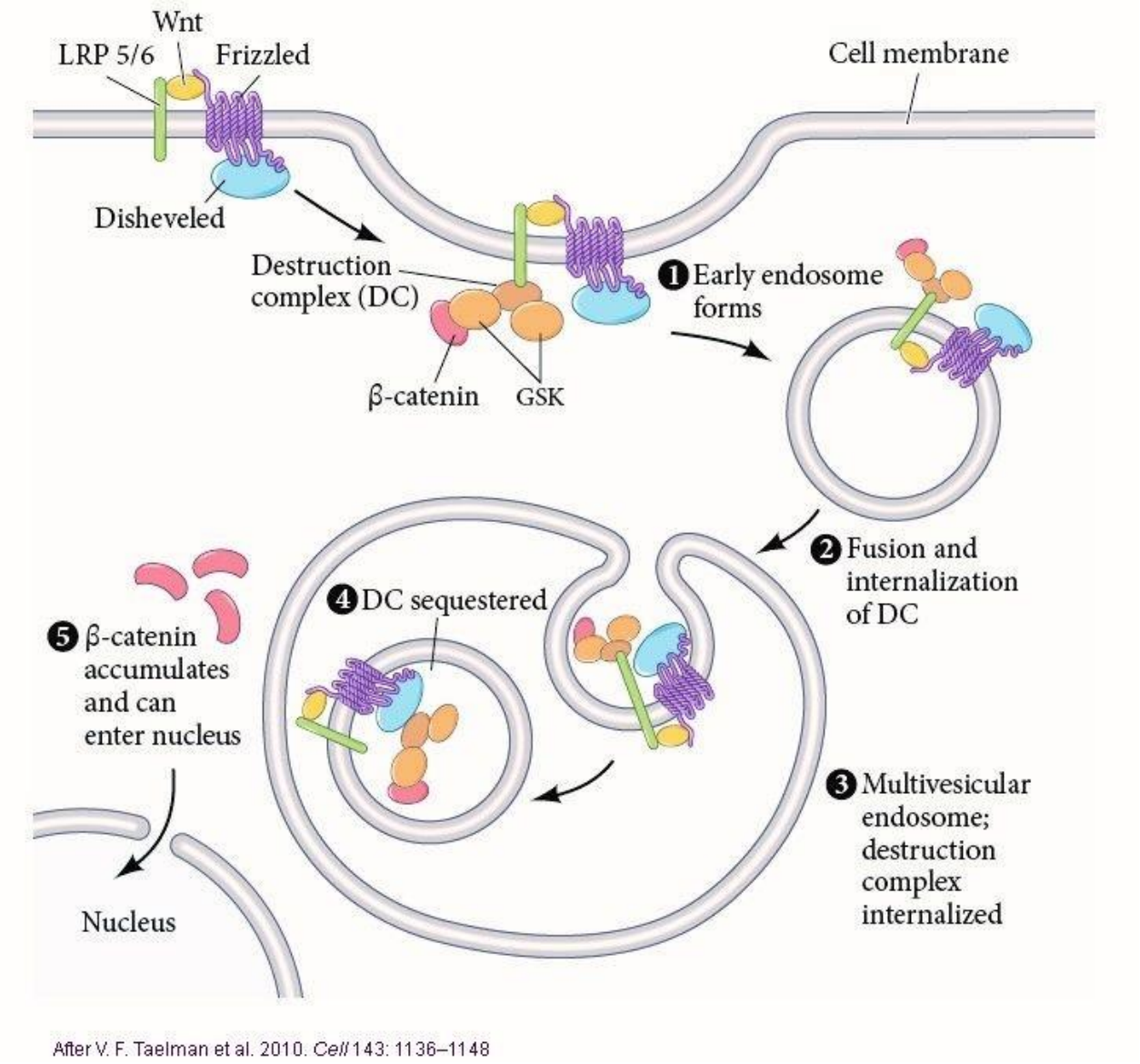

Figure 1 A Wnt pathway: packaging the β-catenin destruction apparatus into endosomes. A major mechanism for separating β-catenin from enzymes that would otherwise destroy it is to package the complex in membrane-bound vesicles called endosomes. When Wnt binds to Frizzled, Frizzled can bind the destruction complex (DC); the entire complex (including the bound Wnt and its receptor) is internalized, allowing β-catenin to accumulate rather than being degraded. (After Taelman et al. 2010.)