Wnt3a nanodisks promote ex vivo expansion of hematopoietic stem and progenitor cells - DTU Orbit (28/12/2018)

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**Background:** Wnt proteins modulate development, stem cell fate and cancer through interactions with cell surface receptors. Wnts are cysteine-rich, glycosylated, lipid modified, two domain proteins that are prone to aggregation. The culprit responsible for this behavior is a covalently bound palmitoleoyl moiety in the N-terminal domain.

**Results:** By combining murine Wnt3a with phospholipid and apolipoprotein A-I, ternary complexes termed nanodisks (ND) were generated. ND-associated Wnt3a is soluble in the absence of detergent micelles and gel filtration chromatography revealed that Wnt3a co-elutes with ND. In signaling assays, Wnt3a ND induced β-catenin stabilization in mouse fibroblasts as well as hematopoietic stem and progenitor cells (HSPC). Prolonged exposure of HSPC to Wnt3a ND stimulated proliferation and expansion of Lin- Sca-1+ c-Kit+ cells. Surprisingly, ND lacking Wnt3a contributed to Lin- Sca-1+ c-Kit+ cell expansion, an effect that was not mediated through β-catenin.

**Conclusions:** The data indicate Wnt3a ND constitute a water-soluble transport vehicle capable of promoting ex vivo expansion of HSPC.