

Drugging a stem cell compartment using wnt3a protein as a therapeutic.

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Public Summary:

The therapeutic potential of Wnt proteins has long been recognized but challenges associated with in vivo stability and delivery have hindered their development as drug candidates. By exploiting the hydrophobic nature of the protein we provide evidence that exogenous Wnt3a can be delivered in vivo if it is associated with a lipid vesicle. Recombinant Wnt3a associates with the external surface of the lipid membrane; this association stabilizes the protein and leads to prolonged activation of the Wnt pathway in primary cells. We demonstrate the consequences of Wnt pathway activation in vivo using a bone marrow engraftment assay. These data provide validation for the development of WNT3A as a therapeutic protein.

Scientific Abstract:

The therapeutic potential of Wnt proteins has long been recognized but challenges associated with in vivo stability and delivery have hindered their development as drug candidates. By exploiting the hydrophobic nature of the protein we provide evidence that exogenous Wnt3a can be delivered in vivo if it is associated with a lipid vesicle. Recombinant Wnt3a associates with the external surface of the lipid membrane; this association stabilizes the protein and leads to prolonged activation of the Wnt pathway in primary cells. We demonstrate the consequences of Wnt pathway activation in vivo using a bone marrow engraftment assay. These data provide validation for the development of WNT3A as a therapeutic protein.

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