Delta-1 or Delta-like 1, Delta-like 3, Delta-like 4, *etc.* Upon ligand binding, Notch receptors are activated by serial cleavage events involving members of the ADAM protease family, as well as an intramembranous cleavage regulated by the gamma secretase presinilin. The result is a translocation of the intracellular domain of Notch to the nucleus, where it transcriptionally activates downstream genes.

A "Notch agonist" as used herein includes a molecule that stimulates a Notch activity in a cell by at least about 10%, at least about 20%, at least about 30%, at least about 50%, at least about 70%, at least about 90%, at least about 100%, at least about 3-fold, 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, 200-fold, 500-fold, 1000-fold or more, relative to a level of a Notch activity in the absence of the Notch agonist. As is known in the art, Notch activity can be determined by, for example, measuring the transcriptional activity of Notch, by a 4xwtCBF1-luciferase reporter construct described by Hsieh *et al.* (*Mol. Cell. Biol.* 16:952-959, 1996, incorporated herein by reference).

In certain embodiments, the Notch agonist is selected from: Jagged-1, Delta-1 and Delta-like 4, or an active fragment or derivative thereof. In certain embodiments, the Notch agonist is DSL peptide (Dontu *et al.*, *Breast Cancer Res.*, 6:R605-R615, 2004), having the amino acid sequence CDDYYYGFGCNKFCRPR (SEQ ID NO:~~36~~ 30). The DSL peptide (ANA spec) may be used at a concentration between 10 μM and 100 nM, or at least 10 μM and not higher than 100 nM. In certain embodiments, the final concentration of Jagged-1 is about 0.1-10 μM; or about 0.2-5 μM; or about 0.5-2 μM; or about 1 μM.

In certain embodiments, any of the specific Notch agonist referenced herein, such as Jagged-1, Jagged-2, Delta-1 and Delta-like 4 may be replaced by a natural, synthetic, or recombinantly produced homologs or fragments thereof that retain at least about 80%, 85%, 90%, 95%, 99% of the respective Notch agonist activity, and/or homologs or fragments thereof that share at least about 60%, 70%, 80%, 90%, 95%, 97%, 99% amino acid sequence identity as measured by any art recognized sequence alignment software based on either a global alignment technique (*e.g.*, the Needleman–Wunsch algorithm) or a local alignment technique (*e.g.*, the Smith–Waterman algorithm).

The sequences of the representative Notch agonists referenced herein are represented in SEQ ID NOs. 28 - 35.

The Notch agonist may be added to the culture medium every 1, 2, 3, or 4 days during the first 1-2 weeks of culturing the stem cells.