

What is claimed is:

1. A nucleic acid comprising a nucleotide sequence encoding a chimeric Notch polypeptide comprising, from N-terminal to C-terminal and in covalent linkage:
 - a) an extracellular domain comprising a binding agent that specifically binds to an antigen;
 - b) one or more proteolytic cleavage sites; and
 - c) an intracellular domain comprising a transcriptional regulator,
 wherein binding of the binding agent to the antigen induces cleavage of the Notch polypeptide at the one or more proteolytic cleavage sites, thereby releasing the intracellular domain and the transcriptional regulator, and wherein said transcriptional regulator comprises a DNA binding domain of human origin and a transactivation domain of human origin; and wherein said transactivation domain is selected from the group consisting of RelA (p65), YAP, WWTR1(TAZ), CREB3(LZIP), and MyoD.
2. A nucleic acid as described in claim 1, wherein said binding agent comprises an antibody.
3. A nucleic acid as described in claim 2, wherein said antibody is selected from the group consisting of scFv, bispecific antibody, nanobody, or bite.
4. A nucleic acid as described in claim 3, wherein said transcriptional regulator is a transcriptional activator.
5. A nucleic acid as described in claim 3, wherein said transcriptional regulator is a transcriptional repressor.
6. A nucleic acid as described in claim 1, wherein said transcriptional regulator is from the HNF transcriptional regulator family.
7. A nucleic acid as described in claim 6, wherein said transcriptional regulator is HNF1 alpha or HNF1 beta.

8. A recombinant vector comprising the nucleic acid of any one of claims 1 to 7.
9. A host cell transformed with the nucleic acid of any one of claims 1 to 7.
10. The host cell of claim 9, wherein the cell is a macrophage.
11. The host cell of claim 10, wherein the macrophage is derived from monocytes.
12. A method of making a chimeric Notch polypeptide comprising a transcriptional regulator wherein said transcriptional regulator comprises a DNA binding domain of human origin comprising culturing a host cell of claim 9.
13. A chimeric Notch polypeptide comprising a humanized transcriptional regulator encoded by the nucleic acid of any one of claims 1 to 7.
14. A chimeric Notch polypeptide of claim 13, wherein said humanized transcriptional regulator is from the HNF transcriptional regulator family.
15. A chimeric Notch polypeptide of claim 14, wherein said humanized transcriptional regulator comprises HNF1 alpha or HNF1 beta.
16. Use of a chimeric Notch polypeptide comprising a humanized transcriptional regulator in the preparation of a medicament for treating disease in a patient in need of said treatment, wherein the chimeric Notch polypeptide is a Notch 2 or Notch 3 polypeptide.
17. Use according to claim 16 wherein the humanized transcriptional regulator is selected from the HNF1 transcriptional regulator family.
18. A use according to claim 16 or 17, wherein said disease is cancer.