CLAIMS

What is claimed is:

1. An isolated polypeptide comprising a targeting moiety and a C-terminus catalytic domain of NPP1.

2. The polypeptide of Claim 1, wherein said catalytic domain is a pyrophosphatase or phosphodiesterase domain of NPP1.

3. The polypeptide of Claim 1, wherein said polypeptide is a recombinant protein.

4. The polypeptide of Claim 1, wherein said targeting moiety is chemically linked to said catalytic domain of NPP1.

5. The polypeptide of Claim 1, wherein said catalytic domain of NPP1 comprises A205 through L591 of SEQ ID NO:1.

6. The polypeptide of Claim 5, wherein said catalytic domain of NPP1 comprises P99 through L591 of SEQ ID NO:1.

7. The polypeptide of Claim 5, wherein said catalytic domain of NPP1 comprises A205 through D925 of SEQ ID NO: 1.

8. The polypeptide of Claim 5, wherein said catalytic domain of NPP1 comprises P99 through D925 of SEQ ID NO: 1.

9. The polypeptide of Claim 8, wherein said polypeptide is a consecutive fragment of the polypeptide having the amino acid sequence of P99 through D925 of SEQ ID NO:1 and containing at least the amino acid resides A205 through L591 of SEQ ID NO:1.

10. The polypeptide of Claim 5, wherein said targeting moiety is a peptide comprising at least four negatively charged amino acid residues.

11. The polypeptide of Claim 5, wherein said targeting moiety is a peptide comprising between about five and about fifteen negatively charged amino acid residues.

12. The polypeptide of Claim 5, wherein said negatively charged amino acid residues comprise at least one aspartic acid or glutamic acid.

13. The polypeptide of Claim 5, wherein said negatively charged amino acid residues comprise at least four aspartic acid residues.

14. The polypeptide of Claim 5, wherein said negatively charged amino acid residues comprise at least four glutamic acid residues.

15. The polypeptide of Claim 5, wherein said negatively charged amino acid residues comprise eight consecutive aspartic acid residues.

16. The polypeptide of Claim 5, wherein said targeting moiety is fused to either N-terminus or C-terminus of said catalytic domain of NPP1.

17. The polypeptide of Claim 5, wherein said targeting moiety is fused to N-terminus and C-terminus of said catalytic domain of NPP1.

18. The polypeptide of Claim 12, wherein said polypeptide further comprises a polypeptide linker between said targeting moiety and said catalytic domain of NPP1.

19. The polypeptide of Claim 1, wherein said polypeptide further comprises an Fc region of an immunoglobulin.

20. The polypeptide of Claim 1, wherein said polypeptide further comprises a signal peptide.

21. The polypeptide of Claim 1, wherein said polypeptide forms a homodimer.

22. The polypeptide of Claim 1, wherein said polypeptide protein is a monomer.

23. An isolated nucleic acid encoding the polypeptide of Claim 1.

24. A replication or expression vector carrying the isolated nucleic acid of Claim 23.

25. A host cell transformed with the replication or expression vector according to Claim 23.

26. The host cell of Claim 25, wherein said host cell is selected from the group consisting of CHO cell, HEK293 cell, or COS cell.

27. The host cell of Claim 20, wherein said host cell is an avian tumor cell.

28. A transgenic animal producing the polypeptide of Claim 1.

29. The transgenic animal of Claim 28, wherein said transgenic animal is mammalian or avian.

30. A method producing said polypeptide of Claim 1 by an avian cell comprising culturing an avian cell transfected with at least one expression vector comprising a transcription unit having a nucleotide sequence encoding said polypeptide of Claim 1 operably linked to a promoter and a transcriptional terminator, and wherein the cultured avian cell produces said polypeptide.

31. A method for producing said polypeptide of Claim 1 in an egg of a chicken, the method comprising:

(a) providing an avian leukosis viral vector comprising a nucleic acid sequence encoding said polypeptide, and a promoter operably linked to said sequence, wherein said promoter drives expression of the encoding sequence in the chicken oviduct;

(b) introducing said vector into chicken stage X embryonic cells;

(c) incubating said embryonic cells under conditions conducive to hatching live chicks;

(d) nurturing growth of a mature chimeric chicken from said chicks;

(e) mating said chimeric chicken, either naturally or via artificial insemination, with a non-transgenic chicken;

(f) identifying a transgenic chicken by screening the progeny of step (e) for germ line incorporation of the protein encoding sequence; and

(g) mating the transgenic progeny with non-transgenic chickens to produce eggs containing the exogenous protein.

32. A method of treating a disorder in a subject in need thereof comprising administering an effective amount of a pharmaceutical composition comprising the polypeptide of Claim 1.

33. The method of claim 32, wherein said subject is a mammal.

34. The method of claim 33, wherein said mammal is a human.

35. The method of Claim 32, wherein said disorder is arterial calcification, insulin resistance, hypophosphatemic rickets, or ossification of posterior longitudinal ligament of spine.

36. The method of Claim 35, wherein said disorder is arterial calcification.

37. The method of Claim 36, wherein the treatment reduces calcification in the artery.

38. The method of Claim 36, wherein the arterial calcification is generalized arterial calcification of infancy.

CLAIMS

What is claimed is:

1. An isolated NPP1 fusion protein, comprising an NPP1 component, a targeting moiety, and an Fc region of an immunoglobulin, wherein a) the NPP1 component comprises the cysteine-rich region and the C-terminus catalytic domain of NPP1, b) the targeting moiety and the Fc region are each located C-terminally to the NPP1 component, and c) the isolated NPP1 fusion protein has NPP1 enzymatic activity.

2. The NPP1 fusion protein of claim 1, wherein said NPP1 enzymatic activity is pyrophosphatase activity, phosphodiesterase activity or pyrophosphatase and phosphodiesterase activity.

3. The NPP1 fusion protein of claim 1, wherein said fusion protein is a recombinant protein.

4. The NPP1 fusion protein of claim 1, wherein said targeting moiety is chemically linked to said catalytic domain of NPP1.

5. The NPP1 fusion protein of claim 1, wherein said NPP1 component consists of P99 through D925 of SEQ ID NO: 1.

6. The NPP1 fusion protein of claim 5, wherein said targeting moiety is a peptide comprising at least four negatively charged amino acid residues.

7. The NPP1 fusion protein of claim 5, wherein said targeting moiety is a peptide comprising between about five and about fifteen negatively charged amino acid residues.

8. The polypeptide NPP1 fusion protein of claim 7, wherein said negatively charged amino acid residues comprise about eight consecutive aspartic acid or glutamic acid residues.

9. The NPP1 fusion protein of claim 7, wherein said negatively charged amino acid residues comprise at least four aspartic acid residues.

10. The NPP1 fusion protein of claim 7, wherein said negatively charged amino acid residues comprise at least four glutamic acid residues.

11. The NPP1 fusion protein of claim 7, wherein said negatively charged amino acid residues comprise eight consecutive aspartic acid residues.

12. The NPP1 fusion protein of claim 5, wherein said targeting moiety is fused to the C-terminus of said catalytic domain of NPP1.

13. The NPP1 fusion protein of claim 5, wherein said Fc region is fused to the C-terminus of said catalytic domain of NPP1.

14. The NPP1 fusion protein of claim 1, wherein said fusion protein further comprises a polypeptide linker between said targeting moiety and said catalytic domain of NPP1.

15. The NPP1 fusion protein of claim 1, wherein said fusion protein further comprises a signal peptide.

16. The NPP1 fusion protein of claim 1, wherein said fusion protein forms a homodimer.

17. The NPP1 fusion protein of claim 1, wherein said fusion protein is a monomer.

18. An isolated nucleic acid encoding the NPP1 fusion protein of claim 1.

19. A replication or expression vector carrying the isolated nucleic acid of claim 18.