

- 5 a) the amino acid sequence ranging from the asparagine (N) residue at position 21 of SEQ ID NO: 1 to the proline (P) residue at position 242 of SEQ ID NO: 1, wherein the serine residue at position 100 is substituted by a phenylalanine residue (S100F), and further comprising at least one mutation selected from the group consisting of:
- the threonine residue at position 36 is substituted by a tyrosine residue (T36Y),
 - the glutamine residue at position 131 is substituted by a phenylalanine residue (Q131F),
 - 10 - the threonine residue at position 36 is substituted by a tryptophan residue (T36W),
 - the threonine residue at position 36 is substituted by a phenylalanine residue (T36F), and
 - the histidine residue at position 56 and the glycine residue at position 112 are both substituted by a cysteine residue (H56C and G112C),
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- b) an amino acid sequence having at least 80% of identity with a sequence defined in a), provided that said polypeptide is an agonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138,
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- c) a fragment of a sequence defined in a) or b), provided that said polypeptide is an agonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138.
- 25 **3.** A mutated IL-34 polypeptide comprising, or consisting of, an amino acid sequence selected from the group consisting of:
- a) the amino acid sequence ranging from the asparagine (N) residue at position 21 of SEQ ID NO: 1 to the proline (P) residue at position 242 of SEQ ID NO: 1, and comprising at least one mutation selected from the group consisting of:
- 30 - the serine residue at position 100 is substituted by an aspartic acid residue (S100D), and

- the glutamine residue at position 131 is substituted by an arginine residue (Q131R),
 - b) an amino acid sequence having at least 80% of identity with a sequence defined in a), provided that said polypeptide is an antagonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138, and
 - c) a fragment of a sequence defined in a) or b), provided that said polypeptide is an antagonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138.
4. A fusion protein consisting of the mutated IL-34 polypeptide according to claim 1 or 2 fused to a heterologous polypeptide.
5. The fusion protein according to claim 4, wherein the mutated IL-34 polypeptide is fused to an Fc region.
6. A fusion protein consisting of the mutated IL-34 polypeptide according to claim 3 fused to a heterologous polypeptide.
7. The fusion protein according to claim 6, wherein the mutated IL-34 polypeptide is fused to an Fc region.
8. An isolated, synthetic or recombinant nucleic acid encoding the mutated IL-34 polypeptide according to any one of claims 1 to 3, or encoding the fusion protein according to any one of claims 4 to 7.
9. A vector comprising the nucleic acid according to claim 8.
10. A host cell comprising the nucleic acid according to claim 8 and/or the vector according to claim 9.
11. Use of the mutated IL-34 polypeptide according to any one of claims 1 to 3, the fusion protein according to any one of claims 4 to 7, the nucleic acid according to claim 8, or the vector according to claim 9, for the manufacture of a medicament.

- 12.** Use of the mutated IL-34 polypeptide according to claim **1** or **2**, or the fusion protein according to claim **4** or **5**, for the manufacture of a medicament for use as an agonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138.
- 5 **13.** Use of the mutated IL-34 polypeptide according to claim **1** or **2**, the fusion protein according to claim **4** or **5**, a nucleic acid encoding said mutated IL-34 polypeptide or said fusion protein, or a vector comprising said nucleic acid, for the manufacture of a medicament for inducing immune tolerance in a patient in need thereof.
- 10 **14.** Use of the mutated IL-34 polypeptide according to claim **1** or **2**, the fusion protein according to claim **4** or **5**, a nucleic acid encoding said mutated IL-34 polypeptide or said fusion protein, or a vector comprising said nucleic acid, for the manufacture of a medicament for preventing or reducing transplant rejection in a patient in need thereof.
- 15 **15.** Use of the mutated IL-34 polypeptide according to claim **1** or **2**, the fusion protein according to claim **4** or **5**, a nucleic acid encoding said mutated IL-34 polypeptide or said fusion protein, or a vector comprising said nucleic acid, for the manufacture of a medicament for preventing or treating neurodegenerative diseases, autoimmune diseases, unwanted immune responses against therapeutic proteins, or allergies in a patient in need thereof.
- 20 **16.** Use of the mutated IL-34 polypeptide according to claim **3**, or the fusion protein according to claim **6** or **7**, for the manufacture of a medicament for use as an antagonist of a ligand of at least one receptor selected from the group consisting of CSF-1R, PTP- ζ and CD138.
- 25 **17.** Use of the mutated IL-34 polypeptide according to claim **3**, the fusion protein according to claim **6** or **7**, a recombinant nucleic acid encoding said mutated IL-34 polypeptide or said fusion protein, or a vector comprising said nucleic acid, for the manufacture of a medicament for the treatment of cancer or of a bone disease involving abnormal proliferation in a patient in need thereof.

- 18.** An *in vitro/ex vivo* method of obtaining a population of immunosuppressive macrophages comprising culturing a population of monocytes with a medium comprising the mutated IL-34 polypeptide according to claim **1** or **2**.
- 19.** A pharmaceutical composition or medicament comprising the mutated IL-34 polypeptide according to any one of claims **1** to **3**, the fusion protein according to any one of claims **4** to **7**, the nucleic acid according to claim **8**, or the vector according to claim **9**, with at least one pharmaceutically acceptable excipient, and optionally further comprising at least one sustained-release matrix such as a biodegradable polymer.