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(54) Title: PEPTIDES TARGETING CKIT AS A THERAPEUTIC AGENT AND METHODS OF USING THE SAME

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 /SCFpeptide_mod/C/C/39     46   51   56
                      LPSHCWISEMVSQLSDSLED                                  SEQ ID NO: 3
/SCFP-CA-BestFit/C/C/39     46   51   56
                      LPSHCWISEMVRQLSDSLRD                                  SEQ ID NO: 2
           /SCFP/C/C/39     46   51   56
                      LPSHCWISEMVVQLSDSLTD                                  SEQ ID NO: 1
           /2E9W/C/C/1    6    11   16   21   26   31   36   41   46   51   56   61
                      EGICRNRVTNNVKDVTKLVANLPKDYMITLKYVPGMDVLPSHCWISEMVVQLSDSLTDLLDKFS
                                                                            SEQ ID NO: 74
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FIG. 1

(57) Abstract: The present technology provides SCF peptides designed to specifically target cKit, delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (e.g., SCF peptides) for delivery of therapeutic payloads to cells expressing cKit, as well as methods of using the same for treating various diseases including cancer, autoimmune disorders, and gastrointestinal disorders.

WO 2024/191848 A2

PEPTIDES TARGETING CKIT AS A THERAPEUTIC AGENT AND METHODS OF USING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/489,666, filed March 10, 2023, which is incorporated herein by reference in its entirety.

SEQUENCE LISTING INCORPORATED BY REFERENCE

[0002] This application contains an ST.26 compliant Sequence Listing, which is submitted concurrently in xml format via Patent Center and is hereby incorporated by reference in its entirety. The .xml copy, created March 8, 2024, is named 134554-8013WO00 Sequence Listing.xml and is 97,000 bytes in size.

BACKGROUND

[0003] The cKit gene encodes a receptor tyrosine kinase, also known as CD117, which has an N-terminal extracellular region with five immunoglobulin-like domains, a transmembrane region, and an intracellular tyrosine kinase domain at the C-terminus. Upon activation by its cytokine ligand, stem cell factor (SCF), cKit phosphorylates multiple intracellular proteins that are important for the proliferation, differentiation, migration, and apoptosis of many cell types and thereby plays a critical role in hematopoiesis, melanogenesis, and gastrointestinal motility. Disruptions in the cKit/SCF interaction have been linked to a variety of diseases, including cancer, autoimmune disorders, and gastrointestinal disorders. Existing therapies targeting cKit suffer from low efficacy and off-target effects. The present technology describes the use of a peptide as a cellular specific therapeutic agent for the targeted delivery of peptide therapeutics that specifically target the cKit/SCF binding surface.

SUMMARY

[0004] The present technology provides SCF-derived peptides designed to specifically target cKit. The peptides may include a sequence that binds to the extracellular domain of

the cKit receptor, or to a proximal region distal to the extracellular domain, and binding of the peptides to cKit activates the receptor. The peptides can be used on delivery vehicles (e.g., nanoparticles) as guides for efficient delivery of therapeutics to cells expressing the cKit receptor, resulting in specific modulation of cKit.

[0005] In some embodiments, the peptide specifically targets cKit and comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1-73, or an amino acid sequence that is at least 80% identical to any one of SEQ ID NOs: 1-73.

[0006] In some aspects, the peptide is conjugated to one or more conditioning agents, for example, busulfan and/or saporin.

[0007] In some aspects, binding of the peptide to cKit results in altered signal transduction of cKit, for example, at least partially activating or at least partially inhibiting or blocking signal transduction of cKit.

[0008] In some embodiments, the present technology provides a delivery vehicle conjugated to the peptide provided herein.

[0009] In some aspects, the delivery vehicle is a nanoparticle.

[0010] In some aspects, the delivery vehicle further comprises a payload comprising a therapeutic agent.

[0011] In some aspects, the therapeutic agent is an RNA, a DNA, or a protein.

[0012] In some aspects, the therapeutic agent is a nucleic acid encoding a protein of interest selected from the group consisting of a transcription factor, a nuclease for gene editing, a secretion, a receptor, and an antibody or antigen-binding potion thereof.

[0013] In some embodiments, the present technology provides a pharmaceutical composition comprising the delivery vehicle provided herein.

[0014] In some embodiments, the present technology provides a method of conditioning a hematopoietic stem cell (HSC), comprising administering an effective amount of the peptide, the delivery vehicle, or the pharmaceutical composition provided herein. In some aspects, the conditioning comprises promoting division and/or expansion of the HSC.

[0015] In some embodiments, the present technology provides a method of treating a hematologic disorder in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide, the delivery vehicle, or the pharmaceutical composition provided herein.

[0016] In some aspects, the hematologic disorder is selected from the group consisting of anemia, hereditary spherocytosis, sickle cell disease (SCD), beta thalassemia, severe combined immunodeficiency (SCID), hemophilia, thrombophilia, and thrombocytopenia.

[0017] In some embodiments, the present technology provides a method of treating a disease associated with cKit in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide, the delivery vehicle, or the pharmaceutical composition provided herein.

[0018] In some aspects, the disease associated with cKit is cancer.

[0019] In some aspects, the cancer is a hematological malignancy selected from the group consisting of monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

[0020] In some aspects, the cancer is a solid tumor selected from the group consisting of lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

[0021] In some aspects, the disease associated with cKit is an autoimmune disorder selected from the group consisting of type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's disease, Graves' disease,

Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

[0022] In some aspects, the disease associated with cKit is gastrointestinal disorder selected from the group consisting of irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] FIG. 1 shows results of the initial peptide design of PEPTIDE-001 (SEQ ID NO: 1), PEPTIDE-002 (SEQ ID NO: 2), and PEPTIDE-003 (SEQ ID NO: 3) based on the extracellular domain of Kit in complex with SCF (PDB ID: 2E9W; SEQ ID NO: 74) from an algorithm with enhanced properties and parameters in accordance with the present technology.

[0024] FIGS. 2A-2C show solubility charts for peptides PEPTIDE-001 (FIG. 2A), PEPTIDE-002 (FIG. 2B), and PEPTIDE-003 (FIG. 2C) in accordance with the present technology.

[0025] FIG. 3 depicts the interaction of the C-terminal end of a SCF peptide with cKit in accordance with the present technology.

[0026] FIG. 4 shows the physiochemical properties of a representative SCF peptide that has been modified at the N-terminal end to replace LP with EE (PEPTIDE-41; SEQ ID NO: 41) in accordance with the present technology.

[0027] FIG. 5 depicts the interaction of a representative SCF peptide that has Glu/Arg mutations with cKit in accordance with the present technology. The mutation sites are shown as the dotted regions on the helical structure at the forefront of FIG. 5.

DETAILED DESCRIPTION

[0028] Described herein are peptides designed to specifically target cKit expressed on certain cells. These peptides can be employed on their own, or, alternatively, on the surface of delivery vehicles, for example, nanoparticles, for targeted delivery of cargos to the cells expressing cKit, thereby modulating cKit signaling and/or cell function via therapeutic agents

(e.g., DNA, RNA, protein) in the payload. The present technology can be used in subjects having cKit-implicated diseases including cancer, autoimmune disorders, and gastrointestinal disorders and offers several advantages, including enhanced specificity and efficacy of therapeutic agents targeting the cKit/SCF interaction; reduced off-target effects and toxicity; increased stability and shelf life of the therapeutic complex; and improved patient outcomes and quality of life for diseases linked to cKit/SCF dysfunction.

[0029] While the present technology is capable of being embodied in various forms, the description below of several embodiments is made with the understanding that the present disclosure is to be considered as an exemplification of the invention and is not intended to limit the invention to the specific embodiments illustrated. Headings are provided for convenience only and are not to be construed to limit the invention in any manner. Embodiments illustrated under any heading may be combined with embodiments illustrated under any other heading.

Definitions

[0030] The use of numerical values in the various quantitative values specified in this application, unless expressly indicated otherwise, are stated as approximations as though the minimum and maximum values within the stated ranges were both preceded by the word "about." It is to be understood, although not always explicitly stated, that all numerical designations are preceded by the term "about." It is to be understood that such range format is used for convenience and brevity and should be understood flexibly to include numerical values explicitly specified as limits of a range, but also to include all individual numerical values or sub-ranges encompassed within that range, as if each numerical value and sub-range is explicitly specified. For example, a ratio in the range of about 1 to about 200 should be understood to include the explicitly recited limits of about 1 and about 200, but also to include individual ratios, such as about 2, about 3, and about 4, and sub-ranges, such as about 10 to about 50, about 20 to about 100, and so forth. It also is to be understood, although not always explicitly stated, that the reagents described herein are merely exemplary and that equivalents of such are known in the art.

[0031] It is to be understood that such range format is used for convenience and brevity and should be understood flexibly to include numerical values explicitly specified as limits of

a range, but also to include all individual numerical values or sub-ranges encompassed within that range as if each numerical value and sub-range is explicitly specified. For example, a ratio in the range of about 1 to about 200 should be understood to include the explicitly recited limits of about 1 and about 200, but also to include individual ratios such as about 2, about 3, and about 4, and sub-ranges such as about 10 to about 50, about 20 to about 100, and so forth. It also is to be understood, although not always explicitly stated, that the reagents of the present technology are merely exemplary and that equivalents of such are known in the art. Furthermore, the term "about," as used herein when referring to a measurable value such as an amount or concentration and the like, is meant to encompass variations of 20%, 10%, 5%, 1%, 0.5%, or even 0.1% of the specified amount.

[0032] Also, the disclosure of ranges is intended as a continuous range, including every value between the minimum and maximum values recited, as well as any ranges that may be formed by such values. Also disclosed herein are any and all ratios (and ranges of any such ratios) that may be formed by dividing a disclosed numeric value into any other disclosed numeric value. Accordingly, the skilled person will appreciate that many such ratios, ranges, and ranges of ratios may be unambiguously derived from the numerical values presented herein and in all instances, such ratios, ranges, and ranges of ratios represent various embodiments of the present technology.

[0033] Compounds having therapeutic applications generated by the present technology include, but are not limited to, peptide ligands of certain receptors. Such compounds are not naturally occurring and are rather designed or otherwise generated by one or more aspects of the present technology. Such peptide ligands may be designed to allosterically and/or orthosterically bind certain receptors. Non-limiting examples of receptors include CD117/ckit (NCBI Gene ID: 3815) and CD34 (NCBI Gene ID: 97).

[0034] The "peptides" and peptoids described herein can be (a) naturally-occurring, (b) produced by chemical synthesis, (c) produced by recombinant DNA technology, (d) produced by biochemical or enzymatic fragmentation of larger molecules, (e) produced by methods resulting from a combination of methods (a) through (d) listed above, or (f) produced by any other means for producing peptides or recombinant proteins.

[0035] The term "peptide" as used herein includes any structure comprised of two or more amino acids, including chemical modifications and derivatives of amino acids. The amino acids forming all or a part of a peptide may be naturally occurring amino acids, stereoisomers and modifications of such amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically modified amino acids, constructs or structures designed to mimic amino acids, peptoids, and the like, so that the term "peptide" includes pseudopeptides and peptidomimetics, including structures which have a non-peptidic backbone. The term "peptide" also includes dimers or multimers of peptides. A "manufactured" peptide includes a peptide produced by chemical synthesis, recombinant DNA technology, biochemical, or enzymatic fragmentation of larger molecules, combinations of the foregoing or, in general, made by any other method. The term "peptide" includes peptides containing a variable number of amino acid residues, optionally with non-amino acid residue groups at the N- and C-termini, such groups including acyl, acetyl, alkenyl, alkyl, N-alkyl, amine, DBCO, or amide groups, among others.

[0036] By employing chemical synthesis, a useful means of production, it is possible to introduce various amino acids which do not naturally occur along the chain, modify the N- or C-terminus, and the like, thereby providing for improved stability and formulation, resistance to protease degradation, and the like. Non-limiting examples of chemical synthesis include solid-phase and solution-phase peptide synthesis.

[0037] The terms "bind," "binding," "complex," and "complexing," refer to all types of physical and chemical binding, reactions, complexing, attraction, chelating and the like.

[0038] The present technology includes various rationales when selecting an amino acid residue at one or more positions in the peptide ligand, one or more of which may be accounted for when designing such compounds. Rationales for features of the peptide ligand include increase or decrease Gibbs free energy, increase or decrease a Van der Waals effect, additions of one or more linkages, improving solubility, zwitterionic effect with a conjugate, positive to negative amino acid residue ratios between 4/2 and 6/2, non charged polar residue compositions of less than about 20%, aliphatic hydrophobic residues from about 40% to about 50%, aromatic hydrophobic residues and tertiary structures such as

beta sheets, location of amino acid residues to promote or inhibit pairing, serum protein corona repulsive behavior, and specific turn character.

[0039] Percent (%) amino acid sequence "identity" with respect to the sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the reference sequence for each of the peptides and/or engineered proteins after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent amino acid sequence identity may be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN, ALIGN-2 or Megalign (DNASTAR) software. Appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full-length of the sequences being compared may be determined. For example, percent amino acid sequence identity values generated using the WU-BLAST-2 computer program uses several search parameters, most of which are set to the default values. Those that are not set to default values (i.e., the adjustable parameters) are set with the following values: overlap span=1, overlap fraction=0.125, word threshold (T)=11 and scoring matrix BLOSUM62.

[0040] "Amino acids" are molecules containing an amine group, a carboxylic acid group, and a side-chain that is specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen and have the generic formula H_2N—CHR—COOH, wherein R represents a side chain group. The various α-amino acids differ in the side-chain moiety that is attached to the α-carbon. The "amino acids" of the present technology include the known naturally occurring protein amino acids, which are referred to by both their common three letter abbreviation and single letter abbreviation. See generally *Synthetic Peptides: A User's Guide*, G. A. Grant, editor, W.H. Freeman & Co., New York (1992), the teachings of which are incorporated herein by reference, including the text and table set forth at pages 11 through 24. As set forth above, the term "amino acid" also includes stereoisomers and modifications of naturally occurring protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino acids, derivatized amino acids, constructs or structures designed to mimic amino acids,

peptoids, and the like. Modified and unusual amino acids are described generally in *Synthetic Peptides: A User's Guide*, supra; Hruby et al., *Biochem. J.* 268:249-262 (1990); and Toniolo, *Int. J. Peptide Protein Res.* 35:287-300 (1990); the teachings of all of which are incorporated herein by reference.

[0041] The phrase "amino acid side chain moiety" used herein, including as used in the specification and claims, includes any side chain of any amino acid, as the term "amino acid" is defined herein. This thus includes the side chain moiety present in naturally occurring amino acids. It further includes side chain moieties in modified naturally occurring amino acids, such as glycosylated amino acids. It further includes side chain moieties in stereoisomers and modifications of naturally occurring protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino acids, derivatized amino acids, constructs, or structures designed to mimic amino acids, and the like. For example, the side chain moiety of any amino acid disclosed herein is included within the definition. A "derivative" of an amino acid side chain moiety is included within the definition of an amino acid side chain moiety.

[0042] The "derivative" of an amino acid side chain moiety includes any modification to or variation in any amino acid side chain moieties, including a modification of naturally occurring amino acid side chain moieties. By way of example, derivatives of amino acid side chain moieties include straight chain or branched, cyclic or noncyclic, substituted or unsubstituted, saturated or unsaturated, alkyl, aryl or aralkyl moieties as well as small molecule ligand conjugates.

[0043] In the peptides described herein, conventional amino acid residues have their conventional meaning as given in Chapter 2400, of the *Manual of Patent Examining Procedure,* 8th Ed. Thus, "A" is alanine; "R" is arginine; "N" is asparagine; "D" is aspartic acid; "C" is cysteine; "Q" is glutamine; "E" is glutamic acid; "G" is glycine; "H" is histidine; "I" is isoleucine; "L" is leucine; "K" is lysine; "M" is methionine; "F" is phenylalanine; "P" is proline; "S" is serine; "T" is threonine; "W" is tryptophan; "Y" is tryosine; and "V" is valine. Unless otherwise indicated, all amino acids abbreviations represent either isomer, i.e., the L-isomer, the D-isomer, or combinations thereof can be used.

[0044] An alpha (α)-amino acid has the generic formula $H_2N—C_\alpha HR—COOH$, where R is a side chain moiety and the amino group is attached to the carbon atom immediately adjacent to the carboxylate group (i.e., the α-carbon). Other types of amino acids exist when the amino group is attached to a different carbon atom. For example, beta (β)-amino acids, the carbon atom to which the amino group is attached is separated from the carboxylate group by one carbon atom, C_β. For example, α-alanine has the formula $H_2N—C_\alpha H(CH_3)—COOH$. In contrast, β-alanine has the general formula $H_2N—C_\beta H_2—C_\alpha H_2—COOH$ (i.e., 3-aminopropanoic acid).

[0045] For additional modified and unusual amino acids, see §2422 of the MPEP, particularly Table 4 at 2400-24. Additionally, "Ac" indicates N-acetyl and "NH_2" indicates an amine group, typically added on the C-terminus of a polypeptide. Accordingly, as used herein, an $—NH_2$ moiety on the C-terminus of a peptide indicates an amidated C-terminus.

[0046] A peptide or aliphatic moiety is "acylated" when an alkyl or substituted alkyl group as defined above is bonded through one or more carbonyl {—(C=O)—} groups. A peptide is most usually acylated at the N-terminus.

[0047] An "amine" includes compounds that contain an amine group ($—NH_2$).

[0048] Amino acids, including stereoisomers and modifications of naturally occurring amino acids, protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino acids, derivatized amino acids, constructs, or structures designed to mimic amino acids (peptide mimetics), and the like, including all of the foregoing, are sometimes referred to herein as "residues."

[0049] A peptide or amino acid "mimetic" is a non-amino acid molecule that mimics a peptide (a chain of amino acids) or one amino acid residue.

[0050] In some embodiments, variants of the peptide ligands of the present technology may be used. "Variants" include protein sequences having one or more amino acid additions, deletions, stop positions, or substitutions, as compared to a peptide sequence disclosed elsewhere herein.

[0051] An amino acid substitution may be a conservative or a non-conservative substitution. Variants of the peptide ligands of the present technology include those having

one or more conservative amino acid substitutions. A “conservative substitution” or “conservative amino acid substitution” involves a substitution found in one of the following conservative substitutions groups: Group 1: A, G, S, T; Group 2: E, D; Group 3: N, Q; Group 4: R, K, H; Group 5: I, L, M, V; and Group 6: F, Y, W.

[0052] Additionally, amino acids may be grouped into conservative substitution groups by similar function, chemical structure, or composition (e.g., hydrophobic with non-polar side chain, hydrophilic with polar side chain, acidic, basic, aliphatic, aromatic, positively charged, negatively charged, containing a side group such as a conjugation group, a small molecule ligand group, a cross-linking group, or a conjugation site for another molecule on its side group, or sulfur-containing). For example, an aliphatic grouping may include, for purposes of substitution, G, A, V, L, and I. Other groups including amino acids that are considered conservative substitutions for one another include: sulfur-containing: M and C; acidic: D, E, N, Q; small aliphatic, nonpolar or slightly polar residues: A, S, T, P, and G; polar, negatively charged residues and their amides: D, N, E, and Q; polar, positively charged residues: H, R, and K; large aliphatic, nonpolar residues: M, L, I, V, and C; and large aromatic residues: F, Y, and W.

[0053] Non-conservative substitutions include those that significantly affect: the structure of the peptide backbone in the area of the alteration (e.g., the alpha-helical or beta-sheet structure); the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. Non-conservative substitutions which in general are expected to produce the greatest changes in the protein's properties are those in which (i) a hydrophilic residue (e.g. S or T) may be substituted for (or by) a hydrophobic residue (e.g. L, I, F, V, or A); (ii) a C or F may be substituted for (or by) any other residue; (iii) a residue having an electropositive side chain (e.g. K, R, or H) may be substituted for (or by) an electronegative residue (e.g. E or D); or (iv) a residue having a bulky side chain (e.g. F), may be substituted for (or by) one not having a bulky side chain, (e.g. G). Additional information is found in Creighton (1984) Proteins, W.H. Freeman and Company.

[0054] To the extent any materials incorporated by reference herein conflict with the present disclosure, the present disclosure controls.

Peptides Targeting cKit

[0055] In some embodiments, provided are SCF peptides that specifically bind to cKit. These SCF peptides are designed by an artificial intelligence (AI) platform based on the wild-type (WT) sequence of SCF, which is a natural ligand for cKit. After the initial design, the platform can also be used to generate non-naturally occurring mutated SCF peptides with enhanced properties using the parameters listed in Table 1. See also FIG. 1.

Table 1. Property improvements made to cKit/SCF peptides

Enhancement	**Parameters**
Solubility	Mutation of proximal residues
	Mutation most distal 3 hydrophobic AA to E/R
	Mutation of residues with G = 0 to E/R

[0056] In some embodiments, the SCF peptide has the same sequence as wild-type (WT) SCF or a portion thereof. For example, the peptide may have an amino acid sequence of LPSHCWISEMVVQLSDSLTD (SEQ ID NO: 1). In some embodiments, the SCF peptide may have one or more mutations, deletions, insertions, or other modifications from the WT SCF sequence. Exemplary sequences of SCF peptides targeting cKit are provided in Table 2 below (natural amino acids are highlighted in bold). Solubility of these SCF peptides may be screened using https://pepcalc.com/peptide-solubility-calculator.php. See also FIGS. 2A-2C. Additionally, in some embodiments, SCF peptides (cKit-targeting peptides) can be designed by incorporating one or more unnatural amino acids and/or introducing one or more polyethylene glycol (PEG) or sarcosine (Sar) linkers at the N- and/or C-terminus. Unnatural amino acids used for the present technology can include, but are not limited to, amino-isobutyric acid (Aib) and ε-azido-Norleucine (Nle).

Table 2. Exemplary cKit/SCF peptides

SEQ ID NO:	Peptide	Sequence	Comments
1	WT	LPSHCWISEMVVQLSDSLTD	
1	PEPTIDE-001	LPSHCWISEMVVQLSDSLTD	No water solubility
2	PEPTIDE-002	LPSHCWISEMV**R**QLSDSL**R**D	Water solubility
3	PEPTIDE-003	LPSHCWISEMV**S**QLSDSL**E**D	Water solubility
4	PEPTIDE-004	LPSHCWISEM(Aib)**R**QLSDSL**R**D	Replaced Val11 with Aib
5	PEPTIDE-005	LPSHCWISEM(Aib)**S**QLSDSL**E**D	Replaced Val11 with Aib
6	PEPTIDE-006	(Aib)PSHCWISEMV**R**QLSDSL**R**D	Replaced Leu1 with Aib
7	PEPTIDE-007	(Aib)PSHCWISEMV**S**QLSDSL**E**D	Replaced Leu1 with Aib
8	PEPTIDE-008	LPSHCWISEMV**R**Q(Aib)SDSL**R**D	Replaced Leu14 with Aib
9	PEPTIDE-009	LPSHCWISEMV**S**Q(Aib)SDSL**E**D	Replaced Leu14 with Aib
10	PEPTIDE-010	LPSHCWISEMV**R**QLSDS(Aib)**R**D	Replaced Leu18 with Aib
11	PEPTIDE-011	LPSHCWISEMV**S**QLSDS(Aib)**E**D	Replaced Leu18 with Aib
12	PEPTIDE-012	(Aib)PSHCWISEM(Aib)**R**QLSDSL**R**D	Replaced Leu1 and Val11 with Aib

SEQ ID NO:	Peptide	Sequence	Comments
13	PEPTIDE-013	(Aib)PSHCWISEM(Aib)**S**QLSDSL**E**D	Replaced Leu1 and Val11 with Aib
14	PEPTIDE-014	LPSHCWISEM(Aib)**R**Q(Aib)SDSL**R**D	Replaced Val11 and Leu14 with Aib
15	PEPTIDE-015	LPSHCWISEM(Aib)**S**Q(Aib)SDSL**E**D	Replaced Val11 and Leu14 with Aib
16	PEPTIDE-016	LPSHCWISEM(Aib)**R**QLSDS(Aib)**R**D	Replaced Val11 and Leu18 with Aib
17	PEPTIDE-017	LPSHCWISEM(Aib)**S**QLSDS(Aib)**E**D	Replaced Val11 and Leu18 with Aib
18	PEPTIDE-018	(Aib)PSHCWISEMV**R**Q(Aib)SDSL**R**D	Replaced Leu1 and Leu14 with Aib
19	PEPTIDE-019	(Aib)PSHCWISEMV**S**Q(Aib)SDSL**E**D	Replaced Leu1 and Leu14 with Aib
20	PEPTIDE-020	(Aib)PSHCWISEMV**R**QLSDS(Aib)**R**D	Replaced Leu1 and Leu18 with Aib

SEQ ID NO:	Peptide	Sequence	Comments
21	PEPTIDE-021	(Aib)PSHCWISEMV**S**QLSDS(Aib)**E**D	Replaced Leu1 and Leu18 with Aib
22	PEPTIDE-022	(Aib)PSHCWISEM(Aib)**R**Q(Aib)SDSL**R**D	Replaced Leu1, Val11, and Leu14 with Aib
23	PEPTIDE-023	(Aib)PSHCWISEM(Aib)**S**Q(Aib)SDSL**E**D	Replaced Leu1, Val11, and Leu14 with Aib
24	PEPTIDE-024	(Aib)PSHCWISEM(Aib)**R**QLSDS(Aib)**R**D	Replaced Leu1, Val11, and Leu18 with Aib
25	PEPTIDE-025	(Aib)PSHCWISEM(Aib)**S**QLSDS(Aib)**E**D	Replaced Leu1, Val11, and Leu18 with Aib
26	PEPTIDE-026	LPSHCWISEM(Aib)**R**Q(Aib)SDS(Aib)**R**D	Replaced Val11, Leu14, and Leu18 with Aib
27	PEPTIDE-027	LPSHCWISEM(Aib)**S**Q(Aib)SDS(Aib)**E**D	Replaced Val11, Leu14, and Leu18 with Aib
28	PEPTIDE-028	(Aib)PSHCWISEMV**R**Q(Aib)SDS(Aib)**R**D	Replaced Leu1, Leu14, and Leu18 with Aib

SEQ ID NO:	Peptide	Sequence	Comments
29	PEPTIDE-029	(Aib)PSHCWISEMV**S**Q(Aib)SDS(Aib)**E**D	Replaced Leu1, Val11, and Leu18 with Aib
30	PEPTIDE-030	(Aib)PSHCWISEM(Aib)**R**Q(Aib)SDS(Aib)**R**D	Replaced Leu1, Vall11, Leu14, and Leu18 with Aib
31	PEPTIDE-031	(Aib)PSHCWISEM(Aib)**S**Q(Aib)SDS(Aib)**E**D	Replaced Leu1, Val11, and Leu18 with Aib
32	PEPTIDE-032	PEG-(Nle)PSHCWISEMV**R**QLSDSL**R**D	Replaced Leu1 with Nle for PEG linker
33	PEPTIDE-033	PEG-(Nle)PSHCWISEMV**S**QLSDSL**E**D	Replaced Leu1 with Nle for PEG linker
34	PEPTIDE-034	LPSHCWISEMV**R**QLSDSL**R**D(Nle)-PEG	Added Nle at C-terminus for PEG linker
35	PEPTIDE-035	LPSHCWISEMV**S**QLSDSL**E**D(Nle)-PEG	Added Nle at C-terminus for PEG linker
36	PEPTIDE-036	Sar-(Nle)PSHCWISEMV**R**QLSDSL**R**D	Replaced Leu1 with Nle for Sar linker

SEQ ID NO:	Peptide	Sequence	Comments
37	PEPTIDE-037	Sar-(Nle)PSHCWISEMV**S**QLSDSL**E**D	Replaced Leu1 with Nle for Sar linker
38	PEPTIDE-038	LPSHCWISEMV**R**QLSDSL**R**D(Nle)-Sar	Added Nle at C-terminus for Sar linker
39	PEPTIDE-039	LPSHCWISEMV**S**QLSDSL**E**D(Nle)-Sar	Added Nle at C-terminus for Sar linker
40	PEPTIDE-040	**EE**SHCWISEMV**R**QLSDSL**R**D	Replaced N-terminal LP with EE
41	PEPTIDE-041	**EE**SHCWISEMV**S**QLSDSL**E**D	Replaced N-terminal LP with EE
42	PEPTIDE-042	**EE**SHCWISEM(Aib)**R**QLSDSL**R**D	Replaced Val11 with Aib; replaced N-terminal LP with EE
43	PEPTIDE-043	**EE**SHCWISEM(Aib)**S**QLSDSL**E**D	Replaced Val11 with Aib; replaced N-terminal LP with EE
44	PEPTIDE-044	**EE**SHCWISEMV**R**Q(Aib)SDSL**R**D	Replaced Leu14 with Aib; replaced

SEQ ID NO:	Peptide	Sequence	Comments
			N-terminal LP with EE
45	PEPTIDE-045	**EE**SHCWISEMV**S**Q(Aib)SDSL**E**D	Replaced Leu14 with Aib; replaced N-terminal LP with EE
46	PEPTIDE-046	**EE**SHCWISEMV**R**QLSDS(Aib)**R**D	Replaced Leu18 with Aib; replaced N-terminal LP with EE
47	PEPTIDE-047	**EE**SHCWISEMV**S**QLSDS(Aib)**E**D	Replaced Leu18 with Aib; replaced N-terminal LP with EE
48	PEPTIDE-048	**EE**SHCWISEM(Aib)**R**Q(Aib)SDSL**R**D	Replaced Val11 and Leu14 with Aib; replaced N-terminal LP with EE
49	PEPTIDE-049	**EE**SHCWISEM(Aib)**S**Q(Aib)SDSL**E**D	Replaced Val11 and Leu14 with Aib; replaced N-terminal LP with EE
50	PEPTIDE-050	**EE**SHCWISEM(Aib)**R**QLSDS(Aib)**R**D	Replaced Val11 and Leu18 with

SEQ ID NO:	Peptide	Sequence	Comments
			Aib; replaced N-terminal LP with EE
51	PEPTIDE-051	**EE**SHCWISEM(Aib)**S**QLSDS(Aib)**E**D	Replaced Val11 and Leu18 with Aib; replaced N-terminal LP with EE
52	PEPTIDE-052	**EE**SHCWISEM(Aib)**R**Q(Aib)SDS(Aib)**R**D	Replaced Val11, Leu14, and Leu18 with Aib; replaced N-terminal LP with EE
53	PEPTIDE-053	**EE**SHCWISEM(Aib)**S**Q(Aib)SDS(Aib)**E**D	Replaced Val11, Leu14, and Leu18 with Aib; replaced N-terminal LP with EE
54	PEPTIDE-054	PEG-(Nle)**E**SHCWISEMV**R**QLSDSL**R**D	Replaced Glu1 with Nle for PEG linker
55	PEPTIDE-055	PEG-(Nle)**E**SHCWISEMV**S**QLSDSL**E**D	Replaced Glu1 with Nle for PEG linker

SEQ ID NO:	Peptide	Sequence	Comments
56	PEPTIDE-056	Sar-(Nle)**E**SHCWISEMV**R**QLSDSL**R**D	Replaced Glu1 with Nle for Sar linker
57	PEPTIDE-057	Sar-(Nle)**E**SHCWISEMV**S**QLSDSL**E**D	Replaced Glu1 with Nle for Sar linker
58	PEPTIDE-058	**EE**SHCWISE**R**V**R**QLSDSL**R**D	
59	PEPTIDE-059	**EE**SHCWISE**R**V**S**QLSDSL**E**D	
60	PEPTIDE-060	**EE**SHCWISE**R**V**RR**LSDSL**R**D	
61	PEPTIDE-061	**EE**SHCWISE**R**V**SR**LSDSL**E**D	
62	PEPTIDE-062	**EE**SHCWISE**R**V**RRR**SDSL**R**D	
63	PEPTIDE-063	**EE**SHCWISE**R**V**SRR**SDSL**E**D	
64	PEPTIDE-064	**EE**SHCWISE**E**V**R**QLSDSL**R**D	
65	PEPTIDE-065	**EE**SHCWISE**E**V**S**QLSDSL**E**D	
66	PEPTIDE-066	**EE**SHCWISE**E**V**RR**LSDSL**R**D	
67	PEPTIDE-067	**EE**SHCWISE**E**V**SR**LSDSL**E**D	
68	PEPTIDE-068	**EE**SHCWISE**E**V**RRR**SDSL**R**D	
69	PEPTIDE-069	**EE**SHCWISE**E**V**SRR**SDSL**E**D	
70	PEPTIDE-070	**EE**SHCWISE**E**V**RER**SDSL**R**D	
71	PEPTIDE-071	**EE**SHCWISE**E**V**SER**SDSL**E**D	
72	PEPTIDE-072	**EE**SHCWISE**E**V**REE**SDSL**R**D	
73	PEPTIDE-073	**EE**SHCWISE**E**V**SEE**SDSL**E**D	

[0057] N-terminal leucine (Leu or L) and proline (Pro or P) (LP) residues are exposed and do not directly interact with cKit. Thus, in some embodiments, the LP residues of SEQ ID NO: 1 or derived sequences can be replaced with two glutamic acid (Glu or E) residues to improve solubility and/or other characteristics of the SCF peptide. Alternatively, the N-terminal LR residues can be replaced with glutamic acid-arginine (ER), glutamic acid-serine (ES), arginine-arginine (RR), or serine-arginine (SR) residues. In the representative example where the LP residues are replaced with EE residues, the isoelectric point (pI, pH(I), IEP) changes from pH 5.25 to 3.27 (FIG. 2D).

[0058] In some embodiments, because the C-terminus of SCF directly interacts with cKit, the C-terminal end of the SCF peptides designed in accordance with the present technology are not conjugated (FIG. 3). Changes at the C-terminus may result in the SCF peptides' inability to bind cKit.

[0059] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) may be conjugated to one or more small molecules or conditioning agents, including, for example, busulfan, saporin, and the like. Conjugation of the peptide with small molecules and/or conditioning agents (optionally small molecule toxins or toxic agents) may be useful as a conditioning approach for *ex vivo* hematopoietic stem cell (HSC) therapies for treatment of certain blood cancers or hematologic conditions. In some embodiments, such conjugations to conditioning agents could replace or otherwise supplement CD117-antibody drug conjugate (ADC) conditioning regimens for *ex vivo* HSC therapies.

[0060] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 1-73, or an amino acid sequence that is at least about 80% identical, (e.g., at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical) to the amino acid sequence set forth in any one of SEQ ID NOs: 1-73.

[0061] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the

amino acid sequence of SEQ ID NO: 1. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 2. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 3. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 3. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 4. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 4. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 5. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 6. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 6. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 7. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 7. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 8. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 8. In some embodiments, the cKit-targeting peptide (e.g., the SCF

peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 9. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 9. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 10.

[0062] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 11. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 11. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 12. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 12. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 13. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 13. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 14. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 14. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 15. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 15. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an

amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 16. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 16. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 17. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 18. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 18. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 19. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 19. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 20. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 20.

[0063] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 21. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 21. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 22. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 22. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an

amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 23. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 23. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 24. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 24. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 25. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 25. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 26. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 26. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 27. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 27. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 28. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 28. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 29. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 29. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 30. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 30.

[0064] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 31. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 31. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 32. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 32. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 33. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 33. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 34. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 34. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 35. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 35. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 36. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 36. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 37. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 37. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 38. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 38. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 39. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 39. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 40. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 40.

[0065] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 41. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 41. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 42. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 42. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 43. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 43. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 44. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 44. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 45. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 45. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 46. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 46. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 47. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 47. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 48. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 48. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 49. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 49. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 50.

[0066] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 51. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 51. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 52. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 52. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 53. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 53. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 54. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 54. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 55. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 55. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 57. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 57. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid

sequence of SEQ ID NO: 58. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 58. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 59. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 59. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 60. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 60.

[0067] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 61. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 1. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 62. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 62. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 63. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 63. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 64. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 64. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid

sequence of SEQ ID NO: 65. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 65. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 66. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 66. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 67. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 67. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 68. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 68. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 69. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 69. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 70.

[0068] In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 71. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 71. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid

sequence of SEQ ID NO: 72. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 72. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises or consists of an amino acid sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the cKit-targeting peptide (e.g., the SCF peptide) comprises the amino acid sequence of SEQ ID NO: 73.

[0069] In some embodiments, binding of the cKit-targeting peptide (e.g., the SCF peptide) to cKit expressed on the surface of a target cell alters signal transduction of the cKit receptor (e.g., CD117), which may comprise at least partially activating (e.g., when the peptide is an agonist) cKit signaling, at least partially inhibiting or blocking (e.g., when the peptide is an antagonist) cKit signaling, or inhibiting or blocking cKit signaling.

Nanoparticles with cKit-targeting Peptides and Pharmaceutical Compositions Thereof

[0070] In some embodiments, provided are delivery vehicles (e.g., nanoparticles) for targeted delivery of payloads (e.g., DNA, RNA, protein) to cells expressing cKit. The delivery vehicles may be conjugated to the SCF peptides that specifically bind to cKit according to various embodiments disclosed herein, so that the SCF peptide will function as a targeting ligand and guide the delivery vehicles to target cells with surface expression of cKit. The payloads will then be incorporated into the target cells to achieve their modulating functions.

[0071] A delivery vehicle is a vehicle for delivering a payload (e.g., nucleic acid and/or protein payload) to a cell. Delivery vehicles can include, but are not limited to, non-viral vehicles, viral vehicles, nanoparticles (e.g., a nanoparticle that includes a targeting ligand and a core comprising an anionic polymer composition, a cationic polymer composition, and/or a cationic polypeptide composition), liposomes, micelles, water-oil-water emulsion particles, oil-water emulsion micellar particles, and multilamellar water-oil-water emulsion particles. For any of the above embodiments, a payload (e.g., DNA, RNA, protein) can be inside the particle, either covalently, bound as nucleic acid complementary pairs, or within a water phase of a particle. In some embodiments, the delivery vehicle may have a solid core

(e.g., metal particle core, quantum dot core, and the like), in which case the payload can be conjugated to (covalently bound to) the core.

[0072] In some embodiments, the delivery vehicle (e.g., nanoparticle) includes a payload. A payload can be any compound one wishes to deliver to a cell, including, for example, nucleic acids, proteins, and/or ribonucleic acid protein (RNP) complexes. The nucleic acid can be any nucleic acid, linear or circular, and can be a plasmid, a viral genome, an RNA (e.g., mRNA, guide RNA (gRNA), short interfering RNA (siRNA), short hairpin RNA (shRNA), microRNA (miRNA), and the like), a DNA, or a locked nucleic acid (LNA) molecule. In some embodiments, the payload comprises a protein of interest and/or a nucleic acid (e.g., an mRNA) that encodes a protein interest. The protein of interest can be any kind of protein, including, for example, transcription factors; nucleases for gene editing such as zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), meganucleases, transposases, clustered regularly interspaced short palindromic repeat (CRISPR)/Cas systems, base editors, prime editing systems (e.g., CRISPR/Cas nuclease-reverse transcriptase fusion proteins), and programmable addition via site-specific targeting elements (PASTE) systems (e.g., CRISPR/Cas nuclease-reverse transcriptase-integrase fusion proteins); secretion proteins such as chemokines, chemokines, and immune checkpoint inhibitors; receptors such as chimeric antigen receptors (CARs) and T cell receptors (TCRs); therapeutic proteins such as antibodies or antigen-binding portions thereof.

[0073] In some embodiments, delivery vehicles (e.g., nanoparticles) decorated with cKit-targeting peptides (SCF peptides) may actively signal the target cells, for example, by signaling gene(s) to be edited inside the target cells, to drive the cells to divide asymmetrically *in vivo* or *ex vivo*. This may result in a greater proportion of nanoparticle/payload positive cells (e.g., HSCs) when compared to a non-signaling variant. In certain of these embodiments, a secondary set of additional payloads such as miRNAs or cell division factors and their genetic encoded precursors may also be introduced in the delivery vehicles to further expand such cells or push them towards specific differentiation paths.

In some embodiments, the cKit-targeting peptides (SCF peptides) or delivery vehicle (e.g., nanoparticle) may be present in a pharmaceutical composition. In some embodiments, the pharmaceutical composition may further comprise one or more pharmaceutically acceptable carriers, excipients, preservatives, or a combination thereof. The term "pharmaceutically acceptable" carriers, excipients, and/or preservatives refers to a pharmaceutically acceptable material, composition, or vehicle that is involved in carrying or transporting a compound of interest from one tissue, organ, or portion of the body to another tissue, organ, or portion of the body. For example, the carrier or excipient may be a liquid or solid filler, diluent, excipient, solvent, or encapsulating material, or some combination thereof. Each component of the carrier or excipient must be "pharmaceutically acceptable" in that it must be compatible with the other ingredients of the formulation. It also must be suitable for contact with any tissue, organ, or portion of the body that it may encounter, meaning that it must not carry a risk of toxicity, irritation, allergic response, immunogenicity, or any other complication that excessively outweighs its therapeutic benefits. Excipients that may be included in the compositions include, for example, fillers, disintegrants, preserving agents, glidants, lubricants, wetting agents, sweetening agents, flavoring agents, and coloring agents. Such pharmaceutically acceptable excipients may be employed in the compositions to improve processability, palatability, stability, and bioavailability of the composition. Suitable excipients include water, saline, dextrose, glycerol, or the like, and combinations thereof.

[0074] In some embodiments, the pharmaceutical composition may be formulated for different routes of administration, including, for example, systemic administration and local administration. In some embodiments, the pharmaceutical composition is formulated for extracorporeal administration, intravenous administration, subcutaneous administration, intralesional administration, intralymphatic administration, intranodal administration, and/or intraperitoneal administration.

[0075] Additional information relating to targeted delivery vehicles, targeting ligands, and payloads can be found in WO 2020223705 and WO2015042585, the entire contents of each of which are incorporated by reference herein.

Methods of Treatment

[0076] In some embodiments, provided herein are methods of conditioning cells including hematopoietic stem cells (HSCs), for example, promoting HSC division and expansion, the methods comprising administering an effective amount of cKit-targeting peptides (SCF peptides), or delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (SCF peptides), according to various embodiments disclosed herein. As discussed herein, conjugation of the cKit-targeting peptides (SCF peptides) with small molecules and/or conditioning agents (e.g., small molecule toxins or toxic agents) may be useful as a conditioning approach for HSC therapies. In certain of these embodiments, the cKit-targeting peptides (SCF peptides) may be included in cell culture or *ex vivo* bioreactor medium to promote HSC divisional and expansion.

[0077] In some embodiments, provided are methods of genetically editing cells including HSCs, the methods comprising administering an effective amount of cKit-targeting peptides (SCF peptides), or delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (SCF peptides), according to various embodiments disclosed herein. Certain hematologic disorders are often caused by gene mutations. Thus, in certain of these embodiments, the cKit-targeting peptides (SCF peptides) may guide the delivery vehicles (e.g., nanoparticles) to target HSCs, and a gene editing system in the payload of the delivery vehicles may exert gene editing functions of the HSCs, so that the genetically corrected HSCs can be used therapeutically for treatment of certain hematologic disorders. The gene editing system may include any suitable systems depending on the specific need, such as ZFNs, TALENs, meganucleases, transposases, CRISPR/Cas systems, base editors, prime editing systems (e.g., CRISPR/Cas nuclease-reverse transcriptase fusion proteins), and PASTE systems (e.g., CRISPR/Cas nuclease-reverse transcriptase-integrase fusion proteins). For example, delivery vehicles of the present technology may be employed to correct E7V substitution mutations for sickle cell disease (SCD) with base editors; BCL11A knockout for SCD and beta thalassemia with prime editors and PASTE technologies (e.g., Beam, Prime, and Aera tech); and IL2Rgamma correction for severe combined immunodeficiency (SCID). See Schiroli et al., *Sci. Transl. Med.* (2017) 9, eaan0820, the teachings of which are incorporated herein by reference.

[0078] Accordingly, in some embodiments, provided are methods of treating a hematologic disorder in a subject in need thereof, the methods comprising administering to the subject a clinically effective amount or a therapeutically effective amount of cKit-targeting peptides (SCF peptides), or delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (SCF peptides), according to various embodiments disclosed herein. In some embodiments, hematologic disorders include, but are not limited to, anemia, hereditary spherocytosis, SCD, beta thalassemia, SCID, hemophilia, thrombophilia, and thrombocytopenia.

[0079] A "therapeutically effective amount" as used herein is an amount that produces a desired effect in a subject for an indication, condition, disease, or disorder. In certain embodiments, the therapeutically effective amount is an amount that yields maximum therapeutic effect. In other embodiments, the therapeutically effective amount yields a therapeutic effect that is less than the maximum therapeutic effect. For example, a therapeutically effective amount may be an amount that produces a therapeutic effect while avoiding one or more side effects associated with a dosage that yields maximum therapeutic effect. A therapeutically effective amount for a particular composition will vary based on a variety of factors, including, but not limited to, the characteristics of the therapeutic composition (e.g., activity, pharmacokinetics, pharmacodynamics, and bioavailability); the physiological condition of the subject (e.g., age, body weight, sex, disease type and stage, medical history, general physical condition, responsiveness to a given dosage, and other present medications); the nature of any pharmaceutically acceptable carriers, excipients, and preservatives in the composition; and the route of administration. One skilled in the clinical and pharmacological arts will be able to determine a therapeutically effective amount through routine experimentation, namely, by monitoring a subject's response to administration of the therapeutic composition and adjusting the dosage accordingly. A "clinically effective amount," "clinically effective concentration," or "clinically effective dose" refers to a concentration or dose of a peptide, composition, or pharmaceutical composition that is shown to be effective in clinical trials or is predicted to be effective based on early phase or pre-clinical trials. In some embodiments, a "clinically effective amount" is the same as a "therapeutically effective amount." In some embodiments, a "clinically effective amount" is higher or lower than a "therapeutically effective amount." For additional guidance, see

Remington: The Science and Practice of Pharmacy, 21st Edition, Univ. of Sciences in Philadelphia (USIP), Lippincott Williams & Wilkins, Philadelphia, PA, 2005.

[0080] Additionally, in some embodiments, provided are methods of treating a disease associated with cKit in a subject in need thereof, the methods comprising administering to the subject a clinically effective amount or a therapeutically effective amount of cKit-targeting peptides (SCF peptides), or delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (SCF peptides), according to various embodiments disclosed herein.

[0081] In some embodiments, the disease associated with cKit is cancer. In some embodiments, the cancer is a hematological malignancy or blood cancer. Non-limiting examples of blood cancers include monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

[0082] In some embodiments, the cancer is a solid tumor. Non-limiting examples of solid tumors include lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

[0083] In some embodiments, the disease associated with cKit is an autoimmune disorder. Non-limiting examples of autoimmune diseases include type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

[0084] In some embodiments, the disease associated with cKit is a gastrointestinal disorder. Non-limiting examples of gastrointestinal disorders include irritable bowel

syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

[0085] In some embodiments, the method comprises administration of at least one dose of the cKit-targeting peptides (SCF peptides). In some embodiments, the method comprises administration of multiple doses (e.g., two doses, three doses, four doses, five doses, or more than five doses) of the cKit-targeting peptides (SCF peptides).

[0086] In some embodiments, the method comprises administration of at least one dose of the targeted delivery vehicles (e.g., delivery vehicles (e.g., nanoparticles) conjugated to cKit-targeting peptides (SCF peptides)). In some embodiments, the method comprises administration of multiple doses (e.g., two doses, three doses, four doses, five doses, or more than five doses) of the targeted delivery vehicles.

[0087] In some embodiments, the cKit-targeting peptides (SCF peptides) are administered systemically. In some embodiments, the targeted delivery vehicles are administered locally. In some embodiments, the cKit-targeting peptides (SCF peptides) are administered by extracorporeal administration, intravenous administration, subcutaneous administration, intralesional administration, intralymphatic administration, intranodal administration, or intraperitoneal administration. In some embodiments, the cKit-targeting peptides (SCF peptides) are delivered preferentially to a tumor or other diseased tissue, for example, by local injection or intralesional injection.

[0088] In some embodiments, the targeted delivery vehicles are administered systemically. In some embodiments, the targeted delivery vehicles are administered locally. In some embodiments, the targeted delivery vehicles are administered by extracorporeal administration, intravenous administration, subcutaneous administration, intralesional administration, intralymphatic administration, intranodal administration, or intraperitoneal administration. In some embodiments, the targeted delivery vehicles are delivered preferentially to a tumor or other diseased tissue, for example, by local injection or intralesional injection.

[0089] In some embodiments, the cKit-targeting peptides (SCF peptides) are administered to the subject in a range of from about 0.1 mg/kg to about 30 mg/kg (dose corresponding to payload), from 0.1 mg/kg to about 10 mg/kg, from 0.1 mg/kg to about 3 mg/kg, for example, at a dose of about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 0.8 mg/kg, about 0.9 mg/kg, about 1 mg/kg, about 2 mg/kg, about 3 mg/kg, about 4 mg/kg, about 5 mg/kg, about 6 mg/kg, about 7 mg/kg, about 8 mg/kg, about 9 mg/kg, about 10 mg/kg, 15 mg/kg, about 20 mg/kg, about 25 mg/kg, or about 30 mg/kg.

[0090] In some embodiments, the targeted delivery vehicles are administered to the subject in a range of from about 0.1 mg/kg to about 30 mg/kg (dose corresponding to payload), from 0.1 mg/kg to about 10 mg/kg, from 0.1 mg/kg to about 3 mg/kg, for example, at a dose of about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 0.8 mg/kg, about 0.9 mg/kg, about 1 mg/kg, about 2 mg/kg, about 3 mg/kg, about 4 mg/kg, about 5 mg/kg, about 6 mg/kg, about 7 mg/kg, about 8 mg/kg, about 9 mg/kg, about 10 mg/kg, 15 mg/kg, about 20 mg/kg, about 25 mg/kg, or about 30 mg/kg.

[0091] In some embodiments, the cKit-targeting peptides (SCF peptides) are administered to the subject once a day or twice a day for a period of about 1 day, about 2 days, about 3 days, about 5 days, about 7 days, about 10 days, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or more than about 5 years. In some embodiments, the cKit-targeting peptides (SCF peptides) may be administered every day, every other day, 3 times a week, every third day, weekly, biweekly (i.e., every other week), every third week, monthly, every other month, every third month, every fourth month, every fifth month, every sixth month, every ninth month, every year, every 18 months, every 2 years, every 5 years, every 10 years, or every 20 years. In some embodiments, the dose regimens listed above could be repeated after a period of about 1 week, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about

9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or more than about 5 years. In some embodiments treatment is continued until disease is eliminated, until no further improvement Is achieved, or as long as the disease does not progress.

[0092] In some embodiments, the targeted delivery vehicles are administered to the subject once a day or twice a day for a period of about 1 day, about 2 days, about 3 days, about 5 days, about 7 days, about 10 days, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or more than about 5 years. In some embodiments, the targeted delivery vehicles may be administered every day, every other day, 3 times a week, every third day, weekly, biweekly (i.e., every other week), every third week, monthly, every other month, every third month, every fourth month, every fifth month, every sixth month, every ninth month, every year, every 18 months, every 2 years, every 5 years, every 10 years, or every 20 years. In some embodiments, the dose regimens listed above could be repeated after a period of about 1 week, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or more than about 5 years. In some embodiments treatment is continued until disease is eliminated, until no further improvement is achieved, or as long as the disease does not progress.

[0093] From the foregoing, it will be appreciated that specific embodiments of the invention have been described herein for purposes of illustration, but that various modifications may be made without deviating from the scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

EXAMPLES

Example 1. Initial Peptide Design

[0094] Using a proprietary AI platform, exemplary SCF peptides (SEQ ID NOs: 1-3) were designed against the cKit receptor. After the initial design, an updated version of the platform was used to design mutated SCF peptides with enhanced properties using the parameters listed in Table 1. The resulting peptides are shown in FIG. 1 and Table 2 as PEPTIDE-001 (SEQ ID NO: 1), PEPTIDE-002 (SEQ ID NO: 2), and PEPTIDE-003 (SEQ ID NO: 3). FIG. 1 also provides the sequence of the extracellular domain of Kit in complex with SCF (EGICRNRVTNNVKDVTKLVANLPKDYMITLKYVPGMDVLPSHCWISEMVVQLSDSL TDLLDKFS; SEQ ID NO: 74)

[0095] The solubility of the three resulting peptides in water was screened using https://pepcalc.com/peptide-solubility-calculator.php. Solubility results are shown in Table 3 and FIGS. 2A-2C.

Table 3. Solubility results of resulting peptides

Peptide	**Sequence**	**Solubility (H_2O)**
PEPTIDE-001	LPSHCWISEMVVQLSDSLTD	No
PEPTIDE-002	LPSHCWISEMV**R**QLSDSL**R**D	Yes
PEPTIDE-003	LPSHCWISEMV**S**QLSDSL**E**D	Yes

Example 2. Additional Peptide Design

[0096] Additional peptides (SEQ ID NOs: 4-73) were designed to incorporate both unnatural amino acids (e.g., amino-isobutyric acid (Aib) and ε-azido-norleucine (Nle)) and/or a polyethylene glycol (PEG) or sarcosine (Sar) linker. The additional peptides are shown in Table 2.

[0097] FIG. 3 depicts the interaction of the C-terminal end of a representative SCF peptide with cKit. Due to this interaction, SCF peptides that modified to include conjugation at the C-terminal end (e.g., SEQ ID NOs: 34, 35, 38, and 39) may have decreased ability to bind to cKit.

[0098] In contrast to the residues at the C-terminal end of the SCF peptides, the N-terminal LP residues are exposed and do not directly interact with cKit. FIG. 4 shows the physiochemical properties of a representative SCF peptide that has been modified at the N-

terminal end to replace LP with EE (PEPTIDE-41; SEQ ID NO: 41). As shown in FIG. 4, such modification decreased the isoeletric point (IEP) of the representative SCF peptide from pH 5.25 to 3.27. Thus, replacing the N-terminal terminal LP resides may eliminate the need for other peptides where Aib is replaced for the terminal Leu.

[0099] FIG. 5 depicts the interaction of a representative SCF peptide that has Glu/Arg mutations with cKit. The mutation sites are shown as the dotted regions on the helical structure at the forefront of FIG. 5.

Additional Embodiments:

[0100] Various embodiments of the present technology are set forth below in paragraphs [0101] to [0129]:

[0101] 1. A peptide that specifically targets cKit, wherein the peptide comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1-73, or an amino acid sequence that is at least 80% identical to any one of SEQ ID NOs: 1-73.

[0102] 2. The peptide of embodiment 1, wherein the peptide is conjugated to one or more small molecule and/or conditioning agents.

[0103] 3. The peptide of embodiment 2, wherein the conditioning agent is busulfan and/or saporin.

[0104] 4. The peptide of any one of embodiments 1-3, wherein binding of the peptide to cKit results in altered signal transduction of cKit.

[0105] 5. The peptide of embodiment 4, wherein the altered signal transduction of cKit comprises at least partially activating or at least partially inhibiting or blocking signal transduction of cKit.

[0106] 6. A delivery vehicle conjugated to the peptide of any one of embodiments 1-5.

[0107] 7. The delivery vehicle of embodiment 6, wherein the delivery vehicle is a nanoparticle.

[0108] 8. The delivery vehicle of embodiment 6 or 7, further comprising a payload comprising a therapeutic agent.

[0109] 9. The delivery vehicle of embodiment 8, wherein the therapeutic agent is an RNA, a DNA, or a protein.

[0110] 10. The delivery vehicle of embodiment 8 or 9, wherein the therapeutic agent is a nucleic acid encoding a protein of interest selected from the group consisting of a transcription factor, a nuclease for gene editing, a secretion, a receptor, and an antibody or antigen-binding potion thereof.

[0111] 11. A pharmaceutical composition comprising the peptide of any one of embodiments 1-5 or the delivery vehicle of any one of embodiments 6-10.

[0112] 12. A method of conditioning a hematopoietic stem cell (HSC), comprising administering an effective amount of the peptide of any one of embodiments 1-5, the delivery vehicle of any one of embodiments 6-10, or the pharmaceutical composition of embodiment 11.

[0113] 13. The method of embodiment 12, wherein the conditioning comprises promoting division and/or expansion of the HSC.

[0114] 14. A method of treating a hematologic disorder in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide of any one of embodiments 1-5, the delivery vehicle of any one of embodiments 6-10, or the pharmaceutical composition of embodiment 11.

[0115] 15. The method of embodiment 14, wherein the hematologic disorder is selected from the group consisting of anemia, hereditary spherocytosis, sickle cell disease (SCD), beta thalassemia, severe combined immunodeficiency (SCID), hemophilia, thrombophilia, and thrombocytopenia.

[0116] 16. A method of treating a disease associated with cKit in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide of any one of embodiments 1-5, the delivery vehicle of any one of embodiments 6-10, or the pharmaceutical composition of embodiment 11.

[0117] 17. The method of embodiment 16, wherein the disease associated with cKit is cancer.

[0118] 18. The method of embodiment 17, wherein the cancer is a hematological malignancy selected from the group consisting of monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

[0119] 19. The method of embodiment 17, wherein the cancer is a solid tumor selected from the group consisting of lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

[0120] 20. The method of embodiment 16, wherein the disease associated with cKit is an autoimmune disorder selected from the group consisting of type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

[0121] 21. The method of embodiment 16, wherein the disease associated with cKit is gastrointestinal disorder selected from the group consisting of irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

[0122] 22. Use of the peptide of any one of embodiments 1-5, the delivery vehicle of any one of embodiments 6-10, or the pharmaceutical composition of embodiment 11 for treating a hematologic disorder in a subject in need thereof.

[0123] 23. The use of embodiment 22, wherein the hematologic disorder is selected from the group consisting of anemia, hereditary spherocytosis, sickle cell disease (SCD), beta thalassemia, severe combined immunodeficiency (SCID), hemophilia, thrombophilia, and thrombocytopenia.

[0124] 24. Use of the peptide of any one of embodiments 1-5, the delivery vehicle of any one of embodiments 6-10, or the pharmaceutical composition of embodiment 11 for treating a disease associated with cKit in a subject in need thereof.

[0125] 25. The use of embodiment 24, wherein the disease associated with cKit is cancer.

[0126] 26. The use of embodiment 25, wherein the cancer is a hematological malignancy selected from the group consisting of monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

[0127] 27. The use of embodiment 25, wherein the cancer is a solid tumor selected from the group consisting of lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

[0128] 28. The use of embodiment 24, wherein the disease associated with cKit is an autoimmune disorder selected from the group consisting of type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

[0129] 29. The use of embodiment 24, wherein the disease associated with cKit is gastrointestinal disorder selected from the group consisting of irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

CLAIMS

I/We claim:

1. A peptide that specifically targets cKit, wherein the peptide comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1-73, or an amino acid sequence that is at least 80% identical to any one of SEQ ID NOs: 1-73.

2. The peptide of claim 1, wherein the peptide is conjugated to one or more small molecules and/or conditioning agents.

3. The peptide of claim 2, wherein the one or more conditioning agent is busulfan and/or saporin.

4. The peptide of any one of claims 1-3, wherein binding of the peptide to cKit results in altered signal transduction of cKit.

5. The peptide of claim 4, wherein the altered signal transduction of cKit comprises at least partially activating or at least partially inhibiting or blocking signal transduction of cKit.

6. A delivery vehicle conjugated to the peptide of any one of claims 1-5.

7. The delivery vehicle of claim 6, wherein the delivery vehicle is a nanoparticle.

8. The delivery vehicle of claim 6 or 7, further comprising a payload comprising a therapeutic agent.

9. The delivery vehicle of claim 8, wherein the therapeutic agent is an RNA, a DNA, or a protein.

10. The delivery vehicle of claim 8 or 9, wherein the therapeutic agent is a nucleic acid encoding a protein of interest selected from the group consisting of a transcription factor, a nuclease for gene editing, a secretion, a receptor, and an antibody or antigen-binding potion thereof.

11. A pharmaceutical composition comprising the peptide of any one of claims 1-5 or the delivery vehicle of any one of claims 6-10.

12. A method of conditioning a hematopoietic stem cell (HSC), comprising administering an effective amount of the peptide of any one of claims 1-5, the delivery vehicle of any one of claims 6-10, or the pharmaceutical composition of claim 11.

13. The method of claim 12, wherein the conditioning comprises promoting division and/or expansion of the HSC.

14. A method of treating a hematologic disorder in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide of any one of claims 1-5, the delivery vehicle of any one of claims 6-10, or the pharmaceutical composition of claim 11.

15. The method of claim 14, wherein the hematologic disorder is selected from the group consisting of anemia, hereditary spherocytosis, sickle cell disease (SCD), beta thalassemia, severe combined immunodeficiency (SCID), hemophilia, thrombophilia, and thrombocytopenia.

16. A method of treating a disease associated with cKit in a subject in need thereof, comprising administering to the subject a clinically effective amount or a therapeutically effective amount of the peptide of any one of claims 1-5, the delivery vehicle of any one of claims 6-10, or the pharmaceutical composition of claim 11.

17. The method of claim 16, wherein the disease associated with cKit is cancer.

18. The method of claim 17, wherein the cancer is a hematological malignancy selected from the group consisting of monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

19. The method of claim 17, wherein the cancer is a solid tumor selected from the group consisting of lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

20. The method of claim 16, wherein the disease associated with cKit is an autoimmune disorder selected from the group consisting of type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

21. The method of claim 16, wherein the disease associated with cKit is gastrointestinal disorder selected from the group consisting of irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

22. Use of the peptide of any one of claims 1-5, the delivery vehicle of any one of claims 6-10, or the pharmaceutical composition of claim 11 for treating a hematologic disorder in a subject in need thereof.

23. The use of claim 22, wherein the hematologic disorder is selected from the group consisting of anemia, hereditary spherocytosis, sickle cell disease (SCD), beta thalassemia, severe combined immunodeficiency (SCID), hemophilia, thrombophilia, and thrombocytopenia.

24. Use of the peptide of any one of claims 1-5, the delivery vehicle of any one of claims 6-10, or the pharmaceutical composition of claim 11 for treating a disease associated with cKit in a subject in need thereof.

25. The use of claim 24, wherein the disease associated with cKit is cancer.

26. The use of claim 25, wherein the cancer is a hematological malignancy selected from the group consisting of monoclonal B cell lymphocytosis, multiple myeloma, myeloid neoplasm, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, acute lymphoid leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blast crisis chronic myelogenous leukemia (bcCML), B cell acute lymphoid leukemia (B-ALL), T cell acute lymphoid leukemia (T-ALL), T cell lymphoma, and B cell lymphoma.

27. The use of claim 25, wherein the cancer is a solid tumor selected from the group consisting of lung cancer, breast cancer, liver cancer, stomach cancer, colon cancer, rectal cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, esophageal cancer, melanoma, bone cancer, pancreatic cancer, skin cancer, uterine cancer, ovarian cancer, testicular cancer, cancer of the thyroid gland, cancer of the adrenal gland, bladder cancer, and glioma.

28. The use of claim 24, wherein the disease associated with cKit is an autoimmune disorder selected from the group consisting of type 1 diabetes, lupus, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Addison's

disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, and celiac disease.

29. The use of claim 24, wherein the disease associated with cKit is gastrointestinal disorder selected from the group consisting of irritable bowel syndrome (IBS), Crohn's disease, celiac disease, ulcerative colitis, gas, hemorrhoids, diverticulosis, diverticulitis, gastroesophageal reflux (GER), and gastroesophageal reflux disease (GERD).

/SCFpeptide_mod/C/C/39 46 51 56
LPSHCWISEMVSQLSDSLED
SEQ ID NO: 3
/SCFP-CA-BestFit/C/C/39 46 51 56
LPSHCWISEMVRQLSDSLRD
SEQ ID NO: 2
/SCFP/C/C/39 46 51 56
LPSHCWISEMVVQLSDSLTD
SEQ ID NO: 1
/2E9W/C/C/1 6 11 16 21 26 31 36 41 46 51 56 61
EGICRNRVTNNVKDVTKLVANLPKDYMITLKYVPGMDVLPSHCWISEMVVQLSDSLTDLLDKFS
SEQ ID NO: 74

FIG. 1

N-terminus | Sequence | C-terminus | AA code used

LPSHCWISEMVVQLSDSLTD **SEQ ID NO: 1** | single-le | **Calculate!**

Disulphide connectivity

Show abbreviations | 20 standard amino acids | modified amino acids | unusual amino acids

Sequence submission

Single letter code: LPSHCWISEMVVQLSDSLTD **Get a quotation**

Sequence interpretation

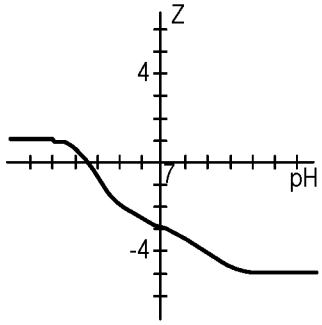
Single letter code: NH2- LPSHCWISEM VVQLSDSLTD -COOH

Triple letter code: NH2- Leu – Pro – Ser – His – Cys – Trp – Ile – Ser – Glu – Met – Val – Val – Gln – Leu – Ser – Asp – Ser – Leu – Thr – Asp -COOH

Physiochemical properties

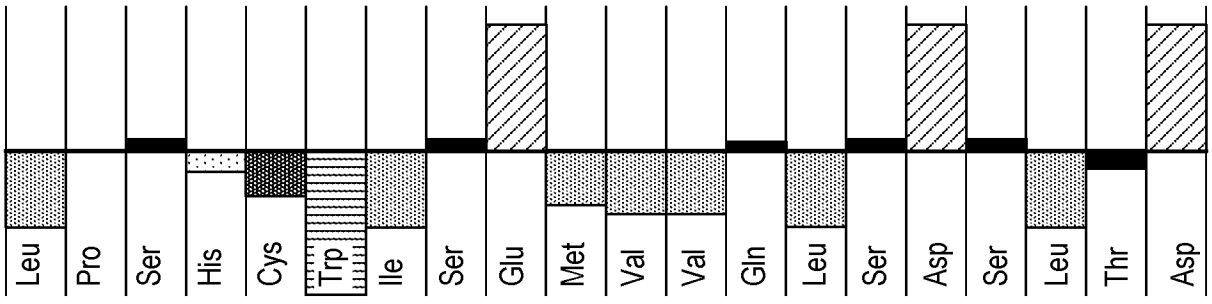
Number of residues:	20	
Molecular weight:	2260.55 g/mol	*notes on MW*
Extinction coefficient:	5690 $M^{-1}cm^{-1}$	*notes on Ext. Coefficient*
Iso-electric point:	pH 3.54	*notes on pI*
Net charge at pH 7:	-3	*notes on net charge*
Estimated solubility:	Poor water solubility.	*notes on solubility*

Net charge vs pH



Hydropathy

Hopp & Woods



Top is hydrophilic

Bottom is hydrophobic

Color codes: Acidic | Aromatic | Basic | Aliphatic | Polar | Cysteine

FIG. 2A

N-terminus	Sequence	C-terminus	AA code used	
	LPSHCWISEMVRQLSDSLRD **SEQ ID NO: 2**		single-le	Calculate!
	Disulphide connectivity			

Show abbreviations | 20 standard amino acids | modified amino acids | unusual amino acids

Sequence submission

Single letter code: LPSHCWISEMVRQLSDSLRD

Get a quotation

Sequence interpretation

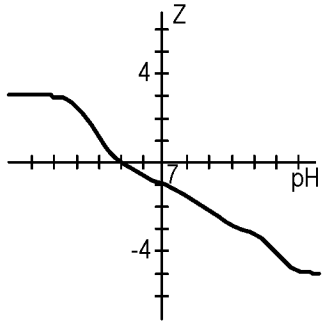
Single letter code: NH2- LPSHCWISEM VRQLSDSLRD -COOH

Triple letter code: NH2- Leu – Pro – Ser – His – Cys – Trp – Ile – Ser – Glu – Met – Val – Arg – Gln – Leu – Ser – Asp – Ser – Leu – Arg – Asp -COOH

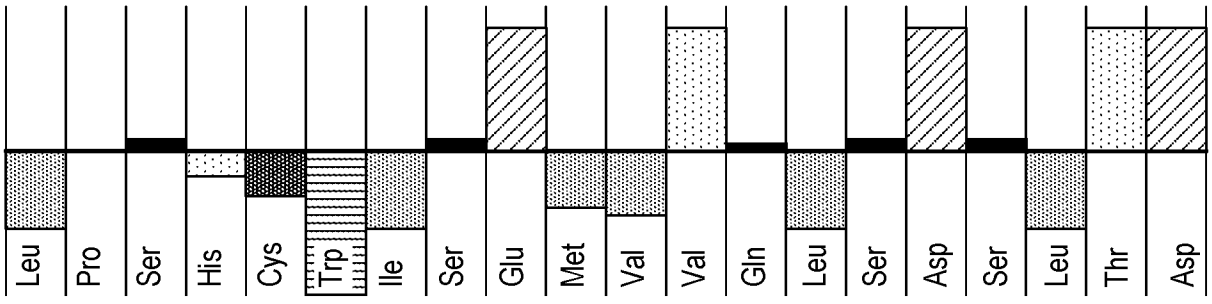
Physiochemical properties

Number of residues:	20	
Molecular weight:	2372.68 g/mol	*notes on MW*
Extinction coefficient:	5690 $M^{-1}cm^{-1}$	*notes on Ext. Coefficient*
Iso-electric point:	pH 5.23	*notes on pI*
Net charge at pH 7:	-1	*notes on net charge*
Estimated solubility:	Good water solubility.	*notes on solubility*

Net charge vs pH



Hydropathy **Hopp & Woods**



Top is hydrophilic
Bottom is hydrophobic
Color codes: Acidic Aromatic Basic Aliphatic Polar Cysteine

FIG. 2B

Sequence submission

Single letter code: LPSHCWISEMVSQLSDSLED **SEQ ID NO: 3**

Get a quotation

Sequence interpretation

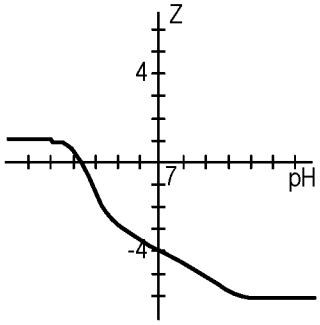
Single letter code: NH2- LPSHCWISEM VSQLSDSLED -COOH

Triple letter code: NH2- Leu – Pro – Ser – His – Cys – Trp – Ile – Ser – Glu – Met – Val – Ser – Gln – Leu – Ser – Asp – Ser – Leu – Glu – Asp -COOH

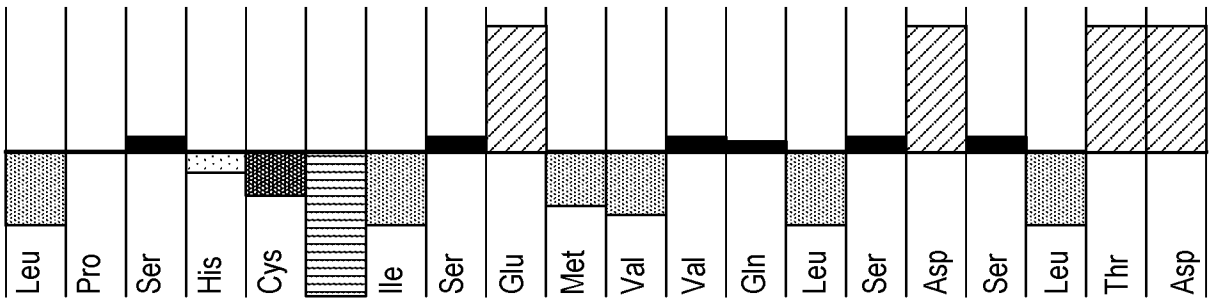
Physiochemical properties

Number of residues:	20	
Molecular weight:	2276.5 g/mol	*notes on MW*
Extinction coefficient:	5690 $M^{-1}cm^{-1}$	*notes on Ext. Coefficient*
Iso-electric point:	pH 3.42	*notes on pI*
Net charge at pH 7:	-4	*notes on net charge*
Estimated solubility:	Good water solubility.	*notes on solubility*

Net charge vs pH



Hydropathy **Hopp & Woods**



Top is hydrophilic

Bottom is hydrophobic

Color codes: Acidic Aromatic Basic Aliphatic Polar Cysteine

FIG. 2C

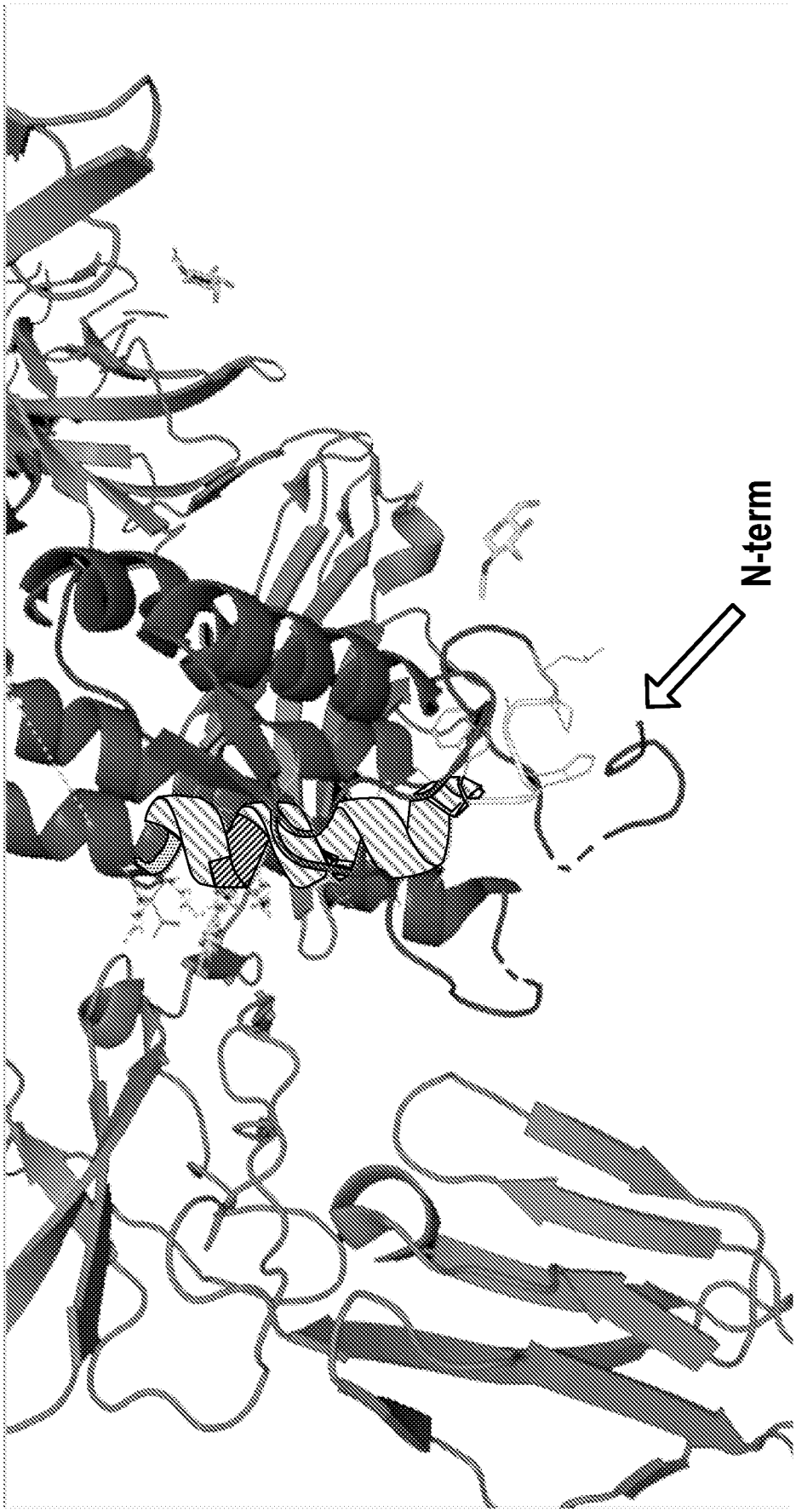


FIG. 3

Sequence submission

Single letter code: EESHCWISEMVSQLSDSLED **SEQ ID NO: 41**

Get a quotation

Sequence interpretation

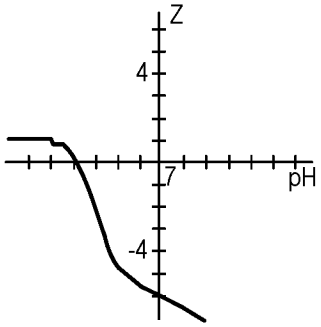
Single letter code: NH2- EESHCWISEM VSQLSDSLED -COOH

Triple letter code: NH2- Glu – Glu – Ser – His – Cys – Trp – Ile – Ser – Glu – Met – Val – Ser – Gln – Leu – Ser – Asp – Ser – Leu – Glu – Asp -COOH

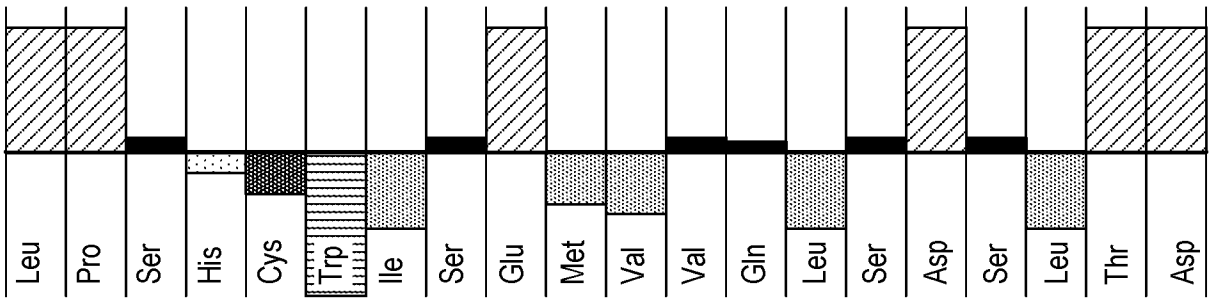
Physiochemical properties

Number of residues:	20	
Molecular weight:	2324.46 g/mol	*notes on MW*
Extinction coefficient:	5690 $M^{-1}cm^{-1}$	*notes on Ext. Coefficient*
Iso-electric point:	pH 3.27	*notes on pI*
Net charge at pH 7:	-6	*notes on net charge*
Estimated solubility:	Good water solubility.	*notes on solubility*

Net charge vs pH



Hydropathy **Hopp & Woods**



Top is hydrophilic

Bottom is hydrophobic

Color codes: Acidic Aromatic Basic Aliphatic Polar Cysteine

FIG. 4

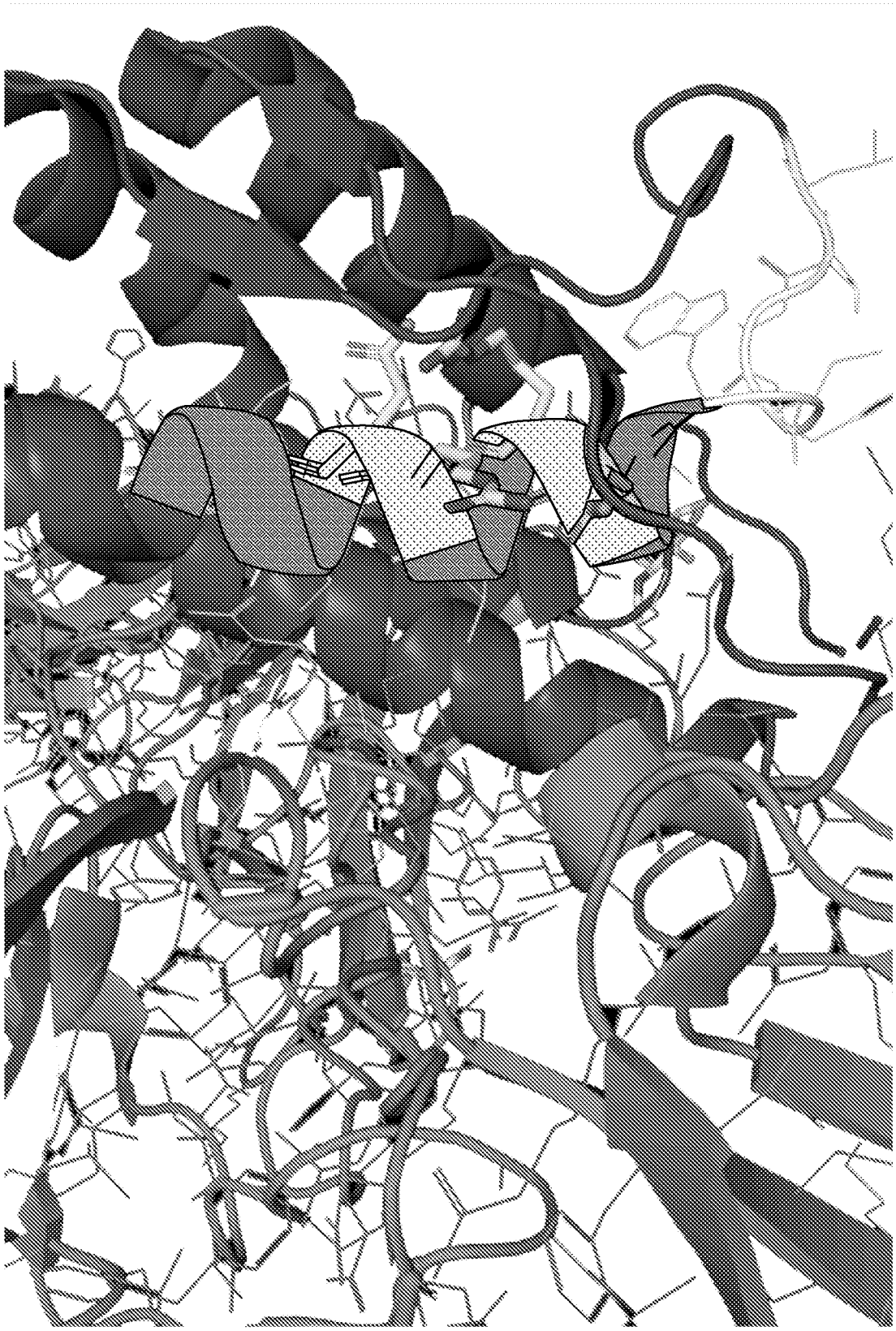


FIG. 5