and unpredictable. The signal intensity for MALDI-generated ions is a function of several intrinsic properties of peptide sequences. These properties include charge of the residue (e.g., guanidine in arginine), length, hydrophobicity, and secondary structure of a particular peptide.

One of the most serious problems associated with MALDI-TOF/TOF-based sequencing of OBOC library is that the peptide fragments containing acidic residues tend to have low signal intensities. The negatively charged groups reduce ionization efficiency and in turn cause low signal-to-noise ratios. There are existing methods to improve the peak intensities of peptide fragments containing such groups, for example, enhancing MALDI-TOF MS signals of a peptide 20- to 35-fold upon picolinamidination. Picolinamidination of amino groups in peptides uses ethyl picolinimidate tetrafluoroborate which is synthesized from picolinamide and triethyloxonium tetrafluoroborate. The N-terminus of the peptide chain and the epsilon-amino group of lysine will undergo the abovementioned reaction. Other approaches include the addition of coumarin tags on the N-terminus of peptide chain, which could potentially enhance the signal intensity by up to 40-fold. These enhancement methods involve the modification of the N-terminus of the peptide chains. This is usually undesirable for ligand- or capture agent-related applications using OBOC library as structural modifications might change the ligand-substrate binding modes.

Accordingly, improvements to screening of OBOC (one-bead-one-compound) combinatorial libraries are still needed.

SUMMARY

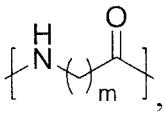
The present ~~invention~~ disclosure generally relates to various peptides and particles, for example, for use in screening of particle-based peptide libraries. The subject matter of the present disclosure ~~invention~~ involves, in some cases, interrelated products, alternative solutions to a particular problem, and/or a plurality of different uses of one or more systems and/or articles.

~~In one aspect, t~~The present disclosure ~~invention~~ is directed to an article. In accordance with one set of embodiments, the article comprises a particle having a peptide attached thereto, having a structure:

(particle)-M-Q-Z_n-X-J,

where M is a methionine residue; Q is a group able to enhance intensity and/or sensitivity of mass spectrometry; X comprises a plurality of amino acid residues; n is a

positive integer; J is an endgroup; and Z is a spacer. In some embodiments, Z has a structure:



where m is a positive integer greater than or equal to 3.

In one aspect, the present disclosure is directed to an article, comprising:

a particle having a peptide attached thereto, having a structure:

(particle)-M-Q-Z_n-X-J,

wherein:

M is a methionine residue;

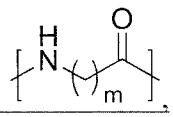
Q is a group able to enhance intensity and/or sensitivity of mass spectrometry;

X comprises a plurality of amino acid residues;

n is a positive integer;

J is an endgroup; and

Z is a spacer having a structure:



wherein m is a positive integer greater than or equal to 3.

In another set of embodiments, the article comprises a collection of particles having peptides attached thereto. At least some of the particles may consist essentially of one type of peptide. The collection of particles may include at least 20 distinguishable types of peptides, where the particles and the peptides have a structure:

(particle)-M-Q-Z_n-X^1-X^2-X^3-X^4-X^5-J,

where M is a methionine residue; Q is a group able to enhance intensity and/or sensitivity of mass spectrometry; Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, where n is a positive integer greater than or equal to 2 when Z is a spacer; X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine; and J is an endgroup.

In another aspect, the present disclosure is directed to an article, comprising:

a collection of particles having peptides attached thereto, at least some of the particles consisting essentially of one type of peptide, the collection including at least 20 distinguishable types of peptides, wherein the particles and the peptides have a structure:

(particle)-M-Q-Z_n-X^1-X^2-X^3-X^4-X^5-J,

wherein:

M is a methionine residue;

Q is a group able to enhance intensity and/or sensitivity of mass spectrometry;

Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, wherein n is a positive integer greater than or equal to 2 when Z is a spacer;

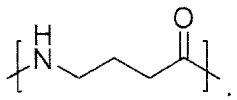
X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine; and

J is an endgroup.

The article, in yet another set of embodiments, includes a particle having a peptide attached thereto, having a structure:

(particle)-M-R-Z_2-X^1-X^2-X^3-X^4-X^5-J,

where M is a methionine residue; R is an arginine residue; X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine; J is an endgroup; and Z is a spacer. In one set of embodiments, Z may have a structure:



In another aspect, the present disclosure is directed to an article, comprising:

a particle having a peptide attached thereto, having a structure:

(particle)-M-R-Z_2-X^1-X^2-X^3-X^4-X^5-J,

wherein:

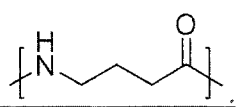
M is a methionine residue;

R is an arginine residue;

X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine;

J is an endgroup; and

Z has a structure:



The article, in still another set of embodiments, includes a particle having a peptide attached thereto, having a structure:

(particle)-M-X^1-X^2-X^3-X^4-X^5-Z_n-Q-J,

where M is a methionine residue; X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine and cysteine; Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, where n is a positive integer when Z is a spacer; Q is either a covalent bond between Z_n and J, or a group able to enhance intensity and/or sensitivity of mass spectrometry; and J is an endgroup.

In another aspect, the present disclosure is directed to an article, comprising:

a particle having a peptide attached thereto, having a structure:

(particle)-M-X^1-X^2-X^3-X^4-X^5-Z_n-Q-J,

wherein:

M is a methionine residue;

X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine and cysteine;

Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, wherein n is a positive integer when Z is a spacer;

Q is either a covalent bond between Z_n and J, or a group able to enhance intensity and/or sensitivity of mass spectrometry; and

J is an endgroup.

In another set of embodiments, the article comprises a particle having a peptide attached thereto, having a structure:

(particle)-M^1-X^1-X^2-X^3-X^4-X^5-Z_n-R-J,

where M^1 is a cleavable linker residue; X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine and cysteine; Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, wherein n is a positive integer when Z is a spacer; Q is either a covalent bond between Z_n and J, or a group able to enhance intensity and/or sensitivity of mass spectrometry; and J is an endgroup.

In another aspect, the present disclosure is directed to an article, comprising:

a particle having a peptide attached thereto, having a structure:

(particle)-M^1-X^1-X^2-X^3-X^4-X^5-Z_n-R-J,

wherein:

M^1 is a cleavable linker residue;

X^1, X^2, X^3, X^4, and X^5 are each independently amino acid residues excluding arginine and cysteine;

Z_n is either a covalent bond or a spacer that does not contain a naturally-occurring amino acid residue, wherein n is a positive integer when Z is a spacer;

Q is either a covalent bond between Z_n and J, or a group able to enhance intensity and/or sensitivity of mass spectrometry; and

J is an endgroup.

~~In another aspect, t~~The present ~~invention~~ disclosure also encompasses methods of making one or more of the embodiments described herein. ~~In still another aspect, t~~The present ~~invention~~ disclosure also encompasses methods of using one or more of the embodiments described herein. In another aspect, the present disclosure is directed to a method, comprising exposing any of the articles as defined herein to a target molecule.

Other advantages and novel features of the present ~~invention~~ disclosure will become apparent from the following detailed description of various non-limiting embodiments of the disclosure ~~invention~~ when considered in conjunction with the accompanying figures. In cases where the present specification and a document incorporated by reference include conflicting and/or inconsistent disclosure, the present specification shall control. If two or more documents incorporated by reference include

conflicting and/or inconsistent disclosure with respect to each other, then the document having the later effective date shall control.

BRIEF DESCRIPTION OF THE DRAWINGS

Non-limiting embodiments of the present invention will be described by way of example with reference to the accompanying figures, which are schematic and are not intended to be drawn to scale. In the figures, each identical or nearly identical component illustrated is typically represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the invention shown where illustration is not necessary to allow those of ordinary skill in the art to understand the invention. In the figures:

Fig. 1 illustrates a particle (represented by a ball) comprising a peptide sequence, in one embodiment of the invention;

Figs. 2A-2B illustrate mass spectrometry data for a peptide comprising FLVFK (SEQ ID NO: 2), in accordance with one embodiment of the invention;