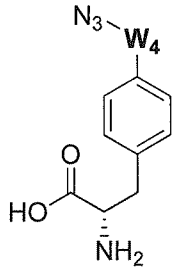
polypeptides are linked to the same conjugate at another location, and some polypeptides might not be linked at all.

[0007] There is a need, therefore, for polypeptides modified at site-specific positions optimized for uniformity, yield and/or activity to further the promising use of polypeptides in, for example, therapy and diagnostics.

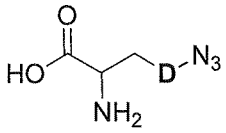
SUMMARY

[0008] Provided herein are modified amino acids comprising an azido group, polypeptides, antibodies and conjugates comprising the modified amino acids, and methods of producing the polypeptides, antibodies and conjugates comprising the modified amino acids. The polypeptides, antibodies and conjugates are useful in methods of treatment and prevention, methods of detection and methods of diagnosis.

[0008a] In a first aspect of the present disclosure, there is provided a compound according to formula II or formula I:



Formula II

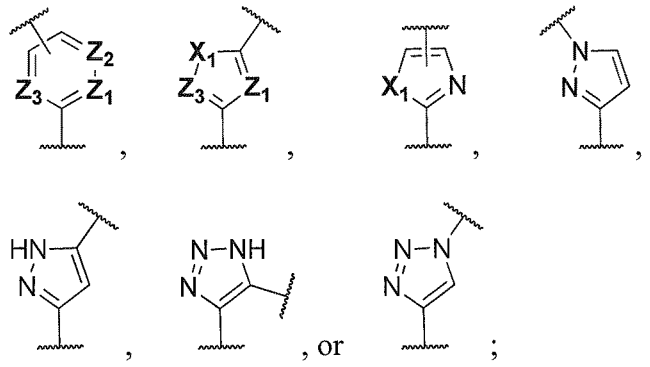


Formula I;

or a salt thereof, wherein:

D is –**Ar**-$\mathbf{W_3}$– or –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–;

Ar is



, , , , , , or ;

each of $\mathbf{W_1}$, $\mathbf{W_2}$, and $\mathbf{W_3}$ is independently a single bond or ~~lower~~ C_1-C_6 alkylene;

$\mathbf{W_4}$ is C_1-C_{10} alkylene;

each $\mathbf{X_1}$ is independently –NH–, –O–, or –S–;

each $\mathbf{Y_1}$ is independently a single bond, –NH–, or –O–;

each $\mathbf{Y_2}$ is independently ~~a single bond, –NH–, –O–, or~~ an N-linked or C-linked pyrrolidinylene; and

one of Z_1, Z_2, and Z_3 is –N– and the others of Z_1, Z_2, and Z_3 are independently –CH–.

[0008b] In a second aspect of the present disclosure, there is provided a polypeptide comprising an amino acid residue corresponding to the compound of the first aspect.

[0008c] In a third aspect of the present disclosure, there is provided a conjugate comprising the polypeptide of the second aspect linked to a payload and optionally comprising a linking moiety between the polypeptide and the payload.

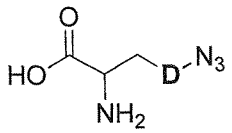
[0008d] In a fourth aspect of the present disclosure, there is provided an antibody comprising an amino acid residue corresponding to the compound of the first aspect.

[0008e] In a fifth aspect of the present disclosure, there is provided a conjugate comprising the antibody of the fourth aspect linked to a payload and optionally comprising a linking moiety between the antibody and the payload.

[0008f] In a sixth aspect of the present disclosure, there is provided an orthogonal tRNA aminoacylated with an amino acid residue corresponding to the compound of the first aspect.

[0008g] In a seventh aspect of the present disclosure, there is provided a method of producing a polypeptide, comprising contacting a polypeptide with the orthogonal tRNA of the sixth aspect under conditions suitable for incorporating the amino acid residue into the polypeptide.

[0009] In one embodiment a compound according to formula I is provided:

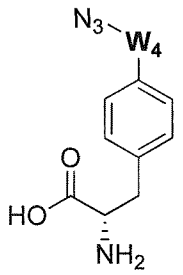


Formula I;

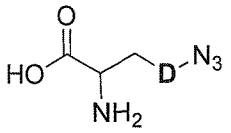
or a salt thereof, wherein: **D** is –**Ar**-$\mathbf{W_3}$– or –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–; **Ar** is

WHAT IS CLAIMED IS:

1. A compound according to formula II or formula I:



Formula II

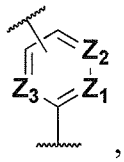
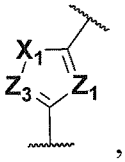
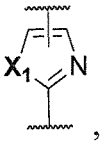
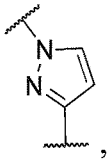


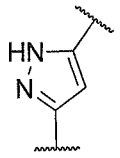
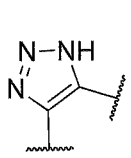
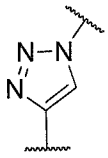
Formula I;

or a salt thereof, wherein:

D is –**Ar**-$\mathbf{W_3}$– or –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–;

Ar is


,

,

,

,


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, or

;

each of $\mathbf{W_1}$, $\mathbf{W_2}$, and $\mathbf{W_3}$ is independently a single bond or ~~lower~~ C_1-C_6 alkylene;

$\mathbf{W_4}$ is C_1-C_{10} alkylene;

each $\mathbf{X_1}$ is independently –NH–, –O–, or –S–;

each $\mathbf{Y_1}$ is independently a single bond, –NH–, or –O–;

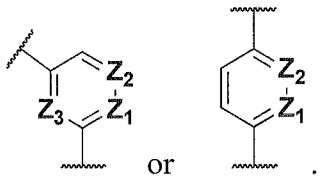
each $\mathbf{Y_2}$ is independently ~~a single bond, –NH–, –O–, or~~ an N-linked or C-linked pyrrolidinylene; and

one of $\mathbf{Z_1}$, $\mathbf{Z_2}$, and $\mathbf{Z_3}$ is –N– and the others of $\mathbf{Z_1}$, $\mathbf{Z_2}$, and $\mathbf{Z_3}$ are independently –CH–.

2. The compound of claim 1, wherein **D** is –**Ar**-$\mathbf{W_3}$–.
3. The compound of claim 1, wherein **D** is –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–.
4. The compound of claim 1, wherein:

D is –**Ar**-$\mathbf{W_3}$–; and

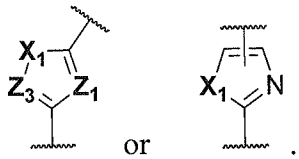
Ar is



5. The compound of claim 1, wherein:

D is –**Ar**-$\mathbf{W_3}$–; and

Ar is

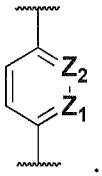


6. The compound of claim 1, wherein:

D is –**Ar**-$\mathbf{W_3}$–;

$\mathbf{W_3}$ is –CH_2–; and

Ar is



7. The compound of claim 1 wherein:

D is –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–; and

~~each~~ $\mathbf{Y_1}$ is independently –NH– or –O–.

8. The compound of claim 1, wherein:

D is –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–;

~~each~~ $\mathbf{Y_2}$ is independently an N-linked or C-linked pyrrolidinylene; and

~~each~~ $\mathbf{W_2}$ is a single bond.

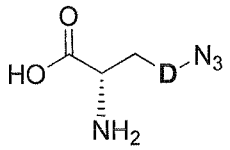
~~9. The compound of claim 1, wherein:~~

~~**D** is –$\mathbf{W_1}$-$\mathbf{Y_1}$-C(O)-$\mathbf{Y_2}$-$\mathbf{W_2}$–;~~

~~each $\mathbf{Y_2}$ is independently a single bond, –NH– or –O–; and~~

~~each $\mathbf{W_2}$ is lower alkylene.~~

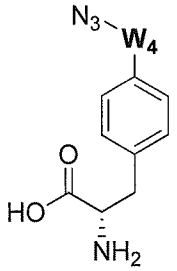
~~10~~9. The compound of claim 1 according to formula Ia:



Formula Ia.

~~11~~10. The compound of claim 1, wherein each of $\mathbf{W_2}$ and $\mathbf{W_3}$ is independently C_1-C_3 alkylene.

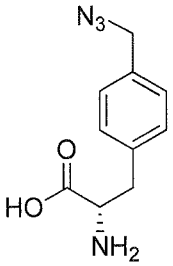
~~12~~11. The compound of claim 1 according to formula II:



Formula II;

or a salt thereof, wherein $\mathbf{W_4}$ is C_1-C_{10} alkylene.

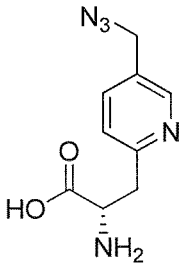
~~13~~12. The compound of claim ~~12~~ 11 according to formula 30:



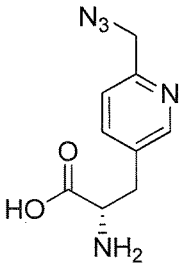
(30);

or a salt thereof.

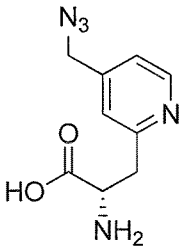
~~14~~13. The compound of claim 1 according to any of formulas ~~1-29 and 40~~1-17 and 24-29:



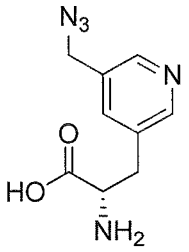
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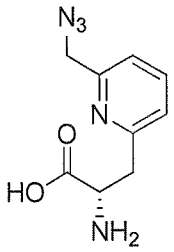
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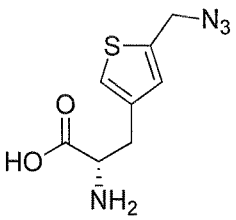
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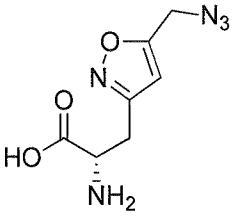
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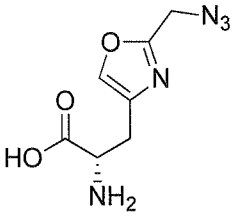
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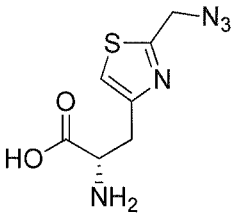
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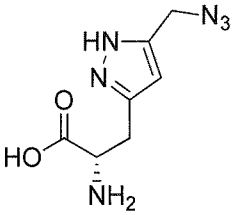
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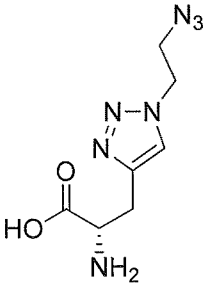
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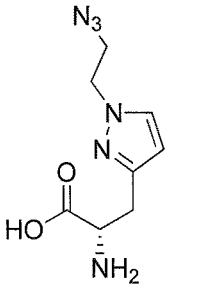
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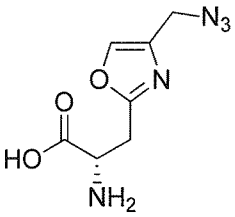
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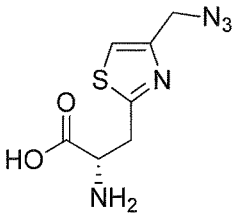
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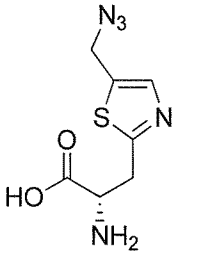
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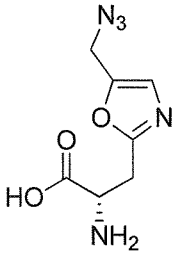
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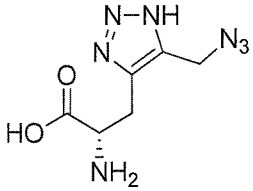
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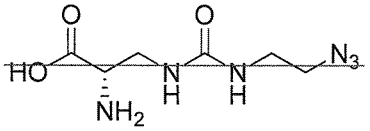
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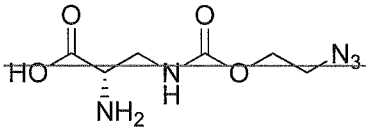
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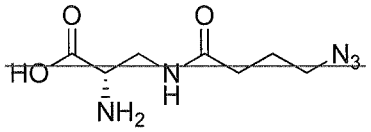
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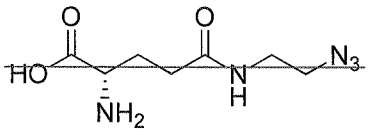
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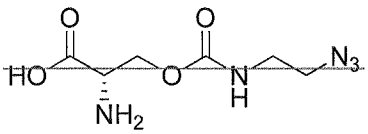
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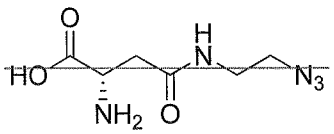
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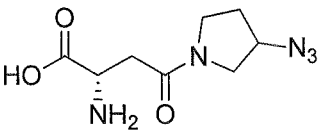
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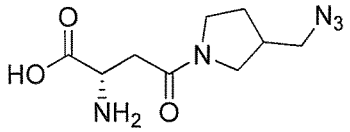
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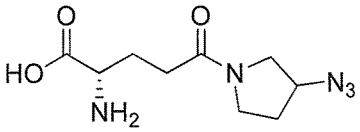
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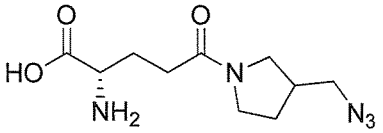
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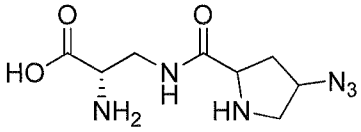
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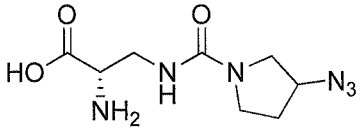
(26)



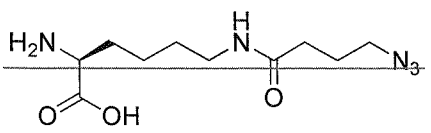
(27)



(28)



(29)



~~(40);~~

or a salt thereof.

~~15~~14. A polypeptide comprising an amino acid residue corresponding to the compound of any of claims 1-~~14~~13.

~~16~~15. A conjugate comprising the polypeptide of claim ~~15~~ 14 linked to a payload and optionally comprising a linking moiety between the polypeptide and the payload.

~~17~~16. An antibody comprising an amino acid residue corresponding to the compound of any of claims 1-~~14~~13.

~~18~~17. A conjugate comprising the antibody of claim ~~17~~ 16 linked to a payload and optionally comprising a linking moiety between the antibody and the payload.

~~19~~18. An orthogonal tRNA aminoacylated with an amino acid residue corresponding to the compound of any of claims 1-~~14~~13.

~~20~~19. A method of producing a polypeptide, comprising contacting a polypeptide with the orthogonal tRNA of claim ~~19~~ 18 under conditions suitable for incorporating the amino acid residue into the polypeptide.

~~21~~20. The method of claim ~~20~~19, wherein the orthogonal tRNA base pairs with a codon that is not normally associated with an amino acid.

~~22~~21. The method of claim ~~20~~19, wherein the contacting occurs in a reaction mixture which comprises a tRNA synthetase capable of aminoacylating the orthogonal tRNA with the compound of any of claims 1-~~14~~13.