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kind of national protection available): AE, AG, AL, AM,
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BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
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HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
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(88) Date of publication of the international search report:

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(54) Title: FLUORESCENT MOLECULAR SENSOR FOR TARGETING CHANGES IN PROTEIN SURFACES, AND METH-
ODS OF USE THEREOF

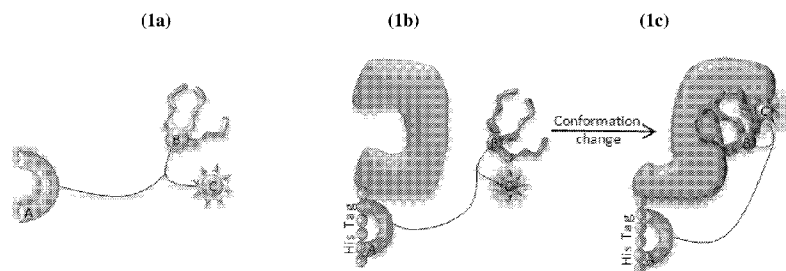


FIGURE 1

(57) Abstract: This invention is directed to monomolecular sensors, comprising a selective binder, a non-selective binder and a fluorophore, which can track changes that occur on the surface of labeled proteins. This invention is further directed to the use of such sensors for identifying binding partners of specific proteins. This invention is further directed to His-tag binding compounds and uses thereof in the preparation of genetically targeted detectable molecules and sensors which can specifically bind tag-labeled proteins.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2015/050441

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/50 C07D249/04 C07C229/76 C07K1/13 C07K14/47
G01N33/533

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N C07D C07C C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/038856 A1 (GEE KYLE [US] ET AL) 6 February 2014 (2014-02-06)	1,3-13, 18,40, 42,43
A	p. 2, paragraph [0017] - p. 15, paragraph [0170], claims 1-52	2,14-17
X	----- LATA SUMAN ET AL: "Specific and stable fluorescence labeling of histidine-tagged proteins for dissecting multi-protein complex formation", JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, US, vol. 128, no. 7, 22 February 2006 (2006-02-22), pages 2365-2372, XP009108035, ISSN: 0002-7863, DOI: 10.1021/JA0563105	1,3-13, 18-23, 40,42,43
A	the whole document ----- -/-	2,14-17



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

30 October 2015

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2015/050441

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GUIGNET E G ET AL: "Reversible site-selective labeling of membrane proteins in live cells", NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, US, vol. 22, no. 4, 21 March 2004 (2004-03-21), pages 440-444, XP002371708, ISSN: 1087-0156, DOI: 10.1038/NBT954	1,3-13, 18-23, 40,42,43
A	the whole document	2,14-17
X	ZHAOHUA HUANG ET AL: "Facile Synthesis of Multivalent Nitrilotriacetic Acid (NTA) and NTA Conjugates for Analytical and Drug Delivery Applications", BIOCONJUGATE CHEMISTRY, vol. 17, no. 6, 1 November 2006 (2006-11-01), pages 1592-1600, XP055075171, ISSN: 1043-1802, DOI: 10.1021/bc0602228	1,3-13, 18-23, 40,42,43
A	the whole document	2,14-17
X	VASSILIOU G ET AL: "Detection of low-affinity adhesion ligands by linking recombinant cell adhesion molecules in uniform orientation to a fluorescently labelled dextran molecule by means of hexahistidine tagging: the case of multimeric CD40", JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 215, no. 1-2, 1 June 1998 (1998-06-01), pages 9-15, XP004146488, ISSN: 0022-1759, DOI: 10.1016/S0022-1759(98)00030-1	1,3-13, 18-23, 40,42,43
A	the whole document	2,14-17
X	NOBUAKI SOH ET AL: "Methodology of reversible proteinlabeling for ratiometric fluorescent measurement", MOLECULAR BIOSYSTEMS, vol. 2, no. 2, 1 January 2006 (2006-01-01), pages 128-131, XP055206426, ISSN: 1742-206X, DOI: 10.1039/B515777C	1,3-13, 18-23, 40,42,43
A	the whole document	2,14-17

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-23, 40, 42(completely); 43(partially)

A monomolecular compound as disclosed in claims 1-17 and its use in tracking changes that occur on the surface of the His-tag protein, in identifying binding partner of the His-tag protein, in localizing the His-tag protein in a cell and in measuring the gene expression of the His-tag protein

2. claims: 24-39, 41(completely); 43(partially)

A His-tag binding compound as disclosed in claims 24-38 and its use in localizing the His-tag protein in a cell and in measuring the gene expression of the His-tag protein

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL2015/050441

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. ☒ forming part of the international application as filed:
 - ☒ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2015/050441

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-23, 40, 42(completely); 43(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2015/050441

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014038856 A1	06-02-2014	AU 2003270619 A1	30-04-2004
		EP 1546359 A2	29-06-2005
		US 2005233307 A1	20-10-2005
		US 2009081722 A1	26-03-2009
		US 2012270757 A1	25-10-2012
		US 2014038856 A1	06-02-2014
		WO 2004025259 A2	25-03-2004
