SUPPORTING INFORMATION

Rapid Discovery of Functional Small Molecule Ligands against Proteomic Targets through Library-Against-Library Screening

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Materials

N, *N*-dimethylformamide (DMF), dichloromethane (DCM), methanol, bovine serum albumin (BSA) and all of the plastic and glassware were purchased from Fisher Scientific (Pittsburgh, PA) unless otherwise noted. All building blocks and other reagents were purchased from Sigma-Aldrich (St. Louis, MO) unless otherwise stated. TentaGel S NH_2 resin (0.26 mmol/g loading, 90 μm diameter) was purchased from Rapp Polymere GmbH (Tubingen, Germany). Rink amide MBHA resin, HOBt (1-hydroxybenzotriazole), HBTU (2-(1H-tribenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate), and Fmoc-OSu were purchased from GL Biochem (Shanghai, China). M13 phage display Jurkat cell cDNA library was purchased from Spring Biosciences (Pleasanton, CA; discontinued). Anti-M13 monoclonal antibody was purchased from GE Healthcare Life Sciences (Piscataway, NJ). Rabbit anti-mouse IgG (H+L) –AP was purchased from Invitrogen (Carlsbad, CA). T7select human liver tumor cDNA library and polymerase chain reaction (PCR) reagents were both purchased from EMD Biosciences (Brookfield, WI). 96-well Genemate® semi-skirted PCR plates were purchased from ISC Bioexpress (Kaysville, UT). 96-well microplate adhesive seals were purchased from USA Scientific (Orlando, FL). PCR product cleaning reagent ExoSAP-IT was purchased from USB (Cleveland, OH). Dimethysulfoxide (DMSO) was purchased from American Type Culture Collection (ATCC, Manassas, VA). RPMI 1640 media was purchased from Invitrogen (Carlsbad, CA). TNT® T7 Quick Coupled Transcription/Translation System, Luciferase control T7 DNA, Dual-Luciferase® Reporter (DLR™) Assay System were purchased from Promega (Madison, WI). Sodium dodecyl sulfate

polyacrylamide gel electrophoresis (SDS-PAGE) gels, sample loading buffer, running buffer, staining buffer and the running system were purchased from PAGEgel (now Expedion in San Diego, CA) and Bio-Rad (Hercules, CA). Precision Plus Protein Kaleidoscope standards, goat anti-mouse IgG-HRP, Western Blot absorbent filter paper, Immun-Blot PVDF membrane and semi-dry blotting system were also purchased from Bio-Rad (Hercules, CA). EIF5B purified MaxPab mouse polyclonal antibody (B01P) was purchased from Abnova (Taoyuan County, Taiwan). High Capacity NeutrAvidin Agarose Resin was purchased from Pierce (Rockford, IL). Protease inhibitor cocktail (EDTA free) was purchased from Roche (Indianapolis, IN).

Nuclear Magnetic Resonance (NMR)

^{1}H NMR spectra were recorded at 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR, using $CDCl_3$ as the solvent and TMS as internal standard (0.00 ppm). MS was recorded in the positive ion mode on a Qtrap spectrometer.

3-(1-(1-(naphthalen-2-yl)ethyl)-2-(3-phenoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)-3-(3-propylureido)propanamide (**LWW31**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87-7.92 (m, 2H), 7.25-7.70 (m, 15H), 7.12-7.18 (m, 2H), 6.89-6.98 (m, 2H), 6.53-6.56 (m, 1H), 5.83 (s, 1H), 5.26-5.28 (m, 2H), 2.80-2.89 (m, 2H), 2.45-2.53 (m, 1H), 2.23 (t, 2H, *J* = 6.3 Hz), 1.25 (bs, 3H), 0.83-0.88 (m, 1H), 0.71 (dt, 3H, *J* = 7.5 Hz, 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 157.9, 154.1, 148.9, 148.7, 133.1, 131.3, 131.1, 130.5, 130.4, 129.8, 129.4, 129.2, 128.8, 128.7, 126.6, 126.3,

125.4, 123.9, 123.5, 123.4, 122.6, 121.5, 120.5, 118.9, 117.1, 114.0, 113.5, 112.4, 54.1, 51.0, 40.9, 28.7, 22.0, 19.3, 10.2; MS: 612.3 ($M + H^+$)

MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) Assay for Measuring IC50 for each Small Molecule against Jurkat Cells and HepG2 Cells

About 10,00 cells were seeded in each well of the 96-well microtiter plate with 100 μL of RPMI 1640 (for Jurkat Cells) or EMEM (for HepG2 Cells) media containing 10% of Fetal Bovine Serum (FBS) and 1% of Penicillin/Streptomycin solution (P/S). To measure the IC_{50}, each compound dissolved in dimethylsulfoxide (DMSO) was diluted in the media mentioned above to the desired concentrations with 0.1% of DMSO. The microtiter plate was incubated in a 37^{o}C incubator at 5% CO_2 for 72 hours. Ten microliter of 5 mg/mL MTT solution in PBS was added to the cell culture and incubated in the same incubator for another 4 hours. The resulting blue precipitation was dissolved by adding 100 μL of 0.04 N HCl in isopropanol and the color density of the solution was measured with a Tecan 96 well plate reader (Seestrasse, Switzerland) at 570 nM at 570nm with reference wavelength of 650 nm. The dose-response curves were then plotted and the percentage of the surviving cells at each concentration was calculated by using the formula: $100\%*(OD_{sample}-OD_{blank})/(OD_{control}-OD_{blank})$.

EIF5B nucleotide and protein sequences

Nucleotide sequence (from 5' end of the complement strand), underlined

sequence matched the database through BLAST search:

TTGGGTTCTGCCTGCCAGCTGCACTGATGCTGCCCCTCATCTCTCTGCCCA

ACCCTTCCCTCAAAGCTTAGCCAGAGCTTCTTGCATAGCTTTAACAGTGGCT

TTGCTAGGTCCTTTTTTCTTCTCTTTCTCTTTTTCTTCCTTTTCTCCTTTCTTTT

TCTTCTTATCTTTCTTCTTTTTGTCTCCTTCATTGTCATCTTCTGCAGCTGTGG

GAGTCTCTGCTTTCTCTTCAGAGGCAGGAATTACTCCAGTATCAACAGTCAC

TTTGGATTTTACAGTTTCTTCTTCAAATTTCCTTTGARATTCCTTTTGTTTACT

CTGATCCTTTTTTACCTGTTTCTAACTCTTCTTTTTCTTTCARCTTCCGCAGTTT

CGCTTTTTTCGCTTGAATTCGGATC

Nucleotide sequence (reverse and complement strand of the above sequence):

GATCCGAATTCAAGCGAAAAAGCGAAACTGCGGAAGYTGAAAGAAAAAGAA

GAGTTAGAAACAGGTAAAAAGGATCAGAGTAAACAAAAGGAATYTCAAAGGA

AATTTGAAGAAGAAACTGTAAAATCCAAAGTGACTGTTGATACTGGAGTAATT

CCTGCCTCTGAAGAGAAAGCAGAGACTCCCACAGCTGCAGAAGATGACAAT

GAAGGAGACAAAAAGAAGAAAGATAAGAAGAAAAAGAAAGGAGAAAAGGAA

GAAAAAGAGAAAGAGAAGAAAAAAGGACCTAGCAAAGCCACTGTTAAAGCTA

TGCAAGAAGCTCTGGCTAAGCTTTGAGGGAAGGGTTGGGCAGAGAGATGAG

GGGCAGCATCAGTGCAGCTGGCAGGCAGAACCCAA

Protein sequence:

DPNSSEKAKLRKLKEKEELETGKKDQSKQKEXQRKFEEETVKSKVTVDTGVIPA

SEEKAETPTAAEDDNEGDKKKKDKKKKKGEKEEKEKEKKKGPSKATVKAMQEA

LAKL*GKGWAER*GAASVQLAGRTQ

MS decoding MATLAB scripts

```
%Bead Decoder Program for Lam Lab, September 7th, 2007
%Written by Daniel Enter (denter@northwestern.edu)for Jimmy Chun-Yi Wu, Dr. Xiaobing Wang,
and Dr. Kit Lam

%Green text is for commenting, black text is the program

%To purchase Matlab software for UC Davis, see
%http://iet.ucdavis.edu/computing/software.cfm

%This program decodes mass spectrometry ASCII files of beads where the
%highest peak is m2, and uses a system of three equations to calculate and
%display between 1 and 2 (rarely more) values for r1, m1, r2, m2, r3 and m3

%System of Equations: r1 = m1 - 753, r2 = m2 - r1 - 810, r3 = m3 - m2 - 42
%Constants in the above equation can be found and modified (Cntl-F for the constants)

%Cutoffs for the program (Can be changed by user, orginal values: brominecutoff =
0.4;intensitycutoffsecondmax = 0.5;intensitycutoffindexr1 = 0.1;intensitycutoffindexr3 =
0.1;intensitycutoffbromine = 0.6;rcutoff = 1;

brominecutoff = 0.4;
intensitycutoffsecondmax = 0.5;
intensitycutoffindexr1 = 0.05;
intensitycutoffindexr3 = 0.05;
intensitycutoffbromine = 0.3;
rcutoff = 1;

%Library of small molecules (extra entries of r1, r2, or r3 can be added, originally 24
for r1, 22 for r2, 32 for r3)
%r1
r1(1) = 59.11;
r1(2) = 71.12;
r1(3) = 73.14;
r1(4) = 75.11;
r1(5) = 87.17;
r1(6) = 89;
r1(7) = 101.15;
r1(8) = 107.16;
r1(9) = 108.14;
r1(10) = 114;
r1(11) = 114;
r1(12) = 127.3;
r1(13) = 128.22;
r1(14) = 130.19;
r1(15) = 131.22;
r1(16) = 139.17;
r1(17) = 142.2;
r1(18) = 143.14;
r1(19) = 151.17;
r1(20) = 156.27;
r1(21) = 162;
r1(22) = 171.24;
r1(23) = 190.29;
r1(24) = 55.08;

%r2
r2(1) = 107.11 ;
r2(2) = 120.15;
r2(3) = 122.12;
r2(4) = 124.11;
r2(5) = 134.18;
r2(6) = 142.11;
```

```
r2(7) = 149.19;
r2(8) = 150.13;
r2(9) = 157.17;
r2(10) = 166.18;
r2(11) = 174.12;
r2(12) = 178.19;
r2(13) = 180.21;
r2(14) = 182.18;
r2(15) = 186.21;
r2(16) = 196.07;
r2(17) =198.22;
r2(18) = 194.23;
r2(19) = 206.24;
r2(20) = 212.25;
r2(21) = 254.33;
r2(22) = 266.22;

%r3
r3(1) = 58 ;
r3(2) = 67;
r3(3) = 69;
r3(4) = 72;
r3(5) = 86;
r3(6) = 98;
r3(7) = 100;
r3(8) = 102;
r3(9) = 105;
r3(10) = 108;
r3(11) = 112;
r3(12) = 116;
r3(13) = 120;
r3(14) = 123;
r3(15) = 126;
r3(16) = 130;
r3(17) = 134;
r3(18) = 138;
r3(19) = 141;
r3(20) = 150;
r3(21) = 157;
r3(22) = 164;
r3(23) = 170;
r3(24) = 176;
r3(25) = 180;
r3(26) = 185;
r3(27) = 188;
r3(28) = 192;
r3(29) = 196;
r3(30) = 210;
r3(31) = 232;
r3(32) = 267;

%Defining blank matrices for all variables to identify m1, r1, m2, r2, m3, r3
m1index =  0;
m1 =  0;
m1poss =  0;
m1close = 0;
m1only1poss = 0;

r1close =  0;
r1only1poss = 0;

m2index =  0;
m2 =  0;
m2poss =  0;

r2close =  0;
r2only1poss = 0;

m3index =  0;
m3 =  0;
m3poss =  0;
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```
m3close =  0;
m3only1poss = 0;

r3close =  0;
r3only1poss = 0;
brominepair2index = 1;
note = 0;

%To save previous possibilities in case increasing sensitivity 1% decreases solutions
from >2 to zero (values set to 1 so this does not happen in the first round), it will use
previous solutions (only case where >2 solutions should be displayed)
prevr2only1poss = 1;
prevr3only1poss = 1;
prevm2only1poss = 1;
prevm3only1poss = 1;
prevr1final = 1;
prevm1final = 1;



%Setting conditions for while...end loop to finish if between 1 and 2 possibilites for
r2,m2,r3,m3, but r1, m1 depends on r2, m2
done= 0;
doner(1) = false;
doner(2) = false;



%Setting molecular weight and intensity to be the columns of chosen dataset
       mw = data(:,1);
intensity = data(:,2);

%Graphing Mass Spec
plot(mw, intensity);
xlabel('Molecular Weight');
ylabel('Intensity');

%Decoding m2

%Find  max intensity
maxint=max(intensity) ;

%Checking which index is the max intensity, display note if not in m2 range
maxindex = 0 ;
while maxindex == 0
    for index = 1:(size(mw))
        if abs(mw(index) - 800) < 0.1
            m1start = index;
        end
             if intensity(index) == maxint;
                 if (min(r1) + min(r2) +800) > mw(index)
                        note = true;
                 end
                 if mw(index) >(max(r1) + max(r2) +820)
                        note = true;
                 end
                 maxindex = index;
             end
    end
end

%Setting an intensity cutoff for the bromine pair of max intensity
intensitycutoffmax = intensity(maxindex) * intensitycutoffsecondmax;

%Cycles through all indices from maxindex downward, and sees if they are 2 mw away from
the mw of maxindex, and of required intensity calculated above, if so, saves their index
and mw
for index = maxindex-200:1:maxindex + 200
    if 2 - brominecutoff <= abs(mw(maxindex) - mw(index)) &  abs(mw(maxindex) - mw(index))
<= 2 + brominecutoff
        if intensity(index) >= intensitycutoffmax
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```
            brominepair2index = index;
            brominepair2mw = mw(index);
        end
    end
end

%Assigning m2 value to whichever has lower mw of the most intense bromine pair
if maxindex < brominepair2index
    m2index = maxindex;
    m2 = mw(maxindex);
else
    m2index = brominepair2index;
    m2 = mw(brominepair2index);
end


%Decoding m1, r1, r2

%Finding all possible m1's with greater than specified % of maxindex intensity (starts at
percentage above, decreases 1% if no possibilities, .1% if already 1% or lower, stops at
0.1%, if more than two solutions, increases by 1% until 99% of max intensity is reached

%Done = 2 means r1,r2,m1,m2 pair and r3,m3 found, doner(1) means r1,m1,r1,m2 found
while done ~= 2
       done = 0;
    if doner(1) == false
        m1index =  0;
%Redefining variables to zero for new percentage
m1 =  0;
m1poss =  0;
m1close = 0;
m1only1poss = 0;
r1close =  0;
r1only1poss = 0;
r2poss = 0;
r2close =  0;
r2only1poss = 0;
r1final = 0;
m1final = 0;

%m1 start indicates index at which an r1 could be possible so scanning is practical
        for index  = m1start:maxindex-200
            if intensity(index) >= (intensitycutoffindexr1 * intensity(maxindex))
                %checking if bromine pair, and making new index, bromineindex for all
over specified %
                bromineindex = index;
                %cycling through increasing indices less than 2 mw above,to see if any
are of high enough intensity to be a bromine pair
               while (mw(bromineindex)- mw(index)) <= (2 + brominecutoff)
                   bromineindex = bromineindex + 1;
                   if 2 <= abs(mw(bromineindex) - mw(index)) & abs(mw(bromineindex) -
mw(index)) <= 2 + brominecutoff
                        if intensity(bromineindex) >= (intensitycutoffbromine *
intensity(index))
                                    m1poss = m1poss + 1 ;
                                    m1index(m1poss) = bromineindex;
                                    m1(m1poss) = mw(index);
                            end
                        end
                end
            end
        end

        %Compare m1 possibilities to library of  r1 MW's
        %m is counter for number of r1 matches
        m = 0;
        for n = 1:size(m1index,2)
            %convert to r1poss
            if m1(n) ~= 0
                r1poss(n) = m1(n) - 753;
                for index = 1:size(r1,2)
```

```
                    %if r1poss and r1 from library are within rcutoff of eachother, then
create a close vector for m1
                    if abs( r1poss(n) - r1(index) ) <= rcutoff
                    m=m+1;
                        r1close(m) = r1(index);
                        m1close(m) = r1(index) +753;
                    end
                end
            end
        end

        %Set duplicate entries to zero
        for n = size(r1close,2):-1:1
            for m = size(r1close,2):-1:1
                if r1close(n) == r1close(m)
                     if n~=m
                         r1close(n) = 0;
                     end
                end
            end
        end


        %Copy non-zero entries to another array
        m=0;
        for n = size(r1close,2):-1:1
            if r1close(n) ~= 0;
                m=m+1;
                r1only1poss(m) = r1close(n);

            end
        end

        %Set duplicate entries to zero
        for n = size(m1close,2):-1:1
            for m = size(m1close,2):-1:1
                if m1close(n) == m1close(m)
                          if n~=m
                              m1close(n) = 0;
                          end
                end
            end
        end

        %Copy non-zero entries to another array
        m=0;
        for n = size(m1close,2):-1:1
            if m1close(n) ~= 0;
                m=m+1;
                m1only1poss(m) = m1close(n);

            end
        end

        %m is counter for number of r2 matches
        m = 0;
        %r2found is false until a match is found for one of the r1only1poss
        %(that name is arbitrary, could be any number of possibilities) for
        %any index, if it stays false, then that entry is not translated to
        %an r value and then the m value is not also translated to next
        %array
        r2found = false;
        for n = 1:size(r1only1poss,2)
            %convert to r1poss
            if r1only1poss(n)~=0
             r2poss(n) = m2 - r1only1poss(n) - 810;
                    for index = 1:size(r2,2)
                        %if r2poss and r2 from library are within rcutoff of eachother,
                        %then create a match vector for m2
                        if abs( r2poss(n) - r2(index) ) <= rcutoff
                            m=m+1;
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```
                    r2close(m) = r2(index);
                r2found = true;
               end
           end
        %to delete r1's that do not result in available r2's
        %if r2matches is less than r1's run through, last r1 must not
        %have matched, so delete it and its corresponding m1
           if r2found == false
                r1only1poss(n) = 0;
                m1only1poss(n) = 0;
           end
           r2found = false;
    end
end

%Set duplicate entries to zero
for n = size(r2close,2):-1:1
    for m = size(r2close,2):-1:1
        if r2close(n) == r2close(m)
             if n~=m
                 r2close(n) = 0;
             end
        end
    end
end

%Copy non-zero entries to another array
m=0;
for n = size(r2close,2):-1:1
    if r2close(n) ~= 0;
               m=m+1;
        r2only1poss(m) = r2close(n);
    end
end

%Set duplicate entries to zero
for n = size(r1only1poss,2):-1:1
    for m = size(r1only1poss,2):-1:1
        if r1only1poss(n) == r1only1poss(m)
             if n~=m
                 r1only1poss(n) = 0;
             end
        end
    end
end

%Copy non-zero entries to another array
m=0;
for n = size(r1only1poss,2):-1:1
    if r1only1poss(n) ~= 0;
        m=m+1;
        r1final(m) = r1only1poss(n);
    end
end

%Set duplicate entries to zero
for n = size(m1only1poss,2):-1:1
    for m = size(m1only1poss,2):-1:1
        if m1only1poss(n) == m1only1poss(m)
                 if n~=m
                     m1only1poss(n) = 0;
                 end
        end
    end
end

%Copy non-zero entries to another array
m=0;
for n = size(m1only1poss,2):-1:1
    if m1only1poss(n) ~= 0;
     m=m+1;
```

```
                m1final(m) = m1only1poss(n);
            end
        end

        doner(1) = true;

        %check if more than 2 possibilites for r2,m2, if so there must also be for r1,m1
        if size(r2only1poss,2) >2
            %check that last time some entries were found, if no will display the >2
entries instead of going down again and up into an infinite loop
            if prevr2only1poss ~= 0
                doner(1) = false;
                %increase % if too many possibilities found
                if intensitycutoffindexr1 <1
                    intensitycutoffindexr1 = intensitycutoffindexr1 + .01;
                else
                   %if cannot increase % any more, tell user
                   doner(1) = true;
                   disp('r2 cannot be found')
                end
            end
        end

        %check if 0 possibilites for r2,m2, if so there must not be enough
        %possibilites for r1,m1
        if size(r2only1poss,2) == 1 & r2only1poss(1) == 0
           if size(prevr2only1poss,2) > 2
                r2only1poss = prevr2only1poss;
                r1final = prevr1final
                m1final = prevm1final
           else
                doner(1) = false;
                %decrease % if no possibilities found
                if intensitycutoffindexr1 >.011
                    intensitycutoffindexr1 = intensitycutoffindexr1 - .01;
                else
                    %decrease % by a smaller amount if no possibilities found
                    if intensitycutoffindexr1 >.0011
                        intensitycutoffindexr1 = intensitycutoffindexr1 - .001;
                    else
                        %if cannot decrease % any more, tell user
                        doner(1) = true;
                        disp('r2 cannot be found')
                    end
                end
           end
        end
    end

    %Decoding m3
    %Using the same mechanism as previously, except r3 does not depend on the value
    %of r1 or r2, so no matches need be excluded as was done above
    if doner(2) == false

    m3index =  0;
    m3 =  0;
    m3poss =  0;
    m3close =  0;
    m3only1poss = 0;
    r3close =  0;
    r3only1poss = 0;

         for index  = maxindex+500:size(intensity)-300
            if intensity(index) >= (intensitycutoffindexr3 * intensity(maxindex))
                %checking if bromine pair, and making new index, bromine index for
                %all over specified %
                bromineindex = index;
               while (mw(bromineindex)- mw(index)) <= (2 + brominecutoff)
                bromineindex = bromineindex + 1;
                   if 2 <= abs(mw(bromineindex) - mw(index)) & abs(mw(bromineindex) -
mw(index)) <= 2 + brominecutoff
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```
                        if intensity(bromineindex) >= (intensitycutoffbromine *
intensity(index))
                              m3poss = m3poss + 1 ;
                              m3index(m3poss) = bromineindex;
                              m3(m3poss) = mw(index);
                         end
                     end
                 end
             end
          end

         %Compare m3poss to library of  r3 MW's
         %set cutoff for how close calculated and actual r mw's can be
         %m is counter for number of r3 matches
         m = 0;
         for n = 1:size(m3,2)
             %convert to r3poss if not zero
             if m3(n) ~= 0
                 r3poss(n) = m3(n) - m2 - 42;
                for index = 1:size(r3,2)
                     %if r3poss and r3 from library are within rcutoff of eachother,
                     %then create a match vector for m3
                    if abs( r3poss(n) - r3(index) ) <= rcutoff
                         m=m+1;
                         r3close(m) = r3(index);
                         m3close(m) = r3(index) + m2 + 42;
                     end
                end
             end
         end
         %Set duplicate entries to zero
         for n = size(r3close,2):-1:1
             for m = size(r3close,2):-1:1
                 if r3close(n) == r3close(m)
                      if n~=m
                          r3close(n) = 0;
                      end
                 end
             end
         end
         %Copy non-zero entries to another array
         m=0;
         for n = size(r3close,2):-1:1
             if r3close(n) ~= 0;
                 m=m+1;
                 r3only1poss(m) = r3close(n);

             end
         end
         %Set duplicate entries to zero
         for n = size(m3close,2):-1:1
             for m = size(m3close,2):-1:1
                 if m3close(n) == m3close(m)
                          if n~=m
                              m3close(n) = 0;
                          end
                 end
             end
         end
         %Copy non-zero entries to another array
         m=0;
         for n = size(m3close,2):-1:1
             if m3close(n) ~= 0;
                 m=m+1;
                 m3only1poss(m) = m3close(n);
             end
       end

        doner(2) = true;

        %check if more than 2 possibilites for r3,m3
```

```
       if  size(r3only1poss,2) > 2
          %check that last time some entries were found, if no will display the >2
entries instead of going down again and up into an infinite loop
          if prevr3only1poss ~= 0
            doner(2) = false;
            %increase % if too many possibilities found
            if intensitycutoffindexr3 <1
                intensitycutoffindexr3 = intensitycutoffindexr3 + .01;
            else
                %if cannot increase % any more, tell user
                doner(2) = true;
                disp('r3 cannot be found')
            end
          end
      end
      %check if 0 possibilites for r3,m3
      if  size(r3only1poss,2) == 1 & r3only1poss(1) == 0
          %check that last time some entries were found, if so will displayprevious
possibilities
        if size(prevr3only1poss,2) > 2
            r3only1poss = prevr3only1poss;
            m3only1poss = prevm3only1poss;
        else
            doner(2) = false;
            %decrease % if no possibilities found
            if intensitycutoffindexr3 >.011
               intensitycutoffindexr3 = intensitycutoffindexr3 - .01;
            else
                 %decrease % by a smaller amount if no possibilities found
                 if intensitycutoffindexr3 >.0011
                    intensitycutoffindexr3 = intensitycutoffindexr3 - .001;
                 else
                    %if cannot decrease % any more, tell user
                    doner(2) = true;
                    disp('r3 cannot be found')
                 end
            end
        end
      end
 end

 %Check that both r1,m1,r2,m2 and r3,m3 found, if so then done will = 2 and overall while
loop to change sensitivity will be exited
 for n = 1:2
     if doner(n) == true
         done = done + 1;
     end
 end

%Saving r1, m1, r2, m2, r3, m3 for next previous entry
prevr1final= r1final;
prevm1final = m1final;
prevr2only1poss = r2only1poss;
prevr3only1poss = r3only1poss;
prevm3only1poss = m3only1poss;

%to end while loop
end

%disp ('intensitycutoffindexr1')
%disp (intensitycutoffindexr1)
%disp ('intensitycutoffindexr3')
%disp (intensitycutoffindexr3)

%Display all final values for  r1, m1, r2, m2, r3, m3, should only display
%1 or 2 values for each unless 0 to >2 encountered by 1% change, then 3 or
%more values could be displayed.  There should be only 1 value for m2

disp('This is the possible m1')
disp(m1final)
disp('This is the possible r1')
```

```
disp(r1final)
disp('This is the possible m2')
disp(m2)
disp('This is the possible r2')
disp(r2only1poss)
disp('This is the possible m3')
disp(m3only1poss)
disp('This is the possible r3')
disp(r3only1poss)

%Displaying not that m2 not in the correct range (calculated from r1, r2 lists)
if note == true
    disp('NOTE: MAXIMUM PEAK IS NOT WITHING M2 RANGE ((min(r1) + min(r2) +800) to (max(r1)
+ max(r2) +820)!')
end

%Clearing all data used in program, necesary to not have extraneous data in the following
run of program with different dataset
Clear
```

Legend of Supplementary Tables, Scheme and Figures

Table S1. List of XBW-SM3 R_1 building blocks, the occurrence of each building block in 91 identified compounds and their molecular weight. R_1 building blocks were all amines.

Table S2. List of XBW-SM3 R_2 building blocks, the occurrence of each building block in 91 identified compounds and their molecular weight. R_2 building blocks were all aldehydes.

Table S3. List of XBW-SM3 R_3 building block, the occurrence of each building block in 91 identified compounds and their molecular weight. R_3 building blocks included amino acids, carboxylic acids and isocyanates. Molecular weight (MW) is adjusted due to losing a water [$-H_2O$, -18]* molecule and/or gaining a proton [$+H^+$, +1]$^{\#}$ during reactions and MS analysis.

Table S4. List of 91 small molecules that bound to the phage display proteomes

Table S5. Result of biopanning over 55 small molecules. NA means peptide sequences are not available due to the failure of DNA sequencing, the failure of translation of DNA to putative peptide sequences or the peptide sequences did not match any sequences in the database after the BLAST search

Scheme S1. The synthesis of OBOC small molecule library, XBW-SM3. The small molecule was synthesized on the surface of the TantaGel resin while its corresponding coding tag ladders were synthesized in the inner topological segregated multi-layers.

Figure S1. The illustration of the small molecule decoding. The molecular weights of the three coding tags M_1, M_2, and M_3 were identified and indicated with arrows. The molecular weights of the three building blocks R_1, R_2 and R_3 were then calculated. Referring to **Supplementary Table S1, 2, and 3**, each building block was identified. $R_1=M_1-753=990-753=156$=1-(3-aminopropyl)-2-pipecoline, $R_2=M_2-M_1-57=174$=α,α,α-trifluoro-*m*-tolualdehyde, $R_3=M_3-M_2-42=193$ which didn't match any MW on Supplementary Table S3; however, 193-1=192 matched the MW of 4-butoxylphenyl isocyanate. Therefore, R_3 was confirmed 4-butoxylphenyl isocyanate

Figure S2.
LWW31 inhibited the expression of luciferase in Promega TnT coupled reticulocyte lysate cell-free protein expression system

Supplementary Tables

Table S1.

Name	Occurrence in 91 identified compounds	MW
Propargylamine	0	55.08
propylamine	1	59.11
cyclobutylamine	3	71.12
isobutylamine	3	73.14
2-methoxyethylamine	0	75.11
1-ethylpropylamine	2	87.17
beta-alanine t-butyl ester HCl	5	89
tetrahydrofurfurylamine	0	101.15
benzylamine	2	107.16
2-(aminomethyl)pyridine	6	108.14
1-Boc-4-(aminomethyl)piperidine	8	114
1-(2-aminoethyl)pyrrolidine	0	114.19
(R)-1-cyclohexylethylamine	1	127.3
1-(2-aminoethyl)piperidine	4	128.22
4-(2-aminoethyl)morpholine	5	130.19
3-butoxypropylamine	3	131.22
4-fluorophenylethylamine	1	139.17
1-(3-aminopropyl)-2-pyrolidione	6	142.2
2,5-difluorobenzylamine	4	143.14
piperonylamine	0	151.17
1-(3-aminopropyl)-2-pipecoline	22	156.27
histamine(Boc)	1	162
1-(1-naphthyl)ethylamine	3	171.24
4-amino-1-benzylpiperidine	11	190.29

Table S2.

Name	Occurrence in 91 identified compounds	MW
4-pyridine carboxaldehyde	13	107.11
m-tolualdehyde	5	120.15
4-hydroxybenzaldehyde	13	122.12
3-fluorobenzaldehyde	8	124.11
2,5-dimethylbenzaldehyde	4	134.18
2,5-difluorobenzaldehyde	1	142.11
4-(dimethylamino)benzaldehyde	1	149.19
4-carboxyl benzaldehyde	1	150.13
2-Quinoline-carboxaldehyde	10	157.17
2,4-dimethoxybenzaldehyde	3	166.18
α,α,α-trifluoro-m-tolualdehyde	2	174.12
4-Hydroxy-3-methoxycinnamaldehyde	0	178.19
3-ethyxy-4-mehoxybenzaldehyde	3	180.21
2,6-Dimethoxy-4-hydroxybenzaldehyde	0	182.18
4-methoxy-1-naphthaldehyde	2	186.21
2-Fluorene-carboxaldehyde	5	194.23
Pentafluoro-benzaldehyde	0	196.07
3-phenoxybenzaldehyde	8	198.22
9-Anthraldehyde	8	206.24
3-(4-methylphenoxy)benzaldehyde	0	212.25
3-(4-tert-butylphenoxy)benzaldehyde	3	254.33
3-(3-(trifluoromethyl)phenoxy)benzaldehyde	1	266.22

Table S3.

Name	Occurrence in 91 identified compounds	MW (adjusted)
Glycine	1	$58^{+\#}$
2-butynoic acid	2	$67^{+\#}$
Cyclopropane carboxyl acid	6	$69^{+\#}$
Alanine	4	$72^{+\#}$
Propyl isocyanate	3	$86^{\#}$
Proline	6	$98^{+\#}$
Tert-butyl isocyanate	5	$100^{\#}$
Threonine	2	$102^{+\#}$
Benzoic acid	1	$105^{+\#}$
1-methyl-2-pyrrole-carboxylic acid	0	$108^{+\#}$
Cyclopentyl isocyanate	4	$112^{\#}$
Aspartic acid	3	$116^{+\#}$
Phenyl isocyanate	1	$120^{\#}$
4-fluorobenzoic acid	3	$123^{+\#}$
Cyclohexyl isocyanate	2	$126^{\#}$
Glutamic acid	3	$130^{+\#}$
o-tolyl isocyanate	3	$134^{\#}$
Histidine	1	$138^{+\#}$
3,4-difluorobenzoic acid	2	$141^{+\#}$
2-methoxyphenyl isocyanate	2	$150^{\#}$
Arginine	3	$157^{+\#}$
Tyrosine	2	$164^{+\#}$
1-naphthyl isocyanate	3	$170^{\#}$
2-tert-butylphenyl isocyanate	0	$176^{\#}$
3,5-dimethoxyphenyl isocyanate	1	$180^{\#}$
(2-naphthoxy)acetic acid	7	$185^{+\#}$
α,α,α-trifluoro-m-tolyl isocyanate	3	$188^{\#}$
4-butoxyphenyl isocyanate	0	$192^{\#}$
2-biphenylyl isocyanate	3	$196^{\#}$
3-benzoyl-2-pyridinecarboxylic acid	13	$210^{+\#}$
2-phenyl-4-quinolinecarboxylic acid	1	$232^{+\#}$
SM	1	$267^{+\#}$

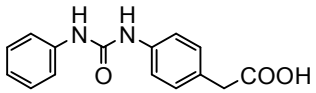

H
N
H
N
O
COOH

Table S4

Compound	R_1 Name	R_2 Name	R_3 Name
LWW1	1-Boc-4-(aminomethyl)piperidine	2-quinoline-carboxyaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW2	1-Boc-4-(aminomethyl)piperidine	2-quinoline-carboxyaldehyde	Arg
LWW3	1-Boc-4-(aminomethyl)piperidine	2-quinoline-carboxyaldehyde	Tert-butyl isocyanate
LWW4	1-(3-aminopropyl)-2-pyrrolidinone	3-ethoxy-4-methoxybenzaldehyde	Cyclopropane carboxylic acid
LWW5	1-(3-aminopropyl)-2-pipecoline	2-quinoline-carboxyaldehyde	(2-naphthoxy)acetic acid
LWW6	1-Boc-4-(aminomethyl)piperidine	2-quinoline-carboxyaldehyde	Tert-butyl isocyanate
LWW7	1-(3-aminopropyl)-2-pipecoline	2-quinoline-carboxyaldehyde	(2-naphthoxy)acetic acid
LWW8	1-Boc-4-(aminomethyl)piperidine	4-pyridine carboaldehyde	2-biphenylyl isocyanate
LWW9	4-(2-aminoethyl)morpholine	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW10	3-butoxypropylamine	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW11	4-fluorophenylethylamine	3-fluorobenzaldehyde	Pro
LWW12	histamine(Boc)	3-phenoxybenzaldehyde	Propyl isocyanate
LWW13	1-(2-aminoethyl)piperidine	4-hydroxybenzaldehyde	Cyclohexyl isocyanate
LWW14	1-(2-aminoethyl)piperidine	4-hydroxybenzaldehyde	4-fluorobenzoic acid
LWW15	1-(3-aminopropyl)-2-pipecoline	4-pyridine carboaldehyde	α,α,α-trifluoro-m-tolyl isocyanate
LWW16	1-(3-aminopropyl)-2-pipecoline	4-pyridine carboaldehyde	(2-naphthoxy)acetic acid
LWW17	4-(2-aminoethyl)morpholine	9-anthraldehyde	Asp
LWW18	4-(2-aminoethyl)morpholine	9-anthraldehyde	Pro
LWW19	1-(3-aminopropyl)-2-pyrrolidinone	3-fluorobenzaldehyde	Tert-butyl isocyanate
LWW20	2,5-difluorobenzylamine	3-fluorobenzaldehyde	Tert-butyl isocyanate
LWW21	beta-alanine t-butyl ester HCl	4-pyridine carboaldehyde	Glu
LWW22	1-(3-aminopropyl)-2-pipecoline	α,α,α-trifluoro-m-tolualdehyde	SM (Ask Ruiwu)
LWW23	beta-alanine t-butyl ester HCl	4-hydroxybenzaldehyde	Cyclopropane carboxylic acid
LWW24	beta-alanine t-butyl ester HCl	4-hydroxybenzaldehyde	2-butynoic acid
LWW25	1-(3-aminopropyl)-2-pipecoline	2,5-dimethylbenzaldehyde	1-naphthyl isocyanate
LWW26	1-(3-aminopropyl)-2-pipecoline	2,4-dimethoxybenzaldehyde	α,α,α-trifluoro-m-tolyl isocyanate
LWW27	1-(3-aminopropyl)-2-pipecoline	2,4-dimethoxybenzaldehyde	(2-naphthoxy)acetic acid
LWW28	1-(naphthyl)ethylamine	4-hydroxybenzaldehyde	Arg
LWW29	4-amino-1-benzylpiperidine	3-phenoxybenzaldehyde	(2-naphthoxy)acetic acid
LWW30	2-(aminomethyl)pyridine	α,α,α-trifluoro-m-tolualdehyde	o-tolyl isocyanate
LWW31	1-(naphthyl)ethylamine	3-phenoxybenzaldehyde	Propyl isocyanate
LWW32	(R)-1-cyclohexylethylamine	2,5-dimethylbenzaldehyde	o-tolyl isocyanate
LWW33	isobutylamine	m-tolualdehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW34	1-(3-aminopropyl)-2-pyrrolidinone	2-fluorene-carboxaldehyde	Ala
LWW35	2,5-difluorobenzylamine	2-fluorene-carboxaldehyde	Ala
LWW36	1-(3-aminopropyl)-2-pyrrolidinone	2-quinoline-carboxyaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW37	Propylamine	4-pyridine carboaldehyde	Arg
LWW38	4-amino-1-benzylpiperidine	9-anthraldehyde	1-naphthyl isocyanate
LWW39	4-amino-1-benzylpiperidine	9-anthraldehyde	2-methoxyphenyl isocyanate
LWW40	2-(aminomethyl)pyridine	3-fluorobenzaldehyde	Benzoic zcid
LWW41	1-(3-aminopropyl)-2-pipecoline	3-(4-tert-butylphenoxy)benzaldehyde	(2-naphthoxy)acetic acid
LWW42	1-(3-aminopropyl)-2-pipecoline	3-(4-tert-butylphenoxy)benzaldehyde	2-methoxyphenyl isocyanate
LWW43	1-(3-aminopropyl)-2-pipecoline	3-(4-tert-butylphenoxy)benzaldehyde	4-fluorobenzoic acid
LWW44	1-(3-aminopropyl)-2-pipecoline	4-carboxylbenzaldehyde	Thr
LWW45	1-(3-aminopropyl)-2-pipecoline	4-(dimethylamine)benzaldehyde	Thr
LWW46	1-Boc-4-(aminomethyl)piperidine	9-anthraldehyde	Cyclopentyl isocyanate
LWW47	1-(naphthyl)ethylamine	2,4-dimethoxybenzaldehyde	Tyr
LWW48	beta-alanine t-butyl ester HCl	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW49	4-amino-1-benzylpiperidine	3-phenoxybenzaldehyde	Cyclohexyl isocyanate
LWW50	4-amino-1-benzylpiperidine	3-phenoxybenzaldehyde	4-fluorobenzoic acid
LWW51	2-(aminomethyl)pyridine	3-phenoxybenzaldehyde	o-tolyl isocyanate
LWW52	1-(3-aminopropyl)-2-pipecoline	4-pyridine carboaldehyde	α,α,α-trifluoro-m-tolyl isocyanate
LWW53	1-(3-aminopropyl)-2-pipecoline	4-pyridine carboaldehyde	(2-naphthoxy)acetic acid
LWW54	isobutylamine	4-pyridine carboaldehyde	Pro
LWW55	4-amino-1-benzylpiperidine	2-quinoline-carboxyaldehyde	2-biphenylyl isocyanate
LWW56	1-(3-aminopropyl)-2-pyrrolidinone	4-pyridine carboaldehyde	Pro
LWW57	2,5-difluorobenzylamine	4-pyridine carboaldehyde	Pro
LWW58	1-(3-aminopropyl)-2-pipecoline	2,5-dimethylbenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW59	1-(3-aminopropyl)-2-pipecoline	2,5-dimethylbenzaldehyde	3,5-dimethoxyphenyl isocyanate
LWW60	benzylamine	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW61	2-(aminomethyl)pyridine	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW62	4-amino-1-benzylpiperidine	3-ethoxy-4-methoxybenzaldehyde	Phenyl isocyanate
LWW63	4-amino-1-benzylpiperidine	3-ethoxy-4-methoxybenzaldehyde	Ala
LWW64	1-(3-aminopropyl)-2-pipecoline	3-[3-(trifluoromethyl)phenoxy]benzaldehyde	Asp
LWW65	3-butoxypropylamine	4-methoxy-1-naphthaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW66	3-butoxypropylamine	4-methoxy-1-naphthaldehyde	2-butynoic acid
LWW67	1-(3-aminopropyl)-2-pipecoline	4-hydroxybenzaldehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW68	1-(3-aminopropyl)-2-pipecoline	4-hydroxybenzaldehyde	Pro
LWW69	beta-alanine t-butyl ester HCl	2-fluorene-carboxaldehyde	Tyr
LWW70	1-Boc-4-(aminomethyl)piperidine	3-fluorobenzaldehyde	His
LWW71	cyclobutylamine	9-anthraldehyde	2-phenyl-4-quinolinecarboxylic acid
LWW72	cyclobutylamine	9-anthraldehyde	3-benzoyl-2-pyridinecarboxylic acid

LWW73	cyclobutylamine	9-anthraldehyde	Gly
LWW74	2-(aminomethyl)pyridine	2,5-difluorobenzaldehyde	Tert-butyl isocyanate
LWW75	1-ethylpropylamine	m-tolualdehyde	3-benzoyl-2-pyridinecarboxylic acid
LWW76	1-ethylpropylamine	m-tolualdehyde	3,4-difluorobenzoic acid
LWW77	1-(3-aminopropyl)-2-pyrrolidinone	3-phenoxybenzaldehyde	Glu
LWW78	2,5-difluorobenzylamine	3-phenoxybenzaldehyde	Glu
LWW79	benzylamine	4-pyridine carboaldehyde	3,4-difluorobenzoic acid
LWW80	isobutylamine	m-tolualdehyde	Cyclopropane carboxylic acid
LWW81	1-(2-aminoethyl)piperidine	4-pyridine carboaldehyde	Asp
LWW82	1-(2-aminoethyl)piperidine	4-pyridine carboaldehyde	Cyclopropane carboxylic acid
LWW83	4-amino-1-benzylpiperidine	3-fluorobenzaldehyde	2-biphenylyl isocyanate
LWW84	4-amino-1-benzylpiperidine	3-fluorobenzaldehyde	1-naphthyl isocyanate
LWW85	4-amino-1-benzylpiperidine	3-fluorobenzaldehyde	Cyclopentyl isocyanate
LWW86	2-(aminomethyl)pyridine	2-quinoline-carboxyaldehyde	Cyclopropane carboxylic acid
LWW87	1-(3-aminopropyl)-2-pipecoline	m-tolualdehyde	Cyclopentyl isocyanate
LWW88	1-(3-aminopropyl)-2-pipecoline	2-quinoline-carboxyaldehyde	Cyclopentyl isocyanate
LWW89	4-(2-aminoethyl)morpholine	2-fluorene-carboxaldehyde	Ala
LWW90	4-(2-aminoethyl)morpholine	2-fluorene-carboxaldehyde	Cyclopropane carboxylic acid
LWW91	1-Boc-4-(aminomethyl)piperidine	4-hydroxybenzaldehyde	Propyl isocyanate

Table S5.

Compound ID	Number of Clones sequenced	Bound Putative Protein ID
LWW1	4 out of 5	Homo sapiens WW domain binding protein 5 (WBP5), transcript variant
	1 out of 5	NA
LWW2	5 out of 5	Homo sapiens ribosomal protein L4 (RPL4), mRNA
LWW4	3 out of 5	Homo sapiens signal recognition particle 19kDa (SRP19)
	1 out of 5	receptor-interacting factor 1
	1 out of 5	NA
LWW5	5 out of 5	NA
LWW7	5 out of 10	Porimin precursor (Transmembrane protein 123) (Pro-oncosis receptor inducing membrane injury) (Keratinocytes-associated transmembrane protein 3) (KCT-3)
	4 out of 10	Zinc finger motifs
	1 out of 10	NA
LWW8	5 out of 5	DNA topoisomerase II, alpha isozyme
LWW9	3 out of 5	Homo sapiens BCL2/adenovirus E1B 19kDa interacting protein 3 (BNIP3), nuclear gene encoding mitochondrial protein, mRNA
	2 out of 5	Homo sapiens albumin (ALB), mRNA
LWW10	2 out of 5	Homo sapiens pericentriolar material 1 (PCM1), mRNA
	3 out of 5	Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 21 (DDX21)
LWW11	1 out of 5	albumin, isoform CRA_l
	4 out of 5	NA
LWW12	5 out of 5	Homo sapiens family with sequence similarity 44, member A (FAM44A)
LWW13	5 out of 5	Homo sapiens retinoblastoma binding protein 6 (RBBP6), transcript
LWW15	2 out of 5	Homo sapiens muscleblind-like 2 (Drosophila) (MBNL2), transcript variant 1, mRNA
	3 out of 5	NA
LWW16	4 out of 5	Homo sapiens nucleolar and coiled-body phosphoprotein 1 (NOLC1), mRNA
	1 out of 5	Homo sapiens actinin, alpha 4 (ACTN4), mRNA
LWW17	5 out of 5	NA
LWW18	1 out of 5	Homo sapiens beta-2-microglobulin (B2M), mRNA
	1 out of 5	Homo sapiens albumin (ALB), mRNA
	3 out of 5	NA
LWW19	1 out of 5	Putative p150
	4 out of 5	NA
LWW20	4 out of 10	Homo sapiens retinoblastoma binding protein 6 (RBBP6), transcript variant 2, mRNA
	6 out of 10	NA
LWW21	2 out of 5	Homo sapiens nuclear casein kinase and cyclin-dependent kinase substrate 1 (NUCKS1)
	3 out of 5	NA
LWW24	5 out of 5	NA
LWW25	5 out of 5	NA
LWW26	3 out of 5	Homo sapiens cortactin (CTTN), transcript variant 1, mRNA
	2 out of 5	NA
LWW27	2 out of 5	Homo sapiens plasminogen (PLG), mRNA
	3 out of 5	NA
LWW28	1 out of 5	Homo sapiens M-phase phosphoprotein 6 (MPHOSPH6), mRNA
	4 out of 5	NA
LWW29	1 out of 5	high-mobility group nucleosomal binding domain 2 (HMGN2)
	1 out of 5	Homo sapiens eukaryotic translation initiation factor 2, subunit 3 gamma, 52kDa (EIF2S3), mRNA
	3 out of 5	NA
LWW30	1 out of 5	Homo sapiens chromosome 1 open reading frame 149 (C1orf149)
	4 out of 5	NA
LWW31	2 out of 10	Homo sapiens nuclear casein kinase and cyclin-dependent

		kinase substrate 1 (NUCKS1)
	4 out of 10	Homo sapiens eukaryotic translation initiation factor 5B (EIF5B)
	1 out of 10	Homo sapiens KRR1, small subunit (SSU) processome component, homolog (yeast) (KRR1)
	3 out of 10	NA
LWW32	3 out of 10	Homo sapiens high-mobility group box 3 (HMGB3)
	3 out of 10	Homo sapiens nucleolar and coiled-body phosphoprotein 1 (NOLC1)
	4 out of 10	NA
LWW33	5 out of 5	Homo sapiens topoisomerase (DNA) I (TOP1)
LWW34	5 out of 5	NA
LWW36	3 out of 5	Homo sapiens nucleolar and coiled-body phosphoprotein 1 (NOLC1)
	2 out of 5	NA
LWW37	5 out of 5	NA
LWW39	5 out of 5	NA
LWW40	1 out of 5	Deformed epidermal autoregulatory factor 1 homolog (Nuclear DEAF-1-related transcriptional regulator) (NUDR) (Suppressin) (Zinc finger MYND domain-containing protein 5)
	4 out of 5	NA
LWW41	5 out of 5	NA
LWW42	5 out of 5	NA
LWW43	5 out of 5	NA
LWW44	5 out of 5	NA
LWW45	5 out of 5	NA
LWW46	5 out of 5	NA
LWW47	5 out of 5	NA
LWW48	5 out of 5	NA
LWW49	5 out of 5	NA
LWW50	5 out of 5	NA
LWW51	5 out of 5	NA
LWW53	5 out of 5	NA
LWW55	1 out of 10	Homo sapiens UTP14, U3 small nucleolar ribonucleoprotein, homolog A (yeast) (UTP14A),
	1 out of 10	p40
	8 out of 19	NA
LWW58	2 out of 5	serum albumin [Homo sapiens]
	1 out of 5	sarcoma antigen NY-SAR-91 [Homo sapiens]
	2 out of 5	NA
LWW60	2 out of 5	sarcoma antigen NY-SAR-91 [Homo sapiens]
	1 out of 5	hCG1820635 [Homo sapiens]
	2 out of 5	NA
LWW64	5 out of 5	NA
LWW65	1 out of 5	ferritin light polypeptide variant [Homo sapiens]
	1 out of 5	aftiphilin protein isoform a [Homo sapiens]
	3 out of 5	NA
LWW66	4 out of 10	KIAA0081 [Homo sapiens]
	1 out of 10	mesoderm development candidate 2 [Homo sapiens]
	2 out of 10	high-mobility group box 3, isoform CRA_b [Homo sapiens].
	1 out of 10	coilin [Homo sapiens]
	2 out of 10	NA
LWW69	5 out of 5	NA
LWW70	2 out of 5	zinc finger protein 354B [Homo sapiens]
	3 out of 5	NA
LWW72	3 out of 5	zinc finger protein 354B [Homo sapiens]
	2 out of 5	NA
LWW73	5 out of 5	NA

Scheme S1

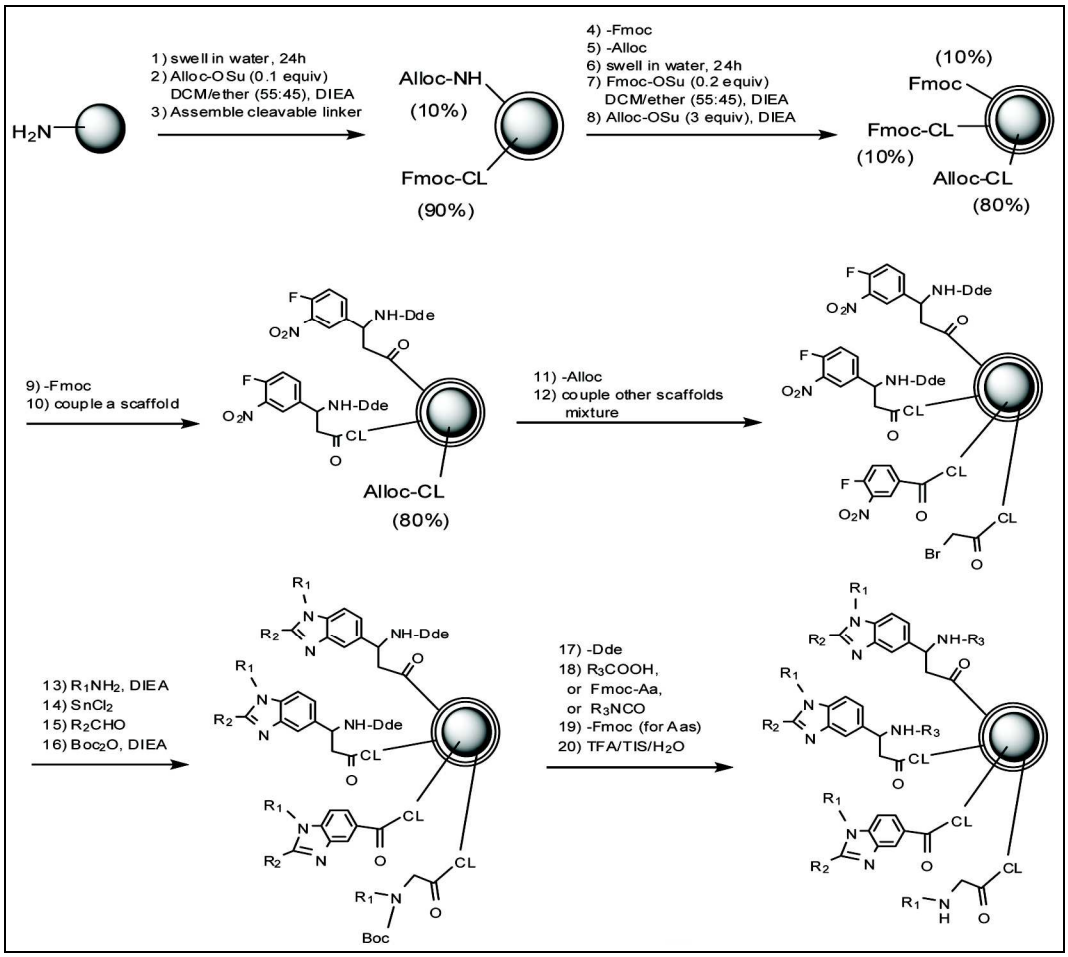

1) swell in water, 24h
2) Alloc-OSu (0.1 equiv)
DCM/ether (55:45), DIEA
3) Assemble cleavable linker
Alloc-NH
(10%)
Fmoc-CL
(90%)
4) -Fmoc
5) -Alloc
6) swell in water, 24h
7) Fmoc-OSu (0.2 equiv)
DCM/ether (55:45), DIEA
8) Alloc-OSu (3 equiv), DIEA
(10%)
Fmoc
Fmoc-CL
(10%)
Alloc-CL
(80%)
9) -Fmoc
10) couple a scaffold
Alloc-CL
(80%)
11) -Alloc
12) couple other scaffolds
mixture
13) R1NH2, DIEA
14) SnCl2
15) R2CHO
16) Boc2O, DIEA
17) -Dde
18) R3COOH,
or Fmoc-Aa,
or R3NCO
19) -Fmoc (for Aas)
20) TFA/TIS/H2O

Figure S1.

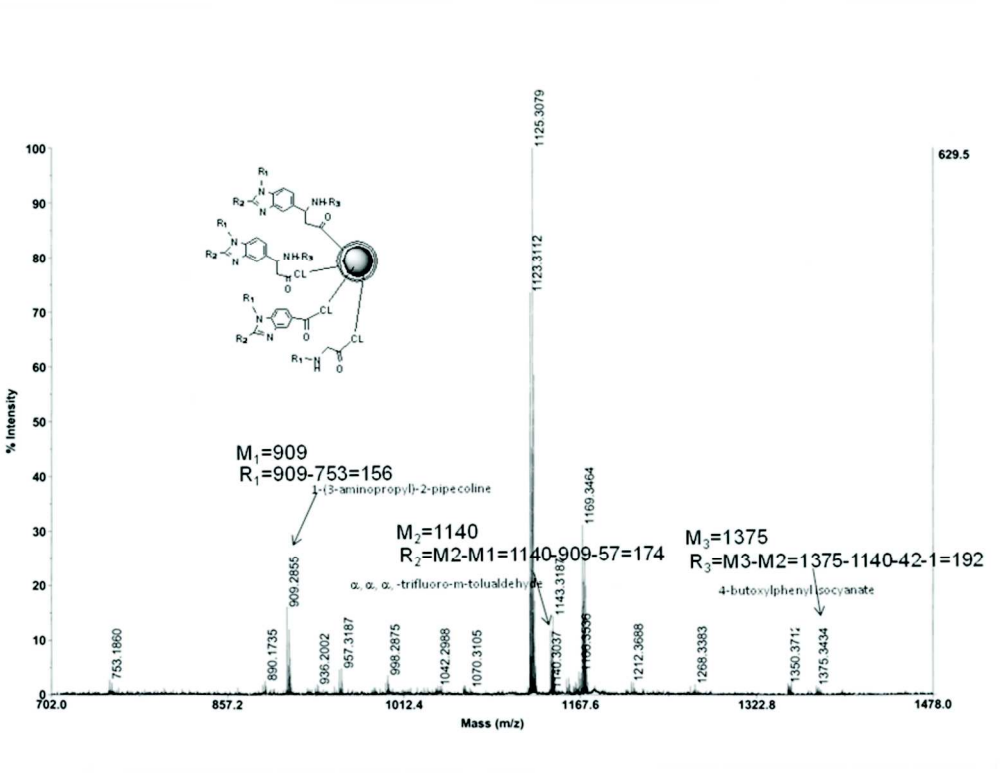
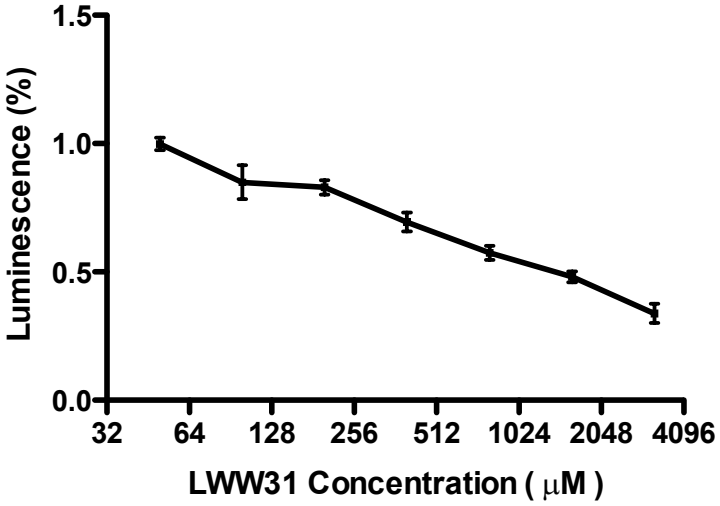

1125.3079
629.5
1123.3112
1169.3464
M1=909
R1=909-753=156
1-(3-aminopropyl)-2-pipecoline
M2=1140
R2=M2-M1=1140-909-57=174
α, α, α, -trifluoro-m-tolualdehyde
M3=1375
R3=M3-M2=1375-1140-42-1=192
4-butoxylphenyl isocyanate
909.2855
1143.3183
753.1860
890.1735
936.2002
957.3187
998.2875
1042.2988
1070.3105
1140.3037
1212.3688
1268.3383
1350.3713
1375.3434
% Intensity
Mass (m/z)
100
90
80
70
60
50
40
30
20
10
0
702.0
857.2
1012.4
1167.6
1322.8
1478.0

Figure S2.


1.5
1.0
0.5
0.0
Luminescence (%)
32
64
128
256
512
1024
2048
4096
LWW31 Concentration (μM)