SUPPORTING INFORMATION

Zebrafish aquaculture and husbandry. All zebrafish (Danio rerio) procedures were performed on embryos obtained from wildtype AB fish (Zebrafish International Resource Center), in compliance with protocol 10511 approved by the Institutional Animal Care and Use Committee of the Stanford University School of Medicine. Embryos used in these studies were obtained by natural matings and cultured in E3 embryo medium at 28.5 °C.

Zebrafish imaging. To permit live imaging of zebrafish at 24 hours post fertilization (hpf), the embryos were manually dechorionated and immobilized in E3 medium containing 0.2% (w/v) low-melt agarose and 0.05% (w/v) tricaine mesylate. Brightfield images were acquired using a Leica M205FA fluorescence stereoscope equipped with a Leica DFC500 digital camera. For imaging of 12-hpf fixed zebrafish, the embryos were mounted in 100% glycerol.

MO and cMO microinjections. MO and cMO solutions containing 100 mM KCl and 0.1% (w/v) phenol red were prepared. Each solution was heated to 100 °C for 30 seconds to dissociate MO aggregates. One to four-cell stage zebrafish embryos were microinjected with this solution (2 nL/embryo). All injections were conducted in E3 medium according to standard procedures, and the embryos were subsequently cultured in E3 medium at 28.5 °C.

cMOs photoactivation. Zebrafish embryos were arrayed in an agarose microinjection template (560-μm x 960-μm wells), with the animal pole facing the light source. To irradiate the cMO-injected embryos with 365-nm light, mercury lamp light was focused onto individual embryos.
for 10 seconds, using a Leica DM4500B compound microscope equipped with an HCX APO 20x/0.5 NA water-immersion objective and a narrow-band DAPI filter cube (Ex: 365 nm, 10-nm bandpass; Chroma). Embryos were similarly irradiated with 470-nm light for 30 seconds, using a GFP filter cube (Ex: 470 nm, 40-nm bandpass; Leica). To irradiate embryos with 405-nm light, a Zeiss LSM700 confocal microscope equipped with a solid-state 405-nm laser and W N-Achroplan 20x/0.5 NA objective was used. The upper and lower limits of the z axis were set to span the entire animal cell mass, and each embryo was irradiated for 60 seconds in 10 optical sections with the maximum laser intensity. Light intensities for each photoactivation wavelength were measured using a digital energy meter (Thor Labs PM100D) and microscope slide sensor (Thor Labs S170C), yielding the following values: 365-nm mercury lamp, 41 mW/cm² (spot diameter = 2.0 mm); 470-nm mercury lamp, 64 mW/cm² (spot diameter = 2.0 mm); 405-nm laser, 230,000 W/cm² (point illumination mode; spot diameter = 0.990 µm; pixel dwell time = 3.15 µs).

**Whole-mount in situ hybridization.** Embryos were fixed at 12 hpf with 4% (w/v) paraformaldehyde in 1X PBS (overnight at 4 °C). Whole-mount in situ hybridization was then performed as previously described,[1] using a myod1 antisense riboprobe labeled with digoxigenin.[2]
**General synthetic procedures.** All reactions were carried out in flame-dried glassware under a nitrogen atmosphere and stirred magnetically. Reactions were monitored by thin layer chromatography (TLC), using glass-backed silica gel 60F254 (Merck or Sorbent Technologies, 250-µm thickness). Tetrahydrofuran, dioxane and toluene were distilled from sodium/benzophenone ketyl prior to use. Dichloromethane, dimethylformamide, acetonitrile, and methanol were distilled from calcium hydride and stored over 4 Å molecular sieves. Other reagents and solvents obtained from commercial sources were stored under nitrogen and used directly without further purification. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Flash chromatography was performed with silica gel (EM Science silica gel 60 Å, 70-230 mesh; Sorbtech silica gel 60 Å, 230-400 mesh) as a stationary phase. The $^1$H NMR and $^{13}$C NMR spectra were recorded on a 300 MHz or 400 MHz Varian NMR spectrometer, and chemical shifts are in δ units (ppm). Electrospray (ESI) mass spectra were obtained using a Micromass ZQ single quadrupole liquid chromatography-mass spectrometer (LC-MS) or a Micromass Q-TOF hybrid quadrupole LC-MS.

**Synthesis of the 4,5-dimethoxy-2-nitrobenzyl (DMNB) linker**

The DMNB bifunctional linker was synthesized as previously described.$^{[3]}$
Synthesis of the 2-nitrobenzyl (NB) linker

2-Hydroxy-2-(2-nitrophenyl)ethyl 4-methylbenzenesulfonate. To a stirred solution of 1-(2-nitrophenyl)ethane-1,2-diol (1) (500 mg, 2.73 mmol) in dry pyridine (4 mL) was added p-toluenesulfonyl chloride (712 mg, 3.73 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 hours and pyridine was removed in vacuo. The resulting residue was dissolved in EtOAc (50 mL), washed with cold aq. 1N HCl and concentrated aq. NaCl, and dried over anhydrous Na₂SO₄. The solvents were removed in vacuo and the monotosylated product was purified by silica gel chromatography (CHCl₃/acetone, stepwise gradient from 1:0 to 20:1) to yield 2-hydroxy-2-(2-nitrophenyl)ethyl 4-methylbenzenesulfonate as colorless flakes (910 mg, 99%). 

1H NMR (400 MHz, CDCl₃) δ = 2.43 (s, 3H), 3.19 (brs, 1H), 4.14 (m, 1H), 4.37 (m, 1H), 5.52 (m, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.46 (m, 1H), 7.65 (m, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.84 (m, 1H), 7.94 (m, 1H). HRMS-ESI: m/z calculated for C₁₅H₁₅NNaO₆S [M + Na]⁺: 360.0502; observed: 360.0512.
2-(Methylamino)-1-(2-nitrophenyl)ethan-1-ol (2). A solution of 2-hydroxy-2-(2-nitrophenyl)ethyl 4-methylbenzenesulfonate (350 mg, 1.04 mmol) and methylamine (10.0 mL of a 2.0 M solution in THF, 20.0 mmol) was stirred overnight at 80 °C. The solvent was removed in vacuo, the residue was co-evaporated twice with MeOH, triturated with dry diethyl ether, and dried in vacuo to yield the tosylate salt of 2 as a colorless solid (346 mg, 91%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 2.32 (s, 3H), 2.48 (brs, 1H), 2.67 (s, 3H), 2.95 (m, 1H), 3.22 (m, 1H), 5.56 (m, 1H), 6.34 (brs, 2H), 7.08 (d, $J$ = 7.6 Hz, 2H), 7.40 (m, 1H), 7.59 (m, 1H), 7.66 (d, $J$ = 7.6 Hz, 2H), 7.88 (m, 1H), 7.93 (m, 1H). HRMS-ESI: m/z calculated for C$_9$H$_{13}$N$_2$O$_3$ [M + H]$^+$: 197.0927; observed: 197.0921.

Methyl 6-((2-hydroxy-2-(2-nitrophenyl)ethyl)(methyl)amino)-6-oxohexanoate (3). The tosylate salt of 2 (346 mg, 0.94 mmol) and N,N-diisopropylethylamine (435 µL, 2.45 mmol) were dissolved in anhydrous CH$_2$Cl$_2$ (15 mL), and the solution was cooled to 0 °C. Methyl adipoyl chloride (298 µL, 1.84 mmol) was added over 10 min, and the reaction mixture was stirred for 4 hours at room temperature. After the solvent was removed in vacuo, the resulting residue was dissolved in EtOAc, washed twice with saturated aq. NaHCO$_3$, and then dried over anhydrous Na$_2$SO$_4$. The solvent was removed in vacuo, and the residue was purified by silica gel chromatography (CHCl$_3$/EtOAc, stepwise gradient from 1:0 to 5:1) to yield 3 as a colorless oil (130 mg, 41%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 1.68-1.62 (m, 4H), 2.39-2.29 (m, 4H), 3.04 (s, 3H), 3.41 (m, 1H), 3.64 (brs, 3H), 4.05 (m, 1H), 5.43 (m, 1H), 5.63 (brs, 1H), 7.42 (m, 1H), 7.66 (m, 1H), 7.95 (m, 1H), 7.97 (m, 1H). HRMS-ESI: m/z calculated for C$_{16}$H$_{23}$N$_2$O$_6$ [M + H]$^+$: 339.1546; observed: 339.1551.
Methyl 1-chloro-11-methyl-9-(2-nitrophenyl)-2,7,12-trioxo-8-oxa-3,6,11-triazaheptadecan-17-oate (4). Compound 3 (130 mg, 0.384 mmol) was dissolved in anhydrous CH₂Cl₂ (900 µL) and added to 1,1′-carbonyldiimidazole (156 mg, 0.961 mmol) in anhydrous CH₂Cl₂ (1.30 mL). The reaction mixture was stirred for 3 hours at room temperature under nitrogen, diluted with CHCl₃, washed twice with water, and dried over anhydrous MgSO₄. The solvents were removed in vacuo to yield crude imidazole carbamate as a yellow gum (150 mg, 0.347 mmol). The imidazole carbamate (150 mg, 0.347 mmol) was dissolved in anhydrous CH₂Cl₂ (3.00 mL) and the solution was cooled to 0 °C. Ethylenediamine (68.5 µL, 1.03 mmol) was added, and the reaction mixture was stirred for 3 hours at room temperature under a nitrogen atmosphere. The solvent was removed in vacuo to yield the crude amine as a colorless oil (130 mg, 0.306 mmol). Without further purification, the obtained amine (130 mg, 0.306 mmol) was dissolved in anhydrous CH₂Cl₂ (2.70 mL) and triethylamine (279 µL, 2.00 mmol) and cooled to 0 °C. 2-Chloroacetyl chloride (62.0 µL, 0.797 mmol) dissolved in anhydrous CH₂Cl₂ (900 µL) was added slowly to this solution. The mixture was allowed to stir at room temperature for 20 minutes, at which time, 5% saturated aq. NaHCO₃ was added. The organic layer was separated, dried over anhydrous MgSO₄, the solvent was removed in vacuo, and the residue was purified by silica gel chromatography (CHCl₃, acetone, stepwise gradient from 1:0 to 1:1) to yield 4 as a colorless oil (100 mg, 65%). ¹H NMR (400 MHz, CDCl₃) δ = 1.74-1.58 (m, 4H), 2.42- 2.31 (m, 4H), 3.11 (m, 3H), 3.29 (m, 2H), 3.39 (m, 2H), 3.67 (brs, 3H), 3.85 (m, 2H), 3.99 (brs, 2H), 5.59 (brs, 1H), 6.42 (m, 1H), 7.18 (brs, 1H), 7.49 (m, 1H), 7.65 (m, 1H), 7.73 (m, 1H), 8.00 (m, 1H). HRMS-ESI: m/z calculated for C₂₁H₳₃ClN₄O₈ [M + H]⁺: 501.1736; observed: 501.1728.
**1-Chloro-11-methyl-9-(2-nitrophenyl)-2,7,12-trioxo-8-oxa-3,6,11-triazahexadecan-17-oic acid.** Compound 4 (100 mg, 0.200 mmol) was dissolved in THF (2.90 mL), cooled to 0 °C, and LiOH (9.24 mg, 0.220 mmol) in aqueous solution (3.86 mL) was added slowly. The reaction mixture was stirred at room temperature for 2 hours, diluted with EtOAc, washed with 2 M HCl (3.86 mL), and the organic layer was dried over MgSO₄. The solvents were removed *in vacuo* to afford the deprotected carboxylic acid as a colorless oil (96.4 mg, 99%). <sup>1</sup>H NMR (400 MHz, CDCl₃) δ = 1.78-1.62 (m, 4H), 2.43-2.32 (m, 4H), 3.15 (m, 3H), 3.26 (m, 2H), 3.37 (m, 2H), 3.98 (m, 2H), 4.11 (brs, 2H), 6.12 (brs, 1H), 6.40 (m, 1H), 7.19 (brs, 1H), 7.48 (m, 1H), 7.68 (m, 1H), 7.73 (m, 1H), 8.01 (m, 1H). HRMS-ESI: *m/z* calculated for C₂₀H₂₇ClN₄O₈Na [M + Na]<sup>+</sup>: 509.1410; observed: 509.1387.

**2,5-Dioxopyrrolidin-1-yl 1-chloro-11-methyl-9-(2-nitrophenyl)-2,7,12-trioxo-8-oxa-3,6,11-triazahexadecan-17-oate (5).** 1-Chloro-11-methyl-9-(2-nitrophenyl)-2,7,12-trioxo-8-oxa-3,6,11-triazahexadecan-17-oic acid (94.6 mg, 0.195 mmol), N,N’-disuccinimidyl carbonate (200 mg, 0.781 mmol) and pyridine (172 µL, 2.14 mmol) were dissolved in CH₃CN (2.40 mL) and stirred at room temperature overnight. The reaction mixture was diluted with EtOAc, washed with 0.1 M aq. HCl and saturated aq. NaHCO₃, and the organic layer was dried over anhydrous MgSO₄. The solvents were removed *in vacuo*, and the residue was purified by silica gel chromatography (CHCl₃/acetone, stepwise gradient from 1/0 to 1/1) to yield 5 as a colorless oil (72.0 mg, 63%). <sup>1</sup>H NMR (400 MHz, CDCl₃) δ = 1.86-1.66 (m, 4H), 2.44-2.35 (m, 4H), 2.92-2.85 (m, 4H), 3.15 (m, 3H), 3.32 (m, 2H), 3.39 (m, 2H), 4.00 (m, 2H), 4.14 (brs, 2H), 5.45 (brs, 1H), 6.44 (m, 1H), 7.15 (brs, 1H), 7.52 (m, 1H), 7.69 (m, 1H), 7.74 (m, 1H), 8.03 (m, 1H). HRMS-ESI: *m/z* calculated for C₂₄H₃₁ClN₅O₁₀ [M + H]<sup>+</sup>: 584.1754; observed: 584.1752.
Synthesis of the 7-diethylamino-coumarin-4-yl-methyl (DEACM) linker

7-Diethylamino-2-oxo-2H-chromene-4-carbaldehyde (7) was prepared according to a previously reported procedure with minor modification.[4] Selenium oxide (3.32 g, 30.0 mmol) was added to a solution of 7-diethylamino-4-methylcoumarin 6 (4.64 g, 20.0 mmol) in 120 mL of dioxane. The reaction was heated to reflux overnight and then filtered through celite. The filtrate was concentrated under reduced pressure and the crude product was purified by silica gel chromatography eluting with hexane/EtOAc (4:1), affording 7 as a red solid (2.06 g, 42%). 1H NMR (300 MHz, CDCl3): δ = 1.12-1.20 (t, J = 7.2 Hz, 6H), 3.33-3.40 (q, J = 7.2 Hz, 4H), 6.36 (s, 1H), 6.42-6.43 (d, J = 2.7 Hz, 1H), 6.53-6.57 (dd, Jₐ = 9.0 Hz, J₉b = 2.7 Hz, 1H), 8.19-8.22 (d, J = 2.7 Hz, 1H), 10.95 (s, 1H). 13C NMR (400 MHz, CDCl3): δ = 12.4, 44.7, 97.4, 103.6, 109.4, 117.1, 126.9, 143.7, 150.9, 157.3, 161.7, 192.5. HRMS-ESI: m/z calculated for C₁₄H₁₅NO₃ [M + H]⁺: 246.1130; observed: 246.1130.

7-Diethylamino-4-(1-hydroxybut-3-en-1-yl)-2H-chromen-2-one (8). Allyltri-n-butyl tin (0.99 mL, 3.00 mmol) and zinc chloride (409 mg, 3.00 mmol) were added to a solution of the
aldehyde 7 (500 mg, 2.00 mmol) in 10 mL of CH$_3$CN/water (4:1). The reaction mixture was stirred overnight at room temperature. The mixture was concentrated under reduced pressure, the residue was taken up in water (10 mL), and was extracted with CH$_2$Cl$_2$ (3 x 10 mL). The organic layers were combined, washed with brine (10 mL), dried over Na$_2$SO$_4$, and concentrated. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (1:1), affording 8 as a green solid (477 mg, 83%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.14$-$1.18$ (t, $J=$ 7.2 Hz, 6H), 2.38-$2.45$ (m, 1H), 2.57-$2.63$ (m, 1H), 3.33-$3.38$ (q, $J=$ 7.2 Hz, 4H), 4.97-$5.00$ (dd, $J_a=$ 8.0 Hz, $J_b=$ 4.0 Hz, 1H), 5.10-$5.17$ (m, 2H), 5.81-$5.90$ (m, 1H), 6.22 (s, 1H), 6.40-$6.41$ (d, $J=$ 2.4 Hz, 1H), 6.52-$6.55$ (dd, $J_a=$ 9.2 Hz, $J_b=$ 2.4 Hz, 1H), 7.36-$7.38$ (d, $J=$ 9.2 Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta =$ 12.5, 41.6, 44.7, 68.7, 97.8, 105.1, 106.2, 108.6, 118.8, 124.9, 133.6, 150.3, 156.4, 158.2, 163.0. HRMS-ESI: m/z calculated for C$_{17}$H$_{21}$NO$_3$ [M + H]$^+$: 288.1660; observed: 288.1602.

4-(1-((tert-Butyldimethylsilyl)oxy)but-3-en-1-yl)-7-diethylamino-2H-chromen-2-one.

TBDMSCl (904 mg, 6.00 mmol) and imidazole (612 mg, 9.00 mmol) were added to a solution of the alcohol 8 (862 mg, 3.00 mmol) in DMF (3.4 mL). The reaction was stirred overnight at room temperature and then quenched with saturated aq. NaHCO$_3$ (15 mL). The aqueous phase was extracted with EtOAc (3 x 10 mL). The organic layers were combined, washed with water (15 mL) and brine (10 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (4:1), affording the TBDMS-protected compound as a yellow solid (1.16 g, 97%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 0.03 (s, 6H), 0.86 (s, 9H), 1.13-1.16 (t, $J=$ 7.2 Hz, 6H), 2.38-2.48 (m, 2H), 3.32-3.37 (q, $J=$ 7.2 Hz, 4H), 4.85-4.88 (m, 1H), 4.97-5.02 (m, 2H), 6.13 (s, 1H), 6.13-6.14 (s, 1H),
6.45-6.46 (d, $J = 2.8$ Hz, 1H), 6.52-6.55 (dd, $J_a = 9.2$ Hz, $J_b = 2.8$ Hz, 1H), 7.43-7.45 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): δ = -5.1, -4.8, -3.6, 12.4, 18.0, 25.7, 42.9, 44.6, 71.0, 97.8, 105.7, 105.9, 108.4, 117.8, 125.2, 133.8, 150.2, 156.5, 158.3, 162.7. HRMS-ESI: m/z calculated for $\text{C}_{23}\text{H}_{35}\text{NO}_3\text{Si} [\text{M} + \text{H}]^+$: 402.2464; observed: 402.2468.

4-(1-((tert-Butyldimethylsilyl)oxy)-4-hydroxybutyl)-7-diethylamino-2H-chromen-2-one (9).

A 2 M solution of BH$_3$•Me$_2$S in THF (0.50 mL, 1.0 mmol) was added to a solution of the TBDMS-protected alkene from the previous step (80 mg, 0.20 mmol) in THF (0.7 mL) at 0 °C and the mixture was stirred for 3 hours at 0 °C. Then, 3 M aq. NaOH (0.5 mL) and 30% hydrogen peroxide in water (0.4 mL) were added. The mixture was allowed to warm to room temperature over 2 hours and was extracted with EtOAc (3 x 2 mL). The organic layers were combined, washed with water (2 mL) and brine (2 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (1:1), affording 9 as a yellow solid (41 mg, 49%). $^1$H NMR (400 MHz, CDCl$_3$): δ = -0.04 (s, 3H) 0.08 (s, 3H), 0.91 (s, 9H), 1.18-1.21 (t, $J = 7.2$ Hz, 6H), 1.62-1.90 (m, 5H), 3.37-3.42 (q, $J = 7.2$ Hz, 3H), 3.62-3.67 (m, 2H), 4.91-4.93 (dd, $J_a = 6.4$ Hz, $J_b = 4.0$ Hz, 1H), 6.17 (s, 1H), 6.49-6.50 (d, $J = 2.8$ Hz, 1H), 6.54-6.57 (dd, $J_a = 9.2$ Hz, $J_b = 2.8$ Hz, 1H), 7.47-7.49 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): δ = -5.0, -4.6, 12.6, 18.3, 25.9, 28.5, 34.5, 44.8, 62.7, 71.0, 97.9, 105.9, 106.1, 108.5, 125.4, 150.3, 156.6, 158.7, 162.7. HRMS-ESI: m/z calculated for $\text{C}_{23}\text{H}_{37}\text{NO}_4\text{Si} [\text{M} + \text{H}]^+$: 420.2570; observed: 408.4193.
4-((tert-Butyldimethylsilyl)oxy)-4-(7-diethylamino-2-oxo-2H-chromen-4-yl)butyl (2-(2-chloroacetamido)ethyl)carbamate (10). 1,1′-Carbonyldiimidazole (45 mg, 0.28 mmol) was added to a solution of the alcohol 9 (47 mg, 0.11 mmol) in CH$_2$Cl$_2$ (3 mL). The reaction mixture was stirred at room temperature for 3 hours and then diluted with CH$_2$Cl$_2$ (2 mL). The solution was washed with water (5 mL) and brine (5 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was confirmed by $^1$H NMR and used in next step without further purification. The activated alcohol was dissolved in CH$_2$Cl$_2$ (2.5 mL) and ethylenediamine (16 µL, 0.25 mmol) was added. The resulting mixture was stirred for 2 hours at room temperature. The solvent was removed under reduced pressure and the crude product was confirmed by $^1$H NMR and subjected to next step without further purification. The amine residue was redissolved in CH$_2$Cl$_2$ (2 mL), DIPEA (8 µl, 0.05 mmol) was added, and the mixture was stirred at room temperature for 10 minutes and then cooled to 0 °C. 2-Chloroacetyl chloride (16 µL, 0.20 mmol) was added and the solution was stirred at 0 °C for 10 minutes. The reaction was quenched with saturated aq. NaHCO$_3$ (2 mL) and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 2 mL). The organic layers were combined, washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (1:1), affording 10 as a yellow foam (42 mg, 65%).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = -0.04 (s, 3H) 0.08 (s, 3H), 0.91 (s, 9H), 1.18-1.22 (t, $J$ = 7.2 Hz, 6H), 1.71-1.80 (m, 4H), 3.35-3.43 (m, 8H), 4.03 (s, 2H), 4.05-4.06 (m, 2H), 4.89 (m, 1H), 5.04 (m, 1H), 6.17 (s, 1H), 6.50-6.51 (d, $J_a$ = 2.8 Hz, 1H), 6.54-6.57 (dd, $J_a = 8.8$ Hz, $J_b = 2.4$ Hz, 1H), 7.13 (br, 1H), 7.44-7.47 (d, $J = 8.8$ Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta$ = -5.0, -4.5, 12.6, 18.3, 24.9, 25.9, 29.8, 34.6, 40.5, 40.8, 42.6, 44.8, 64.9, 70.8, 97.9, 105.9, 106.1, 108.4, 125.3, 150.4, 156.7, 157.4, 158.4, 162.7, 166.9. HRMS-ESI: $m/z$ calculated for
4-(7-Diethylamino-2-oxo-2H-chromen-4-yl)-4-hydroxybutyl (2-(2-chloroacetamido)ethyl) carbamate. A 1 M TBAF solution in THF (0.1 mL, 0.1 mmol) was added to a solution of 10 (38 mg, 0.060 mmol) in THF (1.5 mL). The reaction mixture was stirred at room temperature for 1 hour and then concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with CHCl₃/acetone (1:1), affording the deprotected alcohol as a yellow foam in 44% yield (13 mg, 0.03 mmol). ¹H NMR (400 MHz, CDCl₃): δ = 1.17-1.21 (t, J = 7.2 Hz, 6H), 1.80-1.90 (m, 4H), 3.34-3.45 (m, 9H), 4.03 (s, 2H), 4.10-4.13 (m, 2H), 5.01 (m, 1H), 5.44 (m, 1H), 6.25 (s, 1H), 6.45-6.46 (d, J = 2.0 Hz, 1H), 6.54-6.57 (dd, Jₐ = 9.2 Hz, Jₖ = 2.4 Hz, 1H), 7.21 (br, 1H), 7.37-7.39 (d, J = 9.2 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ = 12.6, 25.3, 33.7, 40.6, 40.7, 42.7, 44.8, 64.9, 69.3, 97.9, 105.1, 106.2, 108.7, 125.1, 150.5, 156.5, 157.5, 158.9, 163.1, 167.2. HRMS-ESI: m/z calculated for C₂₂H₃₀ClN₃O₆ [M + H]⁺: 468.1901; observed: 468.1870.

4-(7-Diethylamino-2-oxo-2H-chromen-4-yl)-4-(((2,5-dioxopyrrolidin-1-yl)oxy)carbonyl)oxy)butyl (2-(2-chloroacetamido)ethyl)carbamate (11). N,N’-Disuccinimidyl carbonate (36 mg, 0.14 mmol) and a catalytic amount of DMAP were added to a solution of the alcohol from the previous step (13 mg, 0.030 mmol) in CH₂Cl₂ (0.5 mL). The reaction mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with CH₂Cl₂/acetone (2:1), affording 11 as a yellow solid (15 mg, 82%). ¹H NMR (400 MHz, CDCl₃): δ = 1.19-1.22 (t, J = 7.2 Hz, 6H), 1.72-1.86 (m, 2H), 2.10-2.14 (m, 2H), 2.84 (s, 4H), 3.35-3.42 (m, 8H), 4.03 (s, 2H), 4.15-
4.18 (t, $J = 7.2$ Hz, 2H), 5.43 (m, 1H), 5.96-5.99 (t, $J = 6.0$ Hz, 1H), 6.15 (s, 1H), 6.51-6.52 (d, $J = 2.8$ Hz, 1H), 6.59-6.63 (dd, $J_a = 9.2$ Hz, $J_b = 2.8$ Hz, 1H), 7.18 (br, 1H), 7.33-7.35 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta = 12.5$, 14.3, 24.3, 25.5, 25.6, 31.9, 40.3, 42.6, 44.9, 64.5, 78.3, 98.2, 105.1, 124.6, 150.9, 151.2, 151.6, 156.7, 161.8, 167.3, 172.2.

HRMS-ESI: $m/z$ calculated for C$_{27}$H$_{33}$ClN$_4$O$_{10}$ [M + H]$^+$: 609.1963; observed: 609.1990.

**Synthesis of the 4-diethylamino-coumarylidene malononitrilemethyl (DEACM-MN) linker**

$\text{HOOC} - \text{NH}_2 \xrightarrow{\text{SOCl}_2/\text{MeOH}} \text{MeOOC} - \text{NH}_2 \xrightarrow{\text{Cl} - \text{Cl}} \text{MeOOC} - \text{N} - \text{Cl}$

Methyl 6-(2-chloroacetamido)hexanoate. DIPEA (104 µl, 0.600 mmol) was added to a solution of methyl-6-aminohexanoate hydrochloride (36 mg, 0.20 mmol) in CH$_2$Cl$_2$ (2 mL). The mixture was stirred at room temperature for 10 minutes and then cooled to 0 °C. 2-Chloroacetyl chloride (45 µL, 0.40 mmol) was added and the mixture was stirred at 0 °C for 10 minutes. The reaction
was quenched with saturated aq. NaHCO₃ (1 mL) and the aqueous layer was extracted with CH₂Cl₂ (3 x 2 mL). The organic layers were combined, washed with brine (2 mL), dried over Na₂SO₄, and concentrated under reduced pressure, affording methyl 6-(2-chloroacetamido)hexanoate as a light yellow oil (42 mg, 96%). ¹H NMR (300 MHz, CDCl₃): δ = 1.29-1.67 (m, 6 H), 2.28-2.33 (t, J = 7.2 Hz, 2H), 3.25-3.33 (q, J = 6.9 Hz, 2H), 3.64 (s, 3H), 4.03 (s, 2H). ¹³C NMR (400 MHz, CDCl₃): δ = 24.5, 26.4, 29.1, 33.1, 39.7, 42.8, 51.6, 165.9, 174.1. HRMS-ESI: m/z calculated for C₉H₁₆ClNO₃ [M - H]: 220.0735; observed: 220.0743.

6-(2-Chloroacetamido)hexanoic acid. A 2 M solution of LiOH in water (0.5 mL, 1 mmol) was added to a solution of methyl 6-(2-chloroacetamido)hexanoate (44 mg, 0.20 mmol) in MeOH (0.5 mL). The mixture was stirred at room temperature for 1 hour and then concentrated under reduced pressure. The residue was dissolved in water (1 mL), acidified to pH 3-4 with 1 M citric acid, and extracted with EtOAc (3 x 1 mL). The organic layers were combined, washed with brine (2 mL), dried over Na₂SO₄, and concentrated under reduced pressure, affording 6-(2-chloroacetamido)hexanoic acid as an off-white solid (32 mg, 84%). ¹H NMR (400 MHz, CD₃CN): δ = 1.31-1.38 (m, 2 H), 1.47-1.63 (m, 4H), 2.25-2.31 (t, J = 7.2 Hz, 2H), 3.18-3.22 (q, J = 6.8 Hz, 2H), 4.02 (s, 2H). ¹³C NMR (400 MHz, CD₃CN): δ = 25.1, 26.8, 29.6, 34.0, 40.0, 43.6, 167.2, 175.4. HRMS-ESI: m/z calculated for C₈H₁₄ClNO₃ [M - H]: 206.0581; observed: 206.0578.
7-Diethylamino-4-(1-hydroxy-2-nitroethyl)-2H-chromen-2-one (12). Nitromethane (0.54 mL, 10 mmol) and N,N,N′,N′-tetramethylethylene diamine (45 µL, 0.30 mmol) were added to a solution of the aldehyde 7 (245 mg, 1.00 mmol) in THF (2 mL). The reaction mixture was stirred overnight at room temperature, quenched with water (3 mL), and extracted with EtOAc (3 x 3 mL). The organic layers were combined, washed with brine (5 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (3:2), affording 12 as an off-white solid (211 mg, 69%). ¹H NMR (300 MHz, CDCl₃): δ = 1.19-1.23 (t, J = 7.2 Hz, 6H), 3.37-3.44 (q, J = 7.2 Hz, 4H), 3.88 (s, 1H), 4.52-4.65 (m, 2H), 5.81 (br, 1H), 6.35 (s, 1H), 6.48-6.49 (d, J = 2.7 Hz, 1H), 6.58- 6.62 (dd, Jₐ = 9.0 Hz, J₉ = 2.7 Hz, 1H), 7.40-7.43 (d, J = 2.7 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ = 12.6, 45.0, 62.3, 80.0, 98.2, 105.2, 106.7, 109.4, 124.2, 151.0, 152.5, 156.7, 162.5. HRMS-ESI: m/z calculated for C₁₅H₁₈N₂O₅ [M + H]⁺: 307.1294; observed: 307.1298.
4-(1-((tert-Butyldimethylsilyl)oxy)-2-nitroethyl)-7-diethylamino-2H-chromen-2-one.

TBDMSCl (110 mg, 0.73 mmol) and imidazole (60 mg, 0.90 mmol) were added to a solution of alcohol 12 (140 mg, 0.46 mmol) in DMF (4.5 mL). The reaction was stirred overnight at room temperature and then quenched with saturated aq. NaHCO₃ (10 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL). The organic layers were combined, washed with water (5 mL) and brine (5 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (4:1), affording the silyl ether as an off-white solid (162 mg, 84%). ¹H NMR (300 MHz, CDCl₃): δ = -0.01 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.18-1.22 (t, J = 5.4 Hz, 6H), 3.38-3.44 (q, J = 5.4 Hz, 4H), 4.51-4.53 (d, J = 4.5 Hz, 2H), 5.67-5.70 (t, J = 4.5 Hz, 1H), 6.27 (s, 1H), 6.51-6.52 (d, J = 2.1 Hz, 1H), 6.61-6.63 (dd, Jₓ = 6.9 Hz, Jᵧ = 1.8 Hz, 1H), 7.49-7.51 (d, J = 6.6 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ = -5.3, -4.4, 12.8, 18.4, 25.9, 45.2, 69.7, 81.5, 98.5, 105.2, 107.4, 109.4, 124.4, 151.2, 152.8, 157.0, 162.0. HRMS-ESI: m/z calculated for C₂₁H₃₂N₂O₅Si [M + H]⁺: 421.2159; observed: 421.2173.

4-(1-((tert-Butyldimethylsilyl)oxy)-2-nitroethyl)-7-diethylamino-2H-chromene-2-thione (13). Lawesson’s reagent (161 mg, 0.15 mmol) was added to a solution of the silyl protected coumarin (42 mg, 0.10 mmol) in dry toluene (1 mL). The reaction mixture was heated to 90 °C for 24 hours and then concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (4:1), affording 13 as an orange solid (35 mg, 79%). ¹H NMR (300 MHz, CDCl₃): δ = -0.09 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.21-1.24 (t, J = 5.4 Hz, 6H), 3.41-3.46 (q, J = 5.4 Hz, 4H), 4.46-4.59 (m, 2H), 5.63-5.66 (t, J = 7.2 Hz, 1H), 6.68-6.71 (m, 2H), 7.13 (s, 1H), 7.57-7.58 (d, J = 7.2 Hz, 1H). ¹³C NMR (400 MHz,
CDCl₃: δ = -5.8, -4.7, 12.5, 18.2, 25.6, 45.1, 69.2, 80.9, 97.9, 107.2, 110.6, 121.1, 124.4, 144.1, 151.2, 159.5, 197.0. HRMS-ESI: m/z calculated for C₂₁H₃₂N₂O₄Si [M + H]⁺: 437.1930; observed: 437.1933.

2-(4-(1-((tert-Butyldimethylsilyl)oxy)-2-nitroethyl)-7-diethylamino-2H-chromen-2-ylidene)malononitrile (14). Silver nitrate (72 mg, 0.43 mmol) was added to a solution of the thiocoumarin 13 (74 mg, 0.17 mmol), malononitrile (13.5 mg, 1.20 mmol), and Et₃N (88 µL, 0.6 mmol) in dry CH₃CN (0.85 mL). The reaction mixture was stirred for 3 hours at room temperature and then concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with hexane/EtOAc (4:1), affording 14 as an orange solid with (72 mg, 89%). ¹H NMR (300 MHz, CDCl₃): δ = 0.02 (s, 3H), 0.08 (s, 3H), 0.91 (s, 9H), 1.23-1.27 (t, J = 5.4 Hz, 6H), 3.44-3.49 (q, J = 5.4 Hz, 4H), 4.51-4.53 (m, 2H), 5.71-5.74 (t, J = 4.8 Hz, 1H), 6.62-6.63 (d, J = 1.5 Hz, 1H), 6.69-6.72 (dd, Jₐ = 6.9 Hz, Jₜ = 1.5 Hz, 1H), 6.94 (s, 1H), 7.51-7.53 (d, J = 6.9 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ = -5.3, -4.6, 12.6, 18.1, 25.6, 45.2, 56.6, 68.9, 81.0, 97.9, 105.9, 106.6, 111.0, 113.6, 114.2, 124.5, 148.9, 151.9, 155.3, 171.7. HRMS-ESI: m/z calculated for C₂₄H₃₂N₄O₄Si [M + H]⁺: 469.2271; observed: 469.2274.

2-(4-(2-Amino-1-((tert-butyldimethylsilyl)oxy)ethyl)-7-diethylamino-2H-chromen-2-ylidene)malononitrile. Zinc powder (167 mg, 2.50 mmol) was added to a solution of the coumarin 14 (30 mg, 0.06 mmol) in acetic acid (2 mL). The reaction mixture was stirred at room temperature for 1 hour and then filtered through celite. The solution was neutralized to pH 7.0 by adding saturated aq. NaHCO₃, and the aqueous layer was extracted with EtOAc (3 x 1 mL). The organic layers were combined, washed with water (2 mL) and brine (2 mL), dried over Na₂SO₄,
and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with CHCl₃/MeOH (9:1), affording the primary amine as a red solid (20 mg, 70%). ¹H NMR (400 MHz, CDCl₃): δ = 0.02 (s, 3H), 0.13 (s, 3H), 0.96 (s, 9H), 1.21-1.25 (t, J = 5.4 Hz, 6H), 2.24 (s, 2H), 2.89-2.93 (m, 1H), 3.05-3.08 (m, 1H), 3.42-3.47 (q, J = 5.4 Hz, 4H), 5.06 (br, 1H), 6.59-6.60 (d, J = 1.5 Hz, 1H), 6.64-6.66 (dd, Jₐ = 6.9 Hz, Jₖ = 1.5 Hz, 1H), 6.88 (s, 1H), 7.49-7.51 (d, J = 6.9 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ = 4.9, 4.5, 12.6, 18.2, 25.8, 45.0, 48.2, 55.6, 71.3, 97.6, 106.1, 106.9, 111.7, 114.2, 114.7, 125.4, 152.9, 155.3, 171.9. HRMS-ESI: m/z calculated for C₂₄H₃₄N₄O₂Si [M + H]⁺: 439.2524; observed: 439.2525.

N-(2-((tert-Butyldimethylsilyl)oxy)-2-((dicyanomethylene)-7-diethylamino-2H-chromen-4-yl)ethyl)-6-(2-chloroacetamido)hexanamide (15). DIPEA (9.9 µl, 0.054 mmol) followed by HATU (13.7 mg, 0.043 mmol) were added to a solution of the amine from the previous step (15 mg, 0.036 mmol) and 6-(2-chloroacetamido)hexanoic acid (8.9 mg, 0.043 mmol) in THF (0.4 mL). The reaction mixture was stirred for 1 hour at room temperature and then quenched with saturated aq. NaHCO₃ (1 mL). The mixture was then extracted with EtOAc (3 x 1 mL). Organic layers were combined, washed with water (2 mL) and brine (2 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with CH₂Cl₂/acetone (9:1), affording 15 as an orange film (10.3 mg, 44%). ¹H NMR (300 MHz, CDCl₃): δ = 0.01 (s, 3H), 0.06 (s, 3H), 0.96 (s, 9H), 1.21-1.25 (t, J = 7.2 Hz, 6H), 1.40-1.60 (m, 6H), 2.23-2.29 (t, J = 7.8 Hz, 2H), 2.90-2.98 (m, 1H), 3.30-3.36 (m, 2H), 3.41-3.48 (q, J = 7.2 Hz, 4H), 3.81-3.91 (m, 1H), 4.05 (s, 2H), 5.18-5.20 (m, 1H), 5.96 (m, 1H), 6.59-6.60 (d, J = 3.0 Hz, 1H), 6.73-6.77 (dd, Jₐ = 9.3 Hz, Jₖ = 2.7 Hz, 1H), 6.91 (s, 1H),
7.87-7.91 (d, J = 9.3 Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): δ = -4.6, -4.7, 12.5, 18.1, 24.1, 25.8, 26.0, 28.9, 31.0, 39.5, 42.8, 44.9, 54.3, 69.3, 97.2, 105.4, 107.1, 111.1, 114.3, 114.9, 125.9, 151.8, 155.1, 166.1, 172.1, 173.8. HRMS-ESI: m/z calculated for C$_{21}$H$_{32}$N$_2$O$_5$Si [M + H]$^+$: 628.3086; observed: 628.3058.

2-(6-(2-Chloroacetamido)hexanamido)-1-(2-(dicyanomethylene)-7-diethylamino-2H-chromen-4-yl)ethyl (2,5-dioxopyrrolidin-1-yl) carbonate (16). A 1 M TBAF solution in THF (24 µL, 0.024 mmol) was added to a solution of the silyl ether 15 (10.3 mg, 0.016 mmol) at 0 °C in THF (0.5 ml). The reaction mixture was stirred at 0 °C for 1 hour, and then N,N'-disuccinimidyl carbonate (5.8 mg, 0.023 mmol) was added followed by DIPEA (4 µL, 0.03 mmol). The solution was stirred for 2 hours at room temperature and concentrated under reduced pressure. The crude product was purified by silica gel chromatography eluting with Et$_2$O/acetone (2:1), affording 16 as an orange foam (3.1 mg, 32%). $^1$H NMR (400 MHz, CDCl$_3$): δ = 1.21-1.25 (t, J = 7.2 Hz, 6H), 1.40-1.60 (m, 6H), 2.25-2.31 (m, 2H), 2.76 (s, 4H), 3.20-3.36 (m, 4H), 3.41-3.48 (m, 4H), 4.03 (s, 2H), 6.31-6.38 (m, 2H), 6.58-6.59 (d, J = 3.0 Hz, 1H), 6.72-6.78 (m, 2H), 7.91-7.93 (d, J = 9.3 Hz, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): δ = 12.5, 24.1, 25.8, 26.3, 28.9, 29.9, 39.5, 42.4, 45.2, 54.3, 69.3, 97.2, 105.4, 107.1, 111.1, 114.3, 114.9, 125.9, 151.8, 152.2, 155.1, 166.1, 167.9, 172.1, 173.8. HRMS-ESI: m/z calculated for C$_{31}$H$_{36}$ClN$_6$O$_8$ [M + H]$^+$: 655.2278; observed: 655.2282.

**Cyclic MO synthesis**

**DMNB cyclic nita cMO.** The cyclic nita cMO bearing a DMNB chromophore was synthesized as previously described,[3] using a 25-base nita MO oligomer with 5’-amine and 3’-disulfide modifications (5’-GACTTGAGGCAGACATATTTCCGAT-3’) (Gene-Tools, LLC).
**NB cyclic ntla cMO.** Synthetic procedures identical to those for the DMNB cyclic ntla cMO were followed, except for an additional purification step. The 25-base ntla MO oligomer with 5’-amine and 3’-disulfide functionalization (50.0 nmol) was dissolved in 0.1 M Na₂B₄O₇, pH 8.5 (100 µL). The photocleavable linker 5 (172 nmol) was added to this solution in DMSO (15.0 µL), and the reaction was shaken overnight in the dark. The reaction mixture was then purified on a NAP-5 gel-filtration column and lyophilized, and the resulting white solid was dissolved in 200 µL of water. Acetic acid (2.00 µL) was added to the solution, which was then washed with CHCl₃ (3 x 200 µL), washed with EtOAc (2 x 200 µL), and neutralized with 10% aq. NH₄OH. The solution was lyophilized to dryness, affording the linear NB linker-ntla MO intermediate (39.0 nmol, 78%) as a white solid. MS-ESI (m/z): [M+H]⁺ calculated for C₃₄₅H₅₂₉N₁₅₇O₁₁₂P₂₅S₂Cl, 9542; observed 9542.

Resin-immobilized TCEP (100 µL) (Pierce Biotechnology, Inc.) was washed with 0.1 M Tris-HCl buffer, pH 8.4 (3 x 100 µL) in a centrifuge filter tube. The DEACM-ntla MO intermediate (41.7 nmol) was dissolved in 0.1 M Tris-HCl buffer, pH 8.4 (100 µL) and added to the washed gel, and the reaction was shaken overnight in the dark. The supernatant was collected by centrifugation at 1,000 g for 30 seconds. The gel slurry was washed with 0.1 M Tris-HCl buffer, pH 8.4 (3 x 100 µL), and the eluted fractions were combined with the supernatant. This mixture was lyophilized down to 100 µL, and the solution was applied to 100 µL of SulfoLink Coupling Resin (Thermo Scientific) in a centrifuge filter tube. The resin was shaken for 15 minutes at room temperature and then stood upright without shaking for 30 minutes at room temperature. The supernatant was collected by centrifugation at 1,000 g for 30 seconds. The gel slurry was
washed by 0.1 M Tris-HCl buffer pH 8.4 (3 x 100 µL) and washed fractions were combined with the supernatant. The mixture was purified on a NAP-5 column and lyophilized to afford the cyclized cMO (27.7 nmol, 71%). MS- ESI: m/z calculated for C_{333}H_{513}N_{156}O_{111}P_{25}S [M + H]^+: 9284; observed: 9285.

**DEACM cyclic ntlα cMO.** Synthetic procedures identical to those for the NB cyclic ntlα cMO were applied to a DEACM cMO targeting ntlα, using the photocleavable linker 11. The linear DEACM-linker-ntlα MO intermediate was obtained in 83% yield. MS-ESI: m/z calculated for C_{340}H_{523}N_{156}O_{112}P_{25}S_{2}Cl [M+H]^+: 9464; observed: 9464. The cyclized cMO was obtained in 39% yield. MS-ESI: m/z calculated for C_{336}H_{516}N_{155}O_{111}P_{25}S [M + H]^+: 9310; observed: 9310.

**DEACM-MN cyclic ntlα cMO.** Synthetic procedures identical to those for the NB cyclic ntlα cMO were applied to a DEACM-MN cMO targeting ntlα, using the photocleavable linker 16. The linear DEACM-MN linker-ntlα MO intermediate was obtained in 68% yield. MS-ESI (m/z): [M+H]^+ calculated for C_{344}H_{527}N_{158}O_{110}P_{25}S_{2}Cl, 9510; observed 9508. The cyclized cMO was obtained in 35% yield. MS-ESI: m/z calculated for C_{340}H_{518}N_{157}O_{109}P_{25}S [M + H]^+: 9356; observed: 9356.

**DEACM cyclic flh cMO.** Synthetic procedures identical to those for the DEACM cyclic ntlα cMO were applied to a DEACM cMO targeting flh, using a 25-base flh MO oligomer with 5’-amine and 3’-disulfide modifications (5’-GGGAATCTGCGATGGCCTGCTGTTTAG-3’) (GeneTools, LLC). The linear DEACM linker-flh MO intermediate was obtained in 70% yield. MS-ESI (m/z): [M+H]^+ calculated for C_{341}H_{526}N_{155}O_{116}P_{25}S_{2}Cl, 9527; observed 9525. The cyclized
cMO was obtained in 48% yield. MS-ESI: m/z calculated for C_{337}H_{518}N_{154}O_{115}P_{25}S [M + H]^+: 9373; observed: 9371.

**NB cyclic spt cMO.** Synthetic procedures identical to those for the NB cyclic ntlia cMO were applied to a NB cMO targeting spt, using a 25-base spt MO oligomer with 5’-amine and 3’-disulfide modifications (5’-CTCTGATAGCCTGCATTATTTAGCC-3’) (Gene-Tools, LLC). The linear NB linker-spt MO intermediate was obtained in 81% yield. MS-ESI (m/z): [M+H]^+ calculated for C_{335}H_{524}N_{147}O_{116}P_{25}S_{2}Cl, 9341; observed 9339. The cyclized cMO was obtained in 77% yield. MS-ESI: m/z calculated for C_{331}H_{526}N_{146}O_{115}P_{25}S [M + H]^+: 9187; observed: 9186.

**REFERENCES**


