Supporting information for:
Activatable Dendritic $^{19}$F Probes for Enzyme Detection

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Materials and Methods
$^{1}$H-NMR spectra were recorded on a 400 MHz Bruker NMR spectrometer using the residual proton resonance of the solvent as the internal standard. Chemical shifts are reported in parts per million (ppm). $^{13}$C NMR spectra were proton decoupled and recorded on a 100 MHz NMR spectrometer using the carbon signal of the deuterated solvent as the internal standard. $^{19}$F-NMR spectra were collected on a 300 MHz Bruker NMR spectrometer using the fluorine signal of trifluoroacetic acid as the internal standard. MALDI mass spectra data were obtained at the University of Massachusetts mass spectrometry center. Dynamic light scattering (DLS) were determined by Nano-ZS (Malvern Instrument) Zetasizer. Transmission electron microscopy (TEM) images were taken from JEOL JEM-2000FX. All chemicals and reagents were purchased from commercial sources and were used as received, unless otherwise mentioned. Compounds 13-14\cite{1} were prepared according to previously reported procedures.

Synthesis

Synthesis scheme of azido compounds (8-12):

Synthesis of compound 8:
To a solution of 3-bromo-1-propanol (1.0 g, 7.2 mmol) in water was added sodium azide (1.5 g, 21.6 mmol) at room temperature and stirred for 24 hours at 80 °C. The reaction mixture was cooled to room temperature and extracted twice with dichloromethane. Combined organic extracts were dried over
anhydrous Na₂SO₄ and evaporated to dryness. The crude product 8a was taken for next step without further purification.

To a solution of 3,5-bis(trifluoromethyl)benzoic acid (0.59 g, 2.3 mmol) in dry dichloromethane was added 8a (0.23 g, 2.3 mmol) and cooled to ice bath temperature. Then N-(3-dimethylaminopropyl)-N’-ethylcarbodiimide hydrochloride (0.65 g, 3.4 mmol) and 4-(dimethylamino)pyridine (0.028 g, 0.23 mmol) were added at the same temperature. The reaction mixture was stirred for 2 hours at room temperature. Distilled water was added to the reaction mixture and extracted twice with dichloromethane. Combined organic layers were dried over anhydrous Na₂SO₄ and evaporated to dryness. The crude product was purified by silica gel column chromatography using mixture of ethyl acetate/hexane as eluent to yield 0.62g (80%) of compound 8. ¹H NMR (400MHz, CDCl₃) δ: 8.48 (s, 2H), 8.08 (s, 1H), 4.51 (t, J = 6.3 Hz, 2H), 3.50 (t, J = 6.6 Hz, 2H), 2.13-2.07 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ: 163.9, 132.4 (q, JŒF = 33.9 Hz), 132.3, 129.9, 129.8, 126.7-126.6 (m), 123.0 (q, JŒF = 271.4 Hz), 63.3, 48.3, 28.2.

Synthesis of compound 9a, 10a and 11a:

To a solution of 3,5-bis(trifluoromethyl)benzoic acid (1.0 g, 3.9 mmol) in dry dichloromethane was added 5 equivalents of oligoethylene glycol (di, tetra, hexa) and cooled to ice bath temperature. Then N-(3-dimethylaminopropyl)-N’-ethylcarbodiimide hydrochloride (1.1 g, 5.8 mmol) and 4-(dimethylamino)pyridine (0.047 g, 0.39 mmol) were added at the same temperature. The reaction was complete in 2 hours, monitored by TLC. Dichloromethane was added to the reaction mixture and washed with distilled water. The organic layer was dried over anhydrous Na₂SO₄ and evaporated to dryness. The crude product was purified by silica gel column chromatography using mixture of ethyl acetate/hexane as eluent.

Compound 9a, 91%. ¹H NMR (400MHz, CDCl₃) δ: 8.50 (s, 2H), 8.07 (s, 1H), 4.59-4.57 (m, 2H), 3.89-3.86 (m, 2H), 3.77 (t, J = 4.8 Hz, 2H), 3.67-3.65 (m, 2H), 2.00 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ: 164.1, 132.4 (q, JŒF = 33.9 Hz), 132.3, 130.0, 130.0, 126.6-126.5 (m), 123.0 (q, JŒF = 271.3 Hz), 72.6, 69.0, 65.2, 61.9.

Compound 10a, 81%. ¹H NMR (400MHz, CDCl₃) δ: 8.50 (s, 2H), 8.05 (s, 1H), 4.57-4.54 (m, 2H), 3.87-3.84 (m, 2H), 3.72-3.62 (m, 10H), 3.59-3.56 (m, 2H), 2.53 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 164.1, 132.4, 132.2 (q, JŒF = 33.9 Hz), 130.0, 130.0, 126.5-126.4 (m), 123.0 (q, JŒF = 271.0 Hz), 72.6, 70.7, 70.6, 70.3, 69.0, 65.1, 61.7.

Compound 11a, 76%. ¹H NMR (400MHz, CDCl₃) δ: 8.50 (s, 2H), 8.07 (s, 1H), 4.57-4.54 (m, 2H), 3.88-3.85 (m, 2H), 3.73-3.59 (m, 20H), 2.37 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ: 164.0, 132.4, 132.2 (q, JŒF = 33.8 Hz), 130.0, 130.0, 126.5-126.3 (m), 122.9 (q, JŒF = 271.2 Hz), 72.7, 70.7, 70.7, 70.4, 69.1, 65.3, 61.2.

Synthesis of compound 9, 10 and 11:

To a solution of oligoethylene glycol mono(3,5-bis(trifluoromethyl)benzoate) (9a, 10a, 11a) in dry dichloromethane was added triethylamine (1.2 equivalent) and methanesulfonyl chloride (1.2 equivalent) slowly at ice bath temperature. After stirring for 1 hour at room temperature, the reaction mixture was washed with distilled water and then brine. The organic extract was concentrated and re-dissolved in 10 mL DMF. Sodium azide (2 equivalent) was dissolved in 3 mL distilled water and added to the above solution. The reaction mixture was heated for 12 hours at 80 °C. Dichloromethane (200 mL) was added to the reaction mixture after it was cooled to room temperature. The reaction mixture was then washed with distilled water (3 x 200mL) and brine (200 mL). The organic layer was dried over anhydrous Na₂SO₄ and evaporated to dryness to obtain pure products.
Compound 9, 95%. $^1$H NMR (400MHz, CDCl$_3$) δ: 8.51 (s, 2H), 8.07 (s, 1H), 4.59-4.56 (m, 2H), 3.89-3.86 (m, 2H), 3.74 (t, $J = 4.8$ Hz, 2H), 3.40 (t, $J = 4.8$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 164.1, 132.3, 132.3 (q, $J_{CF} = 33.8$ Hz), 130.1, 130.0, 126.6-126.5 (m), 123.0 (q, $J_{CF} = 271.1$ Hz), 70.4, 69.0, 65.0, 50.7.

Compound 10, 91%. $^1$H NMR (400MHz, CDCl$_3$) δ: 8.48 (s, 2H), 8.04 (s, 1H), 4.55-4.52 (m, 2H), 3.86-3.83 (m, 2H), 3.71-3.60 (m, 10H), 3.35 (t, $J = 6.5$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 163.9, 132.3, 132.1 (q, $J_{CF} = 33.8$ Hz), 129.8, 129.8, 126.4-126.2 (m), 122.9 (q, $J_{CF} = 271.2$ Hz), 70.6, 70.0, 68.9, 65.1, 50.6.

Compound 11, 85%. $^1$H NMR (400MHz, CDCl$_3$) δ: 8.50 (s, 2H), 8.07 (s, 1H), 4.57-4.54 (m, 2H), 3.87-3.85 (m, 2H), 3.71-3.61 (m, 18H), 3.38 (t, $J = 4.9$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 163.7, 132.2, 131.9 (q, $J_{CF} = 33.8$ Hz), 129.7, 129.7, 126.3-126.1 (m), 122.8 (q, $J_{CF} = 271.1$ Hz), 70.5, 70.4, 70.4, 69.9, 68.8, 65.0, 50.5.

Synthesis of compound 12a:
To a solution of hexaethylene glycol (2 g, 7.1 mmol) in dry dichloromethane was added triethylamine (1.7 g, 17.0 mmol) and methanesulfonyl chloride (1.9 g, 17.0 mmol) slowly at ice bath temperature. After stirring for 1 hour at room temperature, the reaction mixture was washed with distilled water and then brine. The organic extract was concentrated and re-dissolved in 50 mL distilled water. Sodium azide (1.8 g, 28.4 mmol) was then added to the solution and heated to reflux for 12 hours. The reaction mixture was cooled to room temperature and extracted with dichloromethane (2 x 50 mL). The combined organic extracts were concentrated and re-dissolved in 60 mL of Et$_2$O/THF/1M HCl (v/v/v, 5/1/5). A solution of triphenylphosphine (1.1 g, 7.1 mmol) in diethyl ether (50 mL) was added dropwise to the above mixture over a period of 3 hours. After the addition was completed, the reaction mixture was allowed to stir for 20 h at room temperature. The organic layer was discarded. The aqueous layer was washed with diethyl ether (2 x 30 mL). pH of the aqueous solution was adjusted to 14 using NaOH. The basic aqueous solution was then extracted with dichloromethane (2 x 30 mL). Combined organic layers were dried over anhydrous Na$_2$SO$_4$ and evaporated to dryness to yield 0.87 g (40%) of compound 12a. $^1$H NMR (400MHz, CDCl$_3$) δ: 3.71-3.58 (m, 18H), 3.52 (t, $J = 5.2$ Hz, 2H), 3.39 (t, $J = 4.9$ Hz, 2H), 2.88-2.85 (m, 2H), 1.73 (bs, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 72.5, 70.1, 70.0, 70.0, 69.7, 69.5, 50.1, 41.1.

Synthesis of compound 12:
To a solution of 3,5-bis(trifluoromethyl)benzoic acid (0.5 g, 1.9 mmol) in dry dichloromethane was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.48 g, 2.5 mmol) at ice bath temperature and stirred for 20 minutes at the same temperature. 12a (0.77 g, 2.5 mmol) was dissolved in dichloromethane and added to the above mixture. The reaction mixture was stirred for 2 hours at room temperature. 1M HCl was added to the reaction mixture and extracted twice with dichloromethane. Combined organic layers were dried over anhydrous Na$_2$SO$_4$ and evaporated to dryness. The crude product was purified by silica gel column chromatography using mixture of dichloromethane/methanol as eluent to yield 0.88 g (85%) of compound 12. $^1$H NMR (400MHz, CDCl$_3$) δ: 8.37 (s, 2H), 7.98 (s, 1H), 7.59 (bs, 1H), 3.73-3.57 (m, 22H), 3.34 (t, $J = 4.9$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 164.6, 136.7, 131.6 (q, $J_{CF} = 33.8$ Hz), 127.9, 127.9, 124.5-124.4 (m), 123.0 (q, $J_{CF} = 271.0$ Hz), 70.4, 70.4, 70.3, 70.3, 70.0, 69.8, 69.5, 50.5, 40.2.
Synthesis scheme of dendrons (1-7):

General procedure for incorporation of azido compound using “click” chemistry:
The mixture of dendritic acetylene compound (1.0 equiv), azido compound (5 equiv for G1-dendrons and 10 equiv for G2-dendrons), CuSO₄·5H₂O (0.5 equiv.) and sodium ascorbate (0.5 equiv.) in THF/H₂O (1:1) solvent mixture was heated at 50 °C for 24-48 h (24h for G1-dendrons and 48h for G2-dendrons). The progress of the reaction was monitored by TLC. After completion of the reaction, saturated aqueous NaCl solution was added to the reaction mixture. The aqueous layer was extracted twice with ethyl acetate and the combined organic layer was dried over Na₂SO₄ and evaporated to dryness. The crude product was purified by silica gel column chromatography using mixture of dichloromethane/methanol as eluent.

Synthesis of compound 1:
According to general procedure for click reaction, G1-acetylene (40 mg, 0.031 mmol) was treated with compound 11 (85 mg, 0.155 mmol) to give 81 mg (89%) of dendron 1. ¹H NMR (400MHz, acetone-d₆) δ: 8.54 (s, 6H), 8.36 (s, 3H), 8.09 (s, 2H), 7.84 (s, 1H), 6.94-6.57 (m, 11H), 5.18 (s, 4H), 5.13 (s, 2H), 5.04 (s, 4H), 4.64 (d, J = 5.7 Hz, 2H), 4.58-4.47 (m, 12H), 4.30 (bs, 1H), 4.15-4.13 (m, 4H), 4.07-4.05 (m, 2H), 3.90-3.80 (m, 16H), 3.66-3.42 (m, 98H), 3.26 (s, 6H), 3.25 (s, 3H); ¹³C NMR (100 MHz, acetone-d₆) δ: 164.3, 161.2, 160.7, 159.9, 157.8, 157.2, 144.7, 144.3, 144.0, 141.1, 137.1, 133.8, 132.6 (q, JCF = 33.6 Hz), 130.6, 130.5, 127.5-127.2 (m), 125.4, 125.1, 124.0 (q, JCF = 270.6 Hz), 119.4, 111.4, 107.1, 107.1, 105.3, 105.1, 101.6, 101.5, 72.6, 71.4, 71.2, 71.1, 71.0, 70.4, 70.3, 70.1, 70.0, 69.4, 68.4, 66.1, 64.8, 63.2,
Synthesis of compound 2:
According to general procedure for click reaction, G1-acetylene (40 mg, 0.031 mmol) was treated with compound 12 (85 mg, 0.155 mmol) to give 81 mg (89%) of dendron 2. $^1$H NMR (400MHz, acetone-$d_6$) δ: 8.51 (s, 6H), 8.38 (bs, 3H), 8.20 (s, 3H), 8.10 (s, 2H), 7.84 (s, 1H), 6.95-6.53 (m, 11H), 5.19 (s, 4H), 5.11 (s, 2H), 5.04 (s, 4H), 4.65 (d, $J = 5.9$ Hz, 2H), 4.58-4.56 (m, 4H), 4.50-4.47 (m, 2H), 4.33 (t, $J = 5.9$ Hz, 1H), 4.16-4.13 (m, 4H), 4.07-4.05 (m, 2H), 3.90-3.87 (m, 4H), 3.82-3.79 (m, 6H), 3.60-3.41 (m, 110H), 3.26 (s, 6H), 3.25 (s, 3H); $^{13}$C NMR (100 MHz, acetone-$d_6$) δ: 164.7, 161.1, 160.7, 159.8, 157.7, 157.2, 144.7, 141.0, 138.1, 137.1, 132.1 (q, $J_{CF} = 33.3$ Hz), 128.9, 128.9, 125.5-125.2 (m), 124.2 (q, $J_{CF} = 270.6$ Hz), 119.3, 111.4, 107.1, 107.1, 105.3, 105.1, 101.5, 101.4, 72.5, 71.3, 71.1, 71.1, 70.9, 70.9, 70.9, 70.5, 70.4, 70.2, 70.1, 70.0, 69.3, 68.4, 64.7, 63.1, 62.4, 58.8, 50.7, 40.9; $^{19}$F NMR (300 MHz, acetone-$d_6$) δ: -64.28 (s, 6H), -64.29 (s, 12H); MALDI-TOF m/z 2948.22, 3010.16 (calculated: M$^+$, 2947.21; M+Na$^+$, 3010.31).

Synthesis of dendron 3:
According to general procedure for click reaction, G1-acetylene (40 mg, 0.031 mmol) was treated with compound 10 (71 mg, 0.155 mmol) to give 75 mg (90%) of dendron 3. $^1$H NMR (400MHz, acetone-$d_6$) δ: 8.53 (s, 6H), 8.35 (s, 3H), 8.07 (s, 2H), 7.82 (s, 1H), 6.93-6.58 (m, 11H), 5.17 (s, 4H), 5.12 (s, 2H), 5.04 (s, 4H), 4.64 (d, $J = 5.7$ Hz, 2H), 4.56-4.46 (m, 12H), 4.25 (bs, 1H), 4.14-4.12 (m, 4H), 4.06-4.04 (m, 2H), 3.89-3.77 (m, 16H), 3.66-3.41 (m, 74H), 3.26 (s, 6H), 3.25 (s, 3H); $^{13}$C NMR (100 MHz, acetone-$d_6$) δ: 164.4, 161.2, 160.8, 159.9, 157.8, 157.3, 144.8, 144.3, 144.0, 141.1, 137.1, 133.8, 132.6 (q, $J_{CF} = 33.6$ Hz), 130.6, 130.5, 127.5-127.3 (m), 125.3, 125.0, 124.1 (q, $J_{CF} = 270.6$ Hz), 119.5, 111.4, 107.2, 107.1, 105.6, 105.3, 101.6, 101.5, 72.6, 71.4, 71.3, 71.2, 71.2, 71.0, 71.0, 70.4, 70.3, 70.1, 70.1, 70.0, 69.4, 69.4, 68.4, 66.1, 64.8, 63.3, 62.5, 58.8, 50.7; $^{19}$F NMR (300 MHz, acetone-$d_6$) δ: -64.41 (s, 6H), -64.42 (s, 12H); MALDI-TOF m/z 2708.41, 2709.39, 2710.37 (calculated: M+Na$^+$, 2709.0).

Synthesis of dendron 4:
According to general procedure for click reaction, G1-acetylene (40 mg, 0.031 mmol) was treated with compound 9 (58 mg, 0.155 mmol) to give 69 mg (92%) of dendron 4. $^1$H NMR (400MHz, acetone-$d_6$) δ: 8.53 (s, 4H), 8.49 (s, 2H), 8.35 (s, 2H), 8.33 (s, 1H), 8.06 (s, 2H), 7.80 (s, 1H), 6.89-6.53 (m, 11H), 5.10 (s, 4H), 5.04 (s, 2H), 5.03 (s, 4H), 4.65 (d, $J = 4.5$ Hz, 2H), 4.62-4.44 (m, 12H), 4.26 (bs, 1H), 4.14-4.11 (m, 4H), 4.06-4.04 (m, 2H), 4.00-3.76 (m, 16H), 3.66-3.41 (m, 50H), 3.26 (s, 6H), 3.25 (s, 3H); $^{13}$C NMR (100 MHz, acetone-$d_6$) δ: 164.3, 161.1, 160.7, 159.9, 157.7, 157.2, 144.7, 141.1, 137.1, 133.7, 133.7, 132.6 (q, $J_{CF} = 33.6$ Hz), 132.5 (q, $J_{CF} = 33.6$ Hz), 130.6, 127.6-127.3 (m), 124.0 (q, $J_{CF} = 270.7$ Hz), 119.4, 111.4, 107.1, 107.0, 105.3, 105.1, 101.5, 101.4, 72.6, 71.3, 71.2, 71.1, 71.1, 70.9, 70.3, 70.2, 70.1, 70.0, 69.4, 69.3, 68.4, 65.8, 64.7, 62.4, 58.8, 50.7; $^{19}$F NMR (300 MHz, acetone-$d_6$) δ: -64.36 (s, 6H), -64.40 (s, 12H); MALDI-TOF m/z 2444.21, 2484.82 (calculated: M+Na$^+$, 2444.83; M+Na+K$^+$, 2483.93).

Synthesis of dendron 5:
According to general procedure for click reaction, G1-acetylene (40 mg, 0.031 mmol) was treated with compound 8 (53 mg, 0.155 mmol) to give 66 mg (91%) of dendron 5. $^1$H NMR (400MHz, acetone-$d_6$) δ: 8.56 (s, 4H), 8.52 (s, 2H), 8.35 (s, 2H), 8.33 (s, 1H), 8.11 (s, 2H), 7.81 (s, 1H), 6.91-6.54 (m, 11H), 5.15 (s, 4H), 5.08 (s, 2H), 5.04 (s, 4H), 4.67 (t, $J = 6.9$ Hz, 4H), 4.64 (d, $J = 4.2$ Hz, 2H), 4.57 (t, $J = 6.9$ Hz, 2H), 4.48 (t, $J = 6.1$ Hz, 4H), 4.41 (t, $J = 6.1$ Hz, 2H), 4.29 (bs, 1H), 4.13-4.11 (m, 4H), 4.06-4.04 (m, 2H),
Synthesis of compound 6:
According to general procedure for click reaction, G2-acetylene (40 mg, 0.013 mmol) was treated with compound 9 (48 mg, 0.13 mmol) to give 67 mg (90%) of dendron 6. $^1$H NMR (400MHz, acetone-d$_6$) δ: 8.52-8.30 (m, 21H), 8.04 (s, 4H), 7.83 (s, 1H), 7.78 (s, 2H), 7.09-6.52 (m, 27H), 5.14-5.02 (m, 26H), 4.65 (d, $J = 5.7$ Hz, 2H), 4.61-4.41 (m, 28H), 4.31 (bs, 1H), 4.17-3.35 (m, 168H), 3.25 (s, 12H), 3.22 (s, 3H); $^{13}$C NMR (100 MHz, acetone-d$_6$) δ: 164.3, 161.1, 160.6, 159.9, 159.9, 157.9, 157.7, 157.3, 157.2, 144.8, 144.2, 144.1, 141.0, 139.8, 137.1, 136.8, 133.7, 133.6, 133.6, 132.6 (q, $J_{C,F} = 33.6$ Hz), 132.5 (q, $J_{C,F} = 33.6$ Hz), 130.5, 127.6-127.3 (m), 125.2, 125.0, 124.0 (q, $J_{C,F} = 270.6$ Hz), 120.3, 119.4, 111.5, 111.3, 107.2, 107.1, 106.5, 106.4, 105.3, 105.2, 101.8, 101.7, 101.4, 72.5, 72.5, 71.3, 71.3, 71.2, 71.1, 71.0, 71.0, 70.9, 70.9, 70.6, 70.4, 70.2, 70.0, 69.5, 69.2, 68.4, 65.8, 64.7, 63.3, 63.0, 62.4, 58.8, 50.6; $^{19}$F NMR (300 MHz, acetone-d$_6$) δ: -64.35 (s, 6H), -64.41 (s, 12H); MALDI-TOF m/z 2331.92, 2354.72 (calculated: M$^+$, 2331.81; M+Na$^+$, 2354.80).

Synthesis of compound 7:
According to general procedure for click reaction, G2-acetylene (40 mg, 0.013 mmol) was treated with compound 11 (71 mg, 0.13 mmol) to give 78 mg (86%) of dendron 7. $^1$H NMR (400MHz, acetone-d$_6$) δ: 8.55-8.34 (m, 21H), 8.09 (s, 4H), 7.88 (s, 1H), 7.83 (s, 2H), 7.13-6.58 (m, 27H), 5.19-5.04 (m, 26H), 4.66 (d, $J = 5.2$ Hz, 2H), 4.58-4.45 (m, 28H), 4.35 (bs, 1H), 4.16-3.38 (m, 280H), 3.25 (s, 12H), 3.23 (s, 3H); $^{13}$C NMR (100 MHz, acetone-d$_6$) δ: 164.4, 161.2, 160.7, 160.0, 159.9, 157.9, 157.8, 157.4, 157.3, 144.2, 144.2, 144.0, 141.0, 139.8, 137.1, 136.8, 133.8, 132.6 (q, $J_{C,F} = 33.6$ Hz), 130.6, 130.5, 127.5-127.2 (m), 125.4, 125.2, 124.0 (q, $J_{C,F} = 270.6$ Hz), 120.3, 111.5, 111.3, 107.2, 107.1, 106.6, 106.3, 101.7, 101.5, 72.6, 71.7, 71.4, 71.2, 71.0, 70.7, 70.4, 70.3, 70.0, 69.4, 68.4, 66.1, 63.3, 62.5, 58.8, 50.7; $^{19}$F NMR (300 MHz, acetone-d$_6$) δ: -64.38 (s, 18H), -64.40 (s, 24H); MALDI-TOF m/z 6933.31, 6955.83 (calculated: M$^+$, 6931.70; M+Na$^+$, 6954.60).

Procedures for preparing probe solutions:
To a 980 µL solution of 25 mM Tris buffer was slowly added 10 µL (2.5 mM) solution of dendron in dimethyl sulfoxide (DMSO) under vigorously stirring. The solution was allowed to stir for 10 min at room temperature after the addition was complete. To prepare solutions with an enzyme, 10 µL (100 µM) solution of the enzyme in 25 mM Tris buffer was added to the above solution. To prepare solutions without enzymes, 10 µL 25 mM Tris buffer was added. Solutions were immediately taken for DLS or $^{19}$F-NMR measurements, unless otherwise mentioned.

![Figure S1](image1.png)

**Figure S1.** Size distribution of dendron 1 (25 µM) alone in 25 mM Tris buffer measured by (a) DLS, (b)TEM (scale bar 500 nm).

**Control Experiment with dendron 2:**
To support that the $^{19}$F NMR signal generated was indeed due to the hydrolysis of ester functionalities, we performed control experiment where we utilized dendron 2 that does not contain ester functionalities. Dendron 2 (25 µM) was incubated with PLE (1 µM) for 3 hours before taking the $^{19}$F NMR spectrum. The $^{19}$F NMR and DLS studies upon exposing to PLE are shown below

![Figure S2](image2.png)

**Figure S2.** (a) $^{19}$F NMR spectra of 2 (25 µM) in the presence or absence of PLE (1 µM). (b) Size evolution of 2 (25 µM) in the presence of PLE (1 µM) using DLS.
Enzyme specificity experiment:
Dendron 1 was incubated with different enzymes for 3 hours before taking the $^{19}$F spectra.

Figure S3. $^{19}$F NMR spectra of 1 (25 µM) in the presence of different enzymes (1 µM).

$^{19}$F-NMR spectra of dendron probes:
$^{19}$F-NMR spectra were collected on a 300 MHz Bruker NMR spectrometer using the fluorine signal of trifluoroacetic acid ($\delta = -76.5$) as the internal standard. All spectra were taken in 25 mM Tris buffer (pH 7.4, 0.2 mM TFA, 10%D$_2$O (v/v)).

Figure S4. $^{19}$F NMR spectra of dendrons (25 µM) before or after incubation with PLE (1 µM) for 4 days: (a) 5, (b) 6, (c) 7.

DLS measurements to monitor size evolution of dendron probes:
DLS experiments were performed on a Malvern Nano-ZS Zeta-sizer in 25 mM Tris buffer (pH 7.4, 0.2 mM TFA, 10%D$_2$O (v/v)) using a plastic cuvette (1 mL volume). First measurement was taken right after the addition of PLE. The DLS experiment was then performed during each time intervals. The temperature was maintained at 25 °C throughout the experiment.
Figure S5. Size evolution of dendron probes (25 µM) in the presence of PLE (1 µM): (a) 3, (b) 4, (c) 5, (d) 6, and (e) 7.

Reference:

[1] M. A. Azagarsamy, P. Sokkalingam, S. Thayumanavan, J. Am. Chem. Soc. 2009, 131, 14184.