Supporting Materials

Sdex-isothiocyanate synthesis. Synthesis is done according to published procedures\textsuperscript{1,2}. All chemicals were from Sigma-Aldrich. **Dexamethasone-21-mesylate.** 1 g (2.7 mmole) of dexamethasone was dissolved in 20 mL of anhydrous pyridine under argon at 0 °C. To this solution was added 250 µL (3.2 mmole) of methanesulfonyl chloride with stirring. After 1 h at 0 °C another 165 µL (2.1 mmole) of methanesulfonyl chloride was added and the reaction was continued for 5 h. The solution was added to 400 mL of icy water. The white precipitant was filtrated, washed with 400 ml of icy water and dried under vacuum overnight (0.98 g, 82% yield). \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 7.26 (d, \(J = 10.3\) Hz, 1H), 6.19 (d, \(J = 10.1\) Hz, 1H), 5.98 (s, 1H), 5.32 (d, \(J = 20.6\), 1H), 5.24 (s, 1H), 4.87 (d, \(J = 17.8\) Hz, 1H), 4.12 (bs, 1H), 3.21 (s, 3H).

2-[tert-Butoxycarbonyl)amino]-1-ethane-thiol. To a cysteamine hydrochloride (500 mg, 4.4 mmole) solution in dioxane-water (80 : 20) was added 1.4 mL (10 mmole) of triethylamine and 1 g (4.9 mmole) di-tert-butyl dicarbonate. After 10 min, 0.6 mL (4 mmole) more of triethylamine was added and the reaction was allowed at room temperature for 2.5 h. 14 mL of 0.5 N HCl was added to dissolve the precipitant and the solution was extracted with ethylacetate (3 × 16 mL). 4 mL more of 0.5 N HCl was added to the aqueous layer and ethylacetate extraction was done again (3 × 16 mL). The organic solutions were pooled, dried over MgSO\textsubscript{4}, and evaporated under reduced pressure to give 1.05 g (91% yield) semi-clear oil. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 4.96 (bs, 1H), 3.26 (dd, \(J = 6.0, 6.0\) Hz, 2H), 2.60 (dd, \(J = 7.5, 6.6\) Hz, 1H), 1.41 (s, 9H), 1.32 (t, \(J = 8.5\) Hz). **Dex-21-S(CH\textsubscript{2})\textsubscript{2}NHCO\textsubscript{2}-t-Bu.** A mixture of 800 mg (1.7 mmole) Dexamethasone-21-mesylate, 800 mg (4.5 mmole) 2-[tert-Butoxycarbonyl)-amino]-1-ethane-thiol, and
710 µL (5.1 mmole) triethylamine in 50 mL of anhydrous acetone was stirred at 4 °C for 30 h, and then at room temperature for 2 h. To the solution were added 100 mL of acetone, 10 mL of water, and 30 mL of 0.5 N HCl to pH 4. Acetone was removed and 300 mL of icy water was added to give a white precipitate. The solid was extracted with dichloromethane (3 × 170 mL) and ethylacetate (3 × 170 mL). The organic layers were combined, dried over sodium sulfate, and reduced in volume. The residue was purified by silica gel column chromatography (5% methanol in chloroform as the elution solvent) to give 500 mg (53% yield) white solid. ¹H NMR (300 MHz, DMSO-d₆): δ 7.26 (d, J = 10.1 Hz, 1H), 6.93 (m, 2H), 6.19 (d, J = 10.0 Hz, 1H), 5.99 (s, 1H), 5.25 (s, 1H), 5.06 (s, 1H), 4.08 (br s, 1H), 3.81 (d, J = 16.8 Hz, 1H), 3.45 (d, J = 17.0 Hz, 1H), 1.35 (s, 9H).

Dex-21-S(CH₂)₂NH₂•HCl. Dex-21-S(CH₂)₂NHCO₂-t-Bu (600 mg, 1.1 mmole) was dissolved in 6 mL of 1.5 M HCl in glacial acetic acid. After 20 min at room temperature, triturating in 100 mL of cold ethyl ether give white precipitate. Solid was collected by centrifugation and washed with ethyl ether (2 × 25 mL). 370 mg product, 70 % yield. ¹H NMR (300 MHz, DMSO-d₆): 8.15 (br s, 2H), 8.00 (br s, 3H), 7.29 (d, J = 10.1 Hz, 1H), 6.20 (d, J = 10.0 Hz, 1H), 5.99 (s, 1H), 5.37 (s, 1H), 5.14 (s, 1H), 4.12 (br s, 1H), 3.93 (d, J = 17.4 Hz, 1H), 3.45 (d, J = 17.1 Hz, 1H). Dex-21-S(CH₂)₂NCS (Sdex-isothioleyanate). 70 mg (0.14 mmole) Dex-21-S(CH₂)₂NH₂•HCl was mixed with 9 mL of chloroform and 12 mL of saturated Na₂CO₃ at room temperature for 15 min with vigorous agitation. 20 µL of thiophosgene was added and reaction was allowed for 30 min. The organic layer was collected, washed with water (3 × 25 mL), dried over sodium sulfate, and reduced in volume. The gooey residue was dissolved in 20 % ethyl ether in chloroform and purified by silica gel column chromatography (20 % ethyl ether in
chloroform as the elution solvent). 60 mg (84% yield) product was collected. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 7.36 (d, $J = 10.2$ Hz, 1H), 6.29 (d, $J = 10.3$ Hz, 1H), 6.08 (s, 1H), 5.39 (s, 1H), 5.18 (s, 1H), 4.22 (br s, 1H), 3.97 (d, $J = 16.9$ Hz, 1H), 3.91 (m, 2H), 3.47 (d, $J = 17.1$ Hz, 1H). MALDI-TOF: [M+Na]$^+$ calculated 516.18, found 516.12.

Reference.
