Preparation of perflouroadipic acid bis(triethoxysilylpropyl)amide, V, RFS1 and RFS2

Complex **IV** was prepared as described.[3]

Perflouroadipic acid bis(triethoxysilylpropyl)amide
$(EtO)_3Si(CH_2)_3NH(O)C(CF_2)_4C(O)NH(CH_2)_3Si(OEt)_3$

Diethyl octafluoroadipate (3.63 g, 0.0105 mol) (P&M-Invest) was added gradually to APTES (4.67 g, 0.021 mol) with vigorous stirring. The resulting solid product was heated at 36-40^{0}C *in vacuo* to remove ethanol. Vacuum sublimation of the reaction product at 135-170^{o}C gave a white powder in 87% yield. Anal.: Calc. for $C_{24}H_{44}F_8N_2O_8Si_2$: C, 41.37; H, 6.36; Si, 8.06; F, 21.81%. Found: C, 41.29; H, 6.34; Si, 7.97; F, 21.89%. IR (ν, cm^{-1}): 3464, 3297, 3074 (N-H), 1700 (>C=O, amide I), 1548 (N-H, amide II), 1305, 1277, 1182, 1082 (C-N, N-H, C-F), 958, 794 (Si-O-C). NMR ^{1}H (δ, ppm.): 0.66 (m, 4H, -C$\underline{H}_2$-Si-), 1.23 (m, 18H, O-CH$_2$-C$\underline{H}_3$), 1.72 (m, 4H, -CH$_2$-C$\underline{H}_2$-CH$_2$), 3.39 (m, 4H, -NH-C$\underline{H}_2$-), 3.83 (m, 12H, O-C$\underline{H}_2$-CH$_3$), 7.01 (s, 2H, N-H). Mass-spectrum (EI 70eV), *m/z* (I_{rel} (%)): $(EtO)_3Si(CH_2)_3NH(O)C(CF_2)_4C(O)NH(CH_2)_3Si(OEt)_3$: 651 $[M\text{-}OEt]^+$ (7), 605 $[M\text{-}HOEt\text{-}OEt]^+$ (17), 248 $[(EtO)_3Si(CH_2)_3NHCO]^+$ (32), 220 $[(EtO)_3Si(CH_2)_3NH]^+$ (61), 174 $[(EtO)_2Si(CH_2)_3NH]^+$ (47), 79 (100).

Oligomeric precursor V

To a solution of perflouroadipic acid bis(triethoxysilylpropyl)amide (0.102 g: 0.146 mmol) in 5 ml THF was added with stirring 0.1 ml THF containing 11 μl (0.011 g, 0.611 mmol) H_2O and the resulting solution was kept at room temperature for 4 weeks to afford oligomer V. SEC: M_n = 4711, M_w = 5187, M_w/M_n = 1.1. Anal.: Calc. for $C_{146}H_{246}F_{64}N_{16}O_{57}Si_{16}$: C, 36.51; H, 5.16; F, 25.32; Si, 9.36%. Found: C, 36.94; H, 5.26; F, 25.50; Si, 9.38%. IR: 3459 cm^{-1} (O-H), 3318, 3085 (N-H), 1703 (>C=O, amide I), 1546 (N-H, amide II), 1309, 1291, 1274, 1182, 1108 (C-N, N-H, C-F), 957, 795 (Si-O-C).

RFS1

A solution of **IV** (0.004 g) in THF (20 µl) was mixed with 0.5 ml of 5% aqueous solution of PEG with molecular mass 40,000. After intense stirring the resulting mixture can be diluted with water without limit.

RFS2

A solution of complex **IV** (0.004 g) and oligomer **V** (0.010 g) in THF (0.5 ml) was added to an aqueous solution (0.725 g) of 1.65% PEG (MM 40,000) with vigourous stirring over 3 h. The THF was then removed *in vacuo* affording the red-emitting suspension of RFS**2**.

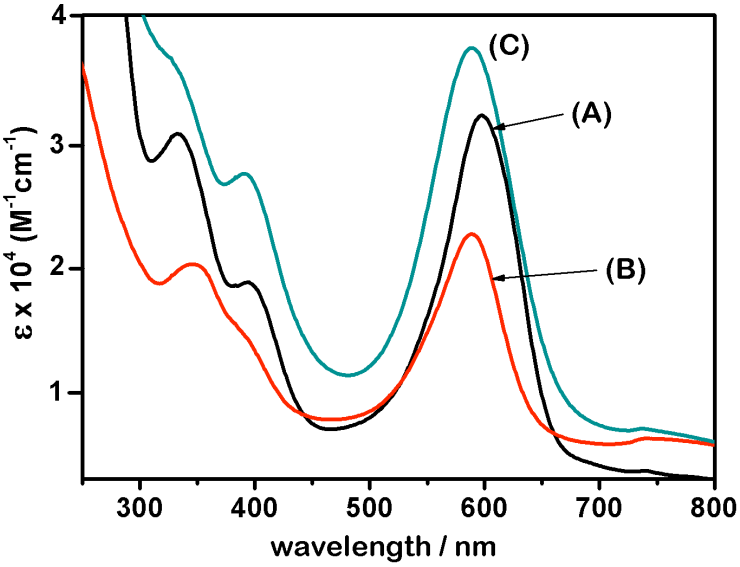

Fig. S1 UV/visible spectra of **IV** (10^{-5} M in THF) (A), RFS**1** (B), and RFS**2** (C).

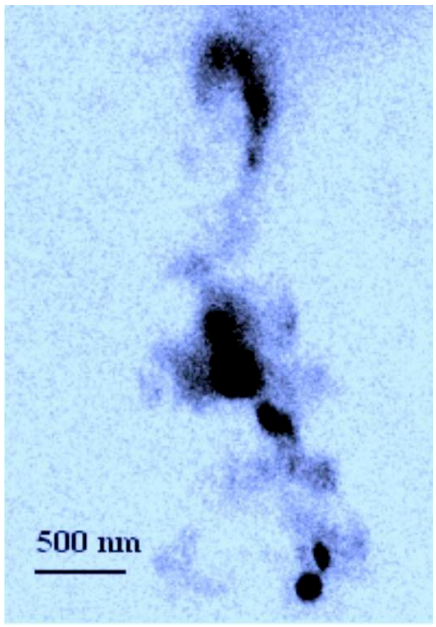

Fig. S2 TEM image of PEG nanoparticles doped with ytterbium cyanoporphyrazine complex: PEG molecular weight 40,000 (drop of water suspension on a copper grid).

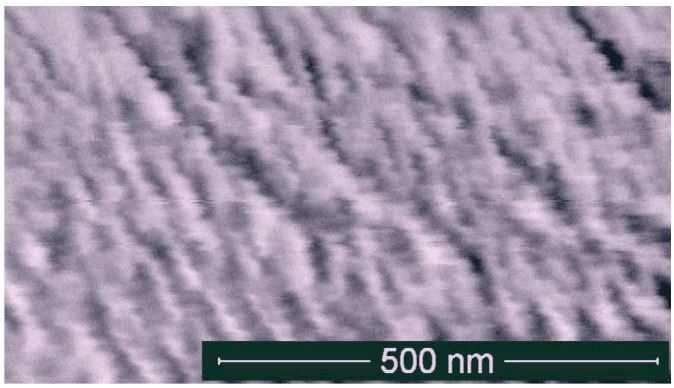

Fig. S3 SEM image of the bicontinuous interconnected PEG-fluorinated hybrid silica framework doped with complex **IV**.

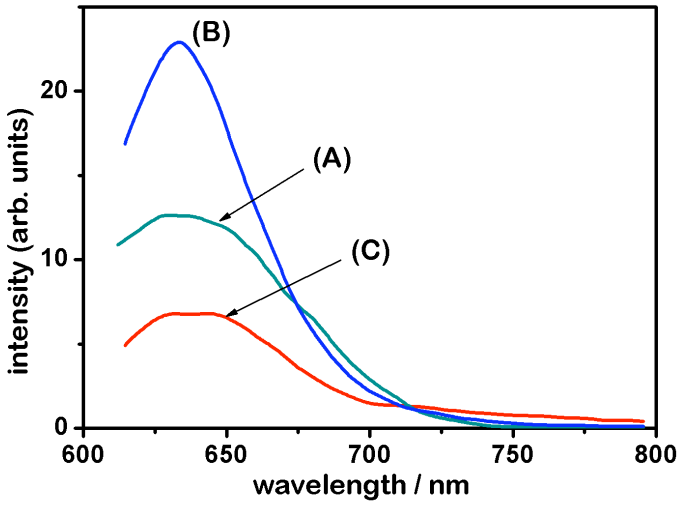

Fig. S4 Fluorescence spectra of **IV** (10^{-5} M in THF) (A), RFS**1** (B), and RFS**2** (C)) ($\lambda_{excit.}$= 595 nm, split 10.5 nm).

Biomedical Studies

By fluorescence spectroscopy an intense fluorescence of porhyrazine was detected in the tumour tissue samples *ex vivo* 6 h post-injection, whereas there was no significant fluorescence in the control samples without porhyrazine (Fig. S5).

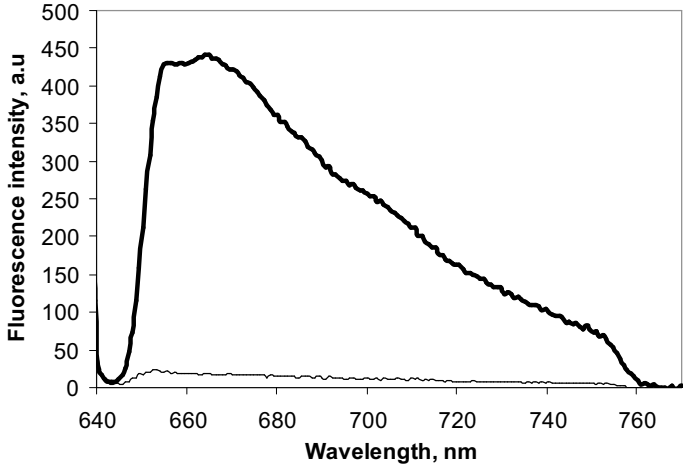

Fig. S5 Fluorescence spectra of the mouse cervical carcinoma *ex vivo*: control without (thin line), 6 h after complex injection (thick line).

In conclusion, preliminary study of the complexes in mice with subcutaneous tumours demonstrated pronounced tumour selective properties.

Materials and Methods

All experiments with live animals were performed in compliance with the relevant national laws and institutional guidelines, and were approved by the Nizhny Novgorod State Medical Academy Institutional Review Board.

Experiments were performed on CBA mice bearing cervical carcinoma. Tumours were transplanted subcutaniously in the subscapular region and used on day 2 0 post-inoculation (1-1.2 cm diameter).

The ytterbium cyanoporphyrazine complex was delivered *via* tail vein injection with dose 15 mg/kg. The complex was administrated in a vehicle composed of 7.5 % DMSO, 6.45 % PEG and 85.9 % normal saline. After dissolution of the complex in minimal volume of DMSO, PEG 6000 (Labtex, Russia) was added. For the study in

which the complex was given intravenously, the drug was additionally dissolved in sterile saline to a final concentration of 1.5 mg/ml.

In vivo fluorescence imaging was performed with a fluorescence transillumination imaging setup developed at the Institute of Applied Physics of the Russian Academy of Sciences (Nizhny Novgorod). In this setup synchronous scanning of the object in the transilluminative configuration is provided by a single pair of a source and a detector set. As a source of excitation light we employed a semiconductor laser at 635 nm. As a detector of fluorescent light we used a high-sensitivity cooled photomultiplier tube Hamamatsu H7422-20. The emission signal was filtered using a 685 to 735 nm band-pass filter. For the scanning procedure, the animal was placed vertically in a glass container and slightly compressed to 1.2 cm. The image acquisition time per animal was 5 minutes. The mice were imaged *in vivo* at 10 min, 0.5 h, 1 h, 2 h, 3h, 4 h, 6 h following the ytterbium cyanoporphyrazine complex administration. The image obtained before administration was used as a control.

6 h after injection the animals were euthanized, and the tumours were removed. Fluorescence was measured *ex vivo* using a spectrometer (QE65000, Ocean Optics Inc., USA). The tissue samples were excited with 635 nm light, and emission was collected between 660 nm and 760 nm using the appropriate interference filter. The tumour tissue samples of the animals which did not receive an ytterbium cyanoporphyrazine complex were used as a control.