***Phosphoiodyns A and B, Unique Phosphorus-Containing Iodinated Polyacetylenes from a
Korean Sponge Placospongia sp.***

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S1. General Experimental Procedures. All NMR spectra were recorded on a Bruker Avance DPX-500 and DPX-600 spectrometer with methanol-*d*₄ or chloroform-*d*. Mass spectral data were obtained on a JEOL, JMS-AX505WA instrument. Optical rotations were measured in MeOH using a 1.0 cm cell on a Rudolph Research Autopol III, #A7214. IR spectra were recorded on KBr plates by a Thermo Electron Corp. NICOLET 570. UV spectra were also recorded in MeOH on a Scinco UVS-2100. Solvents used in partitioning were first grade products of Dae-Jeong & Metals Co., Korea. HPLC grade solvents from Burdick & Jackson were used for TLC and HPLC. WATERS 1525 binary HPLC pump and WATERS 2489 UV/visible detector were used for purifying compounds. NMR solvents were purchased from Cambridge Isotope Laboratories (CIL), Inc.

S2. Animal Material. A species of red-orange marine sponge was collected by SCUBA near Tong-Yong City in the South Sea, Korea. The specimen was frozen at -78 °C immediately after collection. The voucher specimens were deposited in the Center for Marine Natural Products and Drug Discovery, Seoul National University, Korea. The sponge was identified as *Placospongia* species #4830 (registration no. QM G331982) by Dr. Ekins M. of the Queensland Museum, PO Box 3300, South Brisbane, Queensland, 4101, Australia.

S3. Extraction and Isolation. The frozen animal was lyophilized and then when dried (0.94 kg) was extracted three times with 50% MeOH in CH₂Cl₂. The dried extract (138 g) was dissolved in MeOH and washed with hexanes three times. After removal of the solvent, the MeOH-soluble fraction was resuspended in water and partitioned with EtOAc three times. The EtOAc-soluble fraction (1 g) was further fractionated into 9 fractions by MPLC using a step-gradient of CH₂Cl₂ and Methanol as a mobile phase. The PPAR delta active fraction 3 (MeOH 2% fraction) were further fractionated by RP HPLC (Phenomenex Luna C18 (2), 5 μm, 100 Å,

250 × 100 mm, 2.0 mL/min, UV = 210 nm), eluting with 20% MeCN in H₂O to afford pure phosphoiodyns A (4.5 mg) and B (8.8 mg) as yellowish amorphous solids.

S4. In vitro transfection assay The cell-based assay was performed in triplicate as previously reported.¹ CV-1 cells were maintained in Dulbecco's modified Eagle's medium (DMEM) containing 10% charcoal stripped fetal bovine serum and 1% penicillin-streptomycin at 37°C in a humidified atmosphere incubator (5 % CO₂ in air). To transient transfection, CV-1 cells were seeded in 96-well cell culture plates at density of 5×10³ cells/well and incubated overnight. The following day, media were changed to fresh stripped 5% DMEM-FBS and cells were transfected with a pCMX-PPAR expression vector, the TK-PPRE-Luc vector and a β-galactosidase expression vector using SuperFect reagent (QIAGEN) at 70% confluence. After 24 h, media were changed to fresh stripped 5 % DMEM-FBS supplemented with compounds or DMSO vehicle control. After 24 h treatment, luciferase activity was measured by Microlumet Plus luminometer (Berthold) and was normalized to the internal β-galactosidase activity.

(1) Wang, Y. -X.; Zhang, C. -L.; Ruth, T. Y. *PLoS Biol.* **2004**, 2, 1532-1539.

S5. ^1H NMR (700 MHz) spectrum of phosphoiodyne A (**1**) in methanol- d_4

S6-1. ^{13}C NMR (175 MHz) spectrum of phosphiodyn A (**1**) in methanol- d_4

S6-2. Expanded ^{13}C NMR (175 MHz) spectrum of phosphodiodyne A (1) in methanol- d_4

S7. COSY spectrum of phosphiodyn A (**1**) in methanol-*d*₄

S8. HSQC spectrum of phosphiodyn A (**1**) in methanol-*d*₄

S9. HMBC spectrum of phosphoiodyn A (**1**) in methanol- d_4

S10. UV spectrum of phosphoiodyn A (**1**)

S11. IR spectrum of phosphoiodyn A (1)

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S12. HRFABMS spectrum of phosphoiodyn A (1)

[Elemental Composition] Page: 1
 Data : 08HD020E-3-1A-HRFAB Date : 02-Apr-2012 14:33
 Sample: -
 Note : -
 Inlet : Direct Ion Mode : FAB+
 RT : 0.28 min Scan#: (6,7)
 Elements : C 16/0, H 24/1, O 4/1, P 1/1, I 1/1
 Mass Tolerance : 1000ppm, 1mmu if m/z < 1, 3mmu if m/z > 3
 Unsaturation (U.S.) : -0.5 - 200.0

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
438.0459	100.0	+0.4 / +0.2	6.0	C 16 H 24 O 4 P I
439.0494	17.5			

[Theoretical Ion Distribution] Page: 1
 Molecular Formula : C16 H24 O4 P I
 (m/z 438.0457, MW 438.2424, U.S. 6.0)
 Base Peak : 438.0457, Averaged MW : 438.2435(a), 438.2440(w)

m/z	INT.	
438.0457	100.0000	*****
439.0491	18.3082	*****
440.0517	2.3788	*
441.0543	0.2314	
442.0569	0.0182	
443.0595	0.0012	

S13. ^1H NMR (600 MHz) spectrum of phosphiodyn B (**2**) in methanol- d_4 and chloroform- d (5:1)

S14-1. ^{13}C NMR (150 MHz) spectrum of phosphoiodyn B (**2**) in methanol- d_4 and chloroform- d (5:1)

S14-2. ^{13}C NMR (150 MHz) spectrum of phosphoiodyd B (**2**) in methanol- d_4 and chloroform- d (5:1)

S15. COSY spectrum of phosphoiodyn B (**2**) in methanol-*d*₄ and chloroform-*d* (5:1)

S16. HSQC spectrum of phosphoiodyn B (**2**) in methanol-*d*₄ and chloroform-*d* (5:1)

S17. HMBC spectrum of phosphoiodyd B (**2**) in methanol-*d*₄ and chloroform-*d* (5:1)

S18. UV spectrum of phosphoiodyn B (2)

S19. IR spectrum of phosphoiodyn B (2)

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S20. HRFABMS spectrum of phosphoiodyn B (2)

[Elemental Composition] Page: 1
 Data : 1-8HD020E-3-1B-C16H23IO5P Date : 30-Apr-2012 17:05
 Sample: -
 Note : -
 Inlet : Direct Ion Mode : FAB+
 RT : 0.33 min Scan#: (7,8)
 Elements : C 16/0, H 24/1, O 5/1, P 1/1, I 1/1
 Mass Tolerance : 1000ppm, 1mmu if m/z < 1, 3mmu if m/z > 3
 Unsaturation (U.S.) : -0.5 - 200.0

Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
454.0409	100.0	+0.6 / +0.3	6.0	C 16 H 24 O 5 P I
455.0411	18.9			
476.0209	12.9			

[Theoretical Ion Distribution] Page: 1
 Molecular Formula : C16 H24 O5 P I
 (m/z 454.0406, MW 454.2418, U.S. 6.0)
 Base Peak : 454.0406, Averaged MW : 454.2428(a), 454.2433(w)

m/z	INT.
454.0406	100.0000 *****
455.0440	18.3463 *****
456.0465	2.5863 **
457.0491	0.2690
458.0516	0.0231
459.0541	0.0017
460.0567	0.0001

S21. PPAR δ results of phosphoiodyne A (**1**) and phosphoiodyne B (**2**)

PPARs activities for phosphoiodyne A (**1**) and B (**2**)

Compounds	Transactivation EC ₅₀ (nM) ^a		
	hPPAR α	hPPAR γ	hPPAR δ
Phosphoiodyne A	ND	ND	23.7
Phosphoiodyne B	ND	ND	ND
GW501516	220	>1.0 μ M	0.4

^a Compounds were screened for agonist activity on PPARs in transiently transfected CV-1 cells. EC₅₀ value is the molar concentration of the test compound that afforded 50% of the maximal reporter activity. 'ND' means that its EC₅₀ value is bigger than 10 μ M.