Supporting Information

Activation of the c-Jun N-terminal Kinase /Activating Transcription Factor 3 (ATF3) Pathway Characterizes Effective Arylated Diazeniumdiolate-Based Nitric Oxide-Releasing Anticancer Prodrugs.

Anna E. Maciag, [†,#,*] Rahul S. Nandurdikar, [‡,#] Sam Y. Hong, [‡] Harinath Chakrapani,[⊥] Bhalchandra Diwan, [†] Nicole L. Morris, [§] Paul J. Shami, [‖] Yih-Horng Shiao, [‡] Lucy M. Anderson, [‡] Larry K. Keefer, [‡] and Joseph E. Saavedra[†]

[†]*Basic Science Program, SAIC-Frederick, Inc., National Cancer Institute, Frederick, MD 21702*, [‡]*Laboratory of Comparative Carcinogenesis, National Cancer Institute, Frederick, MD 21702*, [⊥]*Department of Chemistry, Indian Institute of Science Education and Research, Pune 411008, India*, [§]*Laboratory Animal Sciences Program, SAIC-Frederick, Inc., National Cancer Institute, Frederick, MD 21702*, [‖]*Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT 84112*

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Table S1. Elemental analysis (CHN) for compounds **6**, **7**, **9** and **11**.

Compound	Molecular formula	Theoretical (%)			Experimental (%)		
		C	**H**	**N**	**C**	**H**	**N**
6	$C_{14}H_{18}N_6O_8$·14% ether	42.89	4.83	20.43	42.60	4.71	20.09
7	$C_{15}H_{20}N_6O_8$	43.69	4.89	20.38	43.96	4.87	20.08
9	$C_{14}H_{18}N_6O_9$	40.58	4.38	20.28	40.45	4.43	20.09
11	$C_{15}H_{20}N_6O_9$	42.06	4.71	19.62	42.24	4.67	19.35

Figure S1. Reaction of compound **6** with 4 mM GSH (glutathione) in pH 7.4 phosphate buffered saline at 37° C followed by HPLC.

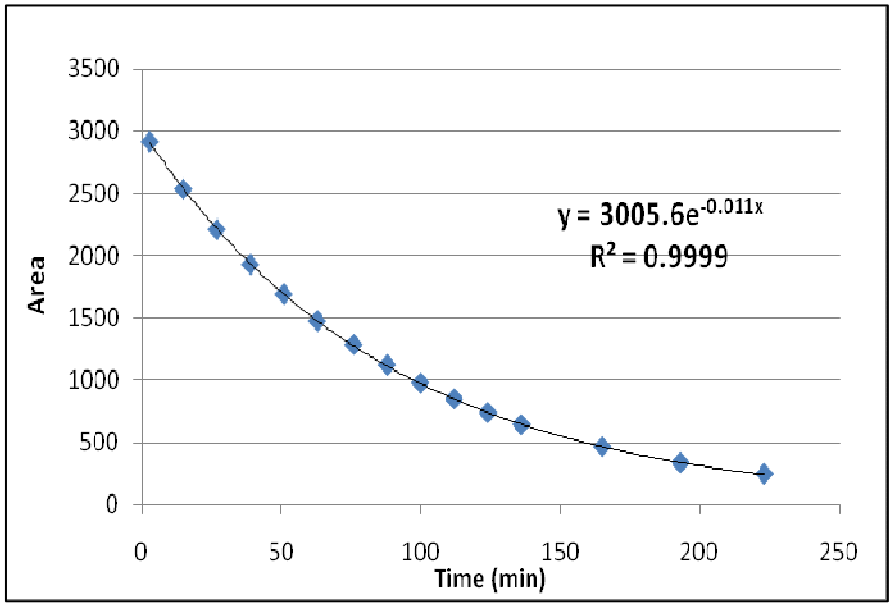

Table S2. Decay of compound **6** over time, in the presence of GSH, as determined by HPLC analysis.

Time (min)	**Peak area**	**%** Compound **6** unreacted
3.0	2914.6	100.0
15.0	2533.6	86.9
27.0	2209.6	75.8
39.0	1928.5	66.2
51.0	1690.0	58.0
63.0	1474.0	50.6
76.0	1284.3	44.1
88.0	1120.9	38.5
100.0	976.2	33.5
112.0	847.1	29.1
124.0	737.5	25.3
136.0	642.2	22.0
165.0	464.1	15.9
193.0	335.7	11.5
223.0	246.0	8.4

[a]Peak area at time 3 min is considered as 100% unreacted compound.

Table S3. Immunohistochemical analysis of xenograft tumors. The staining intensities in tumor tissues were categorized as negative (-), very weak (-/+), weak (+), moderate (++) or strong (+++).

Animal number	Treatment	Histopathology	P-SAPK/JNK	ATF3
2,4	1	Tumor with large areas of necrosis;	+++	+++
2,7	1	A large area of central necrosis, tumor cells at the periphery;	++	+++
2,11	1	A large tumor invading muscles, small area of necrosis;	+++	+++
2,12	1	A large, well-vascularized tumor, area of necrosis at the periphery;	+++	+++
2,13	1	A well-vascularized tumor with multiple focal areas of necrosis in the center;	++	+++
2,14	1	A large tumor with minimal necrosis in the center;	+++	+++
2,20	1	A large, well-vascularized tumor, small area of necrosis at the periphery;	++	++
2,6	Vehicle	A large, well-vascularized tumor with areas of necrosis at the center and periphery;	-/+	+
2,9	Vehicle	A large, well-vascularized tumor, minimal necrosis at the periphery;	-	-/+
2,10	Vehicle	A large, well-vascularized tumor, minimal necrosis at the periphery;	-	-/+
3,2	2	Small tumor, necrosis in the center;	+++	++
3,4	2	A large central area of necrosis, tumor cells only at the periphery;	++	+++
3,5	2	A large tumor, central necrosis;	+++	+++
3,6	2	Necrosis wide spread, both at the center and periphery;	+++	+++
3,7	2	Extensive necrosis in the center of a large tumor;	+++	+++
3,12	2	Extensive necrosis in the center, tumor cells at the periphery;	+++	+++
3,14	2	Small tumor, necrosis at the periphery;	+++	+++
3,16	Vehicle	A well-vascularized large tumor, large blood vessels;	-/+	-/+
3,17	Vehicle	A large tumor invading muscles, many blood vessels;	-	-
3,23	Vehicle	A large tumor with cysts and large blood vessels;	-/+	-
5,1	6	A large tumor, well-vascularized with cysts, no necrosis seen;	-	-/+
5,4	6	A large tumor, small area of necrosis in the center;	-	-/+
5,5	6	A large invasive tumor, no necrosis seen;	-	+
5,6	6	A large invasive tumor, a very small area of necrosis in the center;	-	-/+
5,7	6	A large tumor invading muscles, no necrosis seen;	-	-/+
5,8	6	A small tumor with small areas of necrosis in the center and periphery;	-	+
5,11	6	A large, well-vascularized tumor, no necrosis seen;	-	-/+
5,12	Vehicle	A large tumor with cysts and large blood vessels, no necrosis seen;	-	-/+
5,17	Vehicle	A small tumor with a very small area of necrosis at the periphery;	-	-/+
5,24	Vehicle	A large, well-vascularized tumor, no necrosis seen;	-	-/+