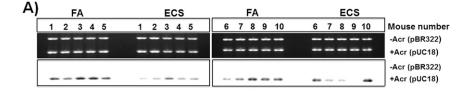
Supporting Information

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	Lung						Bladder					Heart						Liver						
	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS	ST	FA	ECS
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Fig. S1. Methylene blue staining of input DNA used for slot blot antibody hybridization. The same amount of input DNA from different samples were spotted onto two separated membranes, one for slot blot hybridization shown in Fig. 1, and the other was used for methylene blue staining as shown here. The method is the same as previously described (28). Abbreviations are the same as in Fig. 1.



B) Acr-DNA as substrates

Fig. 52. ECS causes a reduction of repair activity toward Acr-modified DNA in lung tissues. Cell-free cell lysates were isolated from lung tissues of mice exposed to ECS (n = 10) or FA (n = 10) the same as described in Fig. 3. The DNA-repair activity toward Acr-modified DNA (modified with 5 mM Acr for 16 h at 37 °C) of these cell lysates was determined using the in vitro DNA-dependent repair synthesis assay. The method of quantification is the same as described Fig. 3. (A) Ethidium-stained gels (*Upper*) and the autoradiograms (*Lower*) of the same gels. (B) Quantifications.

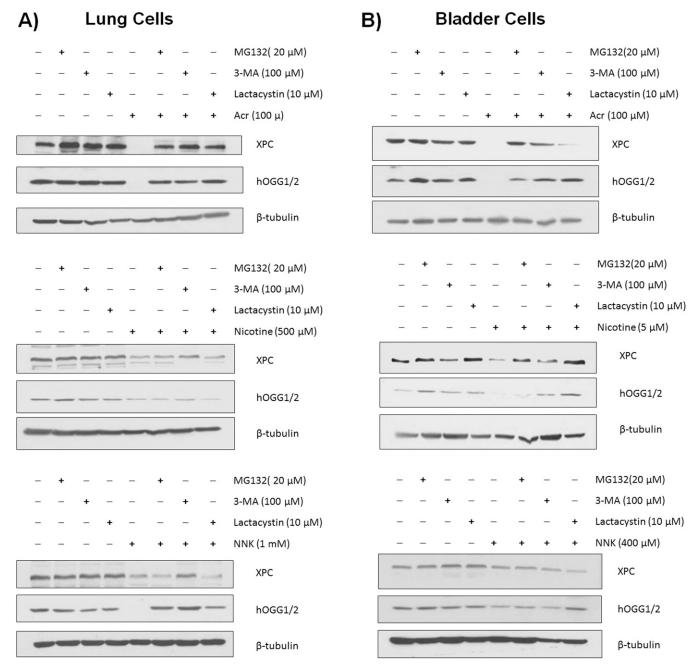


Fig. S3. Nicotine and NNK induce XPC and hOGG1/2 degradation via proteasome and autophagosome pathway. (*A*) Human lung (BEAS-2B) and (*B*) bladder (UROtsa) epithelial cells were preincubated for 1 h in growth medium in the presence of proteasome or autophagosome inhibitor MG132 (20μ M), 3-MA (100μ M), or lactacystin (10μ M). BEAS-2B cells were then treated with Acr (100μ M), nicotine (500μ M), or NNK (1 mM) and UROtsa cells were treated with Acr (100μ M), nicotine (5μ M), or NNK (400μ M) for 1 h at 37 °C. These treatments induce a similar cytotoxicity (10-20%). The XPC and hOGG1/2 were detected by Western blot as described in Figs. 3 and 5.

Table S1. DNA adduct formation (O ⁶ -medG and PdG) in mouse lung, bladder, heart, live	r, and							
DNA-repair (NER and BER) activity in lung in mice exposed to FA ($n = 10$) or ECS ($n = 10$) for								
12 wk								

		O ⁶ -medG	/10 ⁷ dG			PdG/10) ⁷ dG	Lung			
Mouse designation	Lung	Bladder	Heart	Liver	Lung	Bladder	Heart	Liver	Relative NER activity	Relative BER activity	
FA-1	<0.1	0.3	0.2	0.6	9.3	7.6	2.4	1.3	86	100	
FA-2	<0.1	0.1	0.1	0.6	16.3	12.0	2.3	1.9	45	81	
FA-3	0.7	0.1	0.2	0.4	63.4	12.9	0.9	1.2	100	61	
FA-4	<0.1	<0.1	0.1	0.3	21.3	1.4	1.0	1.0	92	51	
FA-5	<0.1	<0.1	0.1	0.9	1.2	1.8	0.3	11.2	36	41	
FA-6	0.8	0.1	0.1	1.3	69.8	0.8	5.8	6.3	66	46	
FA-7	0.3	0.2	0.2	0.9	16.5	1.0	3.4	4.9	41	56	
FA-8	<0.1	0.6	0.4	1.0	18.6	1.1	13.3	3.8	100	92	
FA-9	<0.1	0.1	0.4	2.4	8.3	1.0	17.8	34.5	72	80	
FA-10	<0.1	1.1	0.2	0.9	15.2	16.9	13.6	5.1	71	100	
ECS-1	2.7	1.6	0.8	0.7	54.0	23.2	29.2	3.9	3	14	
ECS-2	3.8	<0.1	0.3	0.7	93.0	2.8	20.0	3.6	6	9	
ECS-3	5.5	2.2	0.2	0.9	112.7	74.2	27.8	4.9	66	24	
ECS-4	6.3	3.4	0.5	1.0	148.9	70.1	28.3	7.0	26	11	
ECS-5	6.7	0.4	0.7	1.0	182.7	14.9	50.2	4.8	60	15	
ECS-6	2.7	4.1	2.2	1.5	89.2	81.6	48.2	5.9	12	45	
ECS-7	2.8	0.4	0.5	1.3	166.1	16.3	38.8	5.0	20	64	
ECS-8	1.2	3.6	0.4	1.0	60.8	81.5	17.0	4.5	13	48	
ECS-9	6.0	2.5	0.3	0.9	104.0	54.1	29.2	7.2	0	5	
ECS-10	2.9	1.8	0.3	0.4	73.9	58.6	19.5	4.9	78	98	

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