Supplemental Material

Long Isoforms of NRF1 Contribute to Arsenic-induced Antioxidant Response in Human Keratinocytes

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Supplemental Material, Table 1:

Primer sequences for Real-time RT-PCR

Gene name	GeneBank Accession	Position	Forward (5' - 3')	Reverse (5' - 3')
NRF1	NM_003204	4172-4259	GCCCTGTTTCACTTATAGGGTCTAGA	GGCAAAGAGAACATTTAGCAGCTT
HMOX1	NM_002133	1216-1294	GCCTGGAAGACACCCTAATGTG	GGCCGTGTCAACAAGGATACTT
NQO1	NM_000903	2154-2264	ACTGCCCTCTTGTGGTGCAT	GCTCGGTCCAATCCCTTCAT
SRX	NM_080725	326-400	GGAGGTGACTACTTCTACTCCTTTGG	GATGGTCTCTCGCTGCAGTTG
GCLC	NM_001498	1521-1625	GATGCTGTCTTGCAGGGAATG	AGCGAGCTCCGTGCTGTT
GCLM	NM_002061	830-910	ACAGGTAAAACCAAATAGTAACAAAGTTAA	TGTTTAGCAAATGCAGTCAAATCTG
β-ACTIN	X00351	1088-1063	GTCCACCTTCCAGCAGATGTG	GCATTTGCGGTGGACGAT

Supplemental Material, Table 2:

Sequence alignment of human *NRF1* (*NFE2L1*) proteins

NRF1-1 (NFE2L1-201): Ensembl Protein ID ENSP00000350072
NRF1-2 (NFE2L1-202): Ensembl Protein ID ENSP00000355190
NRF1-3 (NFE2L1-203): Ensembl Protein ID ENSP00000354855

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NRF1-1    -------------------MLSLKKYLTEGLLQFTILLSLIGVRVDVDTYLTSQLPPLRE
NRF1-3    FVFWKILKTKKHKHSGPSAMLSLKKYLTEGLLQFTILLSLIGVRVDVDTYLTSQLPPLRE
NRF1-2    -------------------MLSLKKYLTEGLLQFTILLSLIGVRVDVDTYLTSQLPPLRE
                              ****************************************

NRF1-1    IILGPSSAYTQTQFHNLRNTLDGYGIHPKSIDLDNYFTARRLLSQVRALDRFQVPTTEVN
NRF1-3    IILGPSSAYTQTQFHNLRNTLDGYGIHPKSIDLDNYFTARRLLSQVRALDRFQVPTTEVN
NRF1-2    IILGPSSAYTQTQFHNLRNTLDGYGIHPKSIDLDNYFTARRLLSQVRALDRFQVPTTEVN
          ************************************************************

NRF1-1    AWLVHRDPEGSVSGSQPNSGLALESSSGLQDVTGPDNGVRESETEQGFGEDLEDLGAVAP
NRF1-3    AWLVHRDPEGSVSGSQPNSGLALESSSGLQDVTGPDNGVRESETEQGFGEDLEDLGAVAP
NRF1-2    AWLVHRDPEGSVSGSQPNSGLALESSSGLQDVTGPDNGVRESETEQGFGEDLEDLGAVAP
          ************************************************************

NRF1-1    PVSGDLTKEDIDLIDILWRQDIDLGAGREVFDYSHRQKEQDVEKELRDGGEQDTWAGEGA
NRF1-3    PVSGDLTKEDIDLIDILWRQDIDLGAGREVFDYSHRQKEQDVEKELRDGGEQDTWAGEGA
NRF1-2    PVSGDLTKEDIDLIDILWRQDIDLGAGREVFDYSHRQKEQDVEKELRDGGEQDTWAGEGA
          ************************************************************

NRF1-1    EALARNLLVDGETGESFPAQFP-----------------------------ADISSITE
NRF1-3    EALARNLLVDGETGESFPAQVPSGEDQTALSLEECLRLLEATCPFGENAEFPADISSITE
NRF1-2    EALARNLLVDGETGESFPAQVPSGEDQTALSLEECLRLLEATCPFGENAEFPADISSITE
          ********************.*                             ********

NRF1-1    AVPSESEPPALQNNLLSPLLTGTESPFDLEQQWQDLMSIMEMQAMEVNTSASEILYSAPP
NRF1-3    AVPSESEPPALQNNLLSPLLTGTESPFDLEQQWQDLMSIMEMQAMEVNTSASEILYSAPP
NRF1-2    AVPSESEPPALQNNLLSPLLTGTESPFDLEQQWQDLMSIMEMQAMEVNTSASEILYSAPP
          ************************************************************

NRF1-1    GDPLSTNYSLAPNTPINQNVSLHQASLGGCSQDFLLFSPEVESLPVASSSTLLPLAPSNS
NRF1-3    GDPLSTNYSLAPNTPINQNVSLHQASLGGCSQDFLLFSPEVESLPVASSSTLLPLAPSNS
NRF1-2    GDPLSTNYSLAPNTPINQNVSLHQASLGGCSQDFLLFSPEVESLPVASSSTLLPLAPSNS
          ************************************************************

NRF1-1    TSLNSTFGSTNLTGLFFPPQLNGTANDTAGPELPDPLGGLLDEAMLDEISLMDLAIEEGF
NRF1-3    TSLNSTFGSTNLTGLFFPPQLNGTANDTAGPELPDPLGGLLDEAMLDEISLMDLAIEEGF
NRF1-2    TSLNSTFGSTNLTGLFFPPQLNGTANDTAGPELPDPLGGLLDEAMLDEISLMDLAIEEGF
          ************************************************************
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NRF1-1    NPVQASQLEEEFDSDSGLSLDSSHSPSSLSSSEGSSSSSSSSSSSSSSASSSASSSFSEE
NRF1-3    NPVQASQLEEEFDSDSGLSLDSSHSPSSLSSSEGSSSSSSSSSSSSSSASSSASSSFSEE
NRF1-2    NPVQASQLEEEFDSDSGLSLDSSHSPSSLSSSEGSSSSSSSSSSSSSSASSSASSSFSEE
          ************************************************************

NRF1-1    GAVGYSSDSETLDLEEAEGAVGYQPEYSKFCRMSYQDPAQLSCLPYLEHVGHNHTYNMAP
NRF1-3    GAVGYSSDSETLDLEEAEGAVGYQPEYSKFCRMSYQDPAQLSCLPYLEHVGHNHTYNMAP
NRF1-2    GAVGYSSDSETLDLEEAEGAVGYQPEYSKFCRMSYQDPAQLSCLPYLEHVGHNHTYNMAP
          ************************************************************

NRF1-1    SALDSADLPPPSALKKGSKEKQADFLDKQMSRDEHRARAMKIPFTNDKIINLPVEEFNEL
NRF1-3    SALDSADLPPPSALKKGSKEKQADFLDKQMSRDEHRARAMKIPFTNDKIINLPVEEFNEL
NRF1-2    SALDSADLPPPSALKKGSKEKQADFLDKQMSRDEHRARAMKIPFTNDKIINLPVEEFNEL
          ************************************************************

NRF1-1    LSKYQLSEAQLSLIRDIRRRGKNKMAAQNCRKRKLDTILNLERDVEDLQRDKARLLREKV
NRF1-3    LSKYQLSEAQLSLIRDIRRRGKNKMAAQNCRKRKLDTILNLERDVEDLQRDKARLLREKV
NRF1-2    LSKYQLSEAQLSLIRDIRRRGKNKMAAQNCRKRKLDTILNLERDVEDLQRDKARLLREKV
          ************************************************************

NRF1-1    EFLRSLRQMKQKVQSLYQEVFGRLRDENGRPYSPSQYALQYAGDGSVLLIPRTMADQQAR
NRF1-3    EFLRSLRQMKQKVQSLYQEVFGRLRDENGRPYSPSQYALQYAGDGSVLLIPRTMADQQAR
NRF1-2    EFLRSLRQMKQKVQSLYQEVFGRLRDENGRPYSPSQYALQYAGDGSVLLIPRTMADQQAR
          ************************************************************

NRF1-1    RQERKPKDRRK
NRF1-3    RQERKPKDRRK
NRF1-2    RQERKPKDRRK
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Supplemental Material, Table 3:

Sequence alignment of human *NRF1* (*NFE2L1*) cDNAs

Nrf1-1 (Nfe2l1-201): Ensembl Transcript ID ENST00000357480
Nrf1-2 (Nfe2l1-202): Ensembl Transcript ID ENST00000361665
Nrf1-3 (Nfe2l1-203): Ensembl Transcript ID ENST00000362042

Red text: Target sites of sh-RNAs
Underline and yellow highlight: Primer sequences for Real-time PCR
Yellow highlight: sequence of PCR products

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Nrf1-1    TTTCCGAGTGCGGTAGCAGGAGGGGGCGGGGAGGTAAGCGGAGGCTCCGAGCTCTAGGCC
Nrf1-3    TTTCCGAGTGCGGTAGCAGGAGGGGGCGGGGAGGTAAGCGGAGGCTCCGAGCTCTAGGCC
Nrf1-2    TTTCCGAGTGCGGTAGCAGGAGGGGGCGGGGAGGTAAGCGGAGGCTCCGAGCTCTAGGCC
          ************************************************************

Nrf1-1    GGCCGGCGGTGGCGGCGGCGAGGCCGGGACTCGGGCTTAGGGCCTGCTGTGGAGGCAGCG
Nrf1-3    GGCCGGCGGTGGCGGCGGCGAGGCCGGGACTCGGGCTTAGGGCCTGCTGTGGAGGCAGCG
Nrf1-2    GGCCGGCGGTGGCGGCGGCGAGGCCGGGACTCGGGCTTAGGGCCTGCTGTGGAGGCAGCG
          ************************************************************

Nrf1-1    GCGGACGCCGAGCTAAGCAGTTTCTCTGGAAACCCCCCTGGTAAGTGTGGAGGAGGCGGG
Nrf1-3    GCGGACGCCGAGCTAAGCAGTTTCTCTGGAAACCCCCCTGGTAAGTGTGGAGGAGGCGGG
Nrf1-2    GCGGACGCCGAGCTAAGCAGTTTCTCTGGAAACCCCCCTGGTAAGTGTGGAGGAGGCGGG
          ************************************************************

Nrf1-1    ACACTCTGACCCAAGACGAAAGGCCTGTAGCTCCAGCCAAAGAAAATAAACCTTAGGAGG
Nrf1-3    ACACTCTGACCCAAGACGAAAGGCCTGTAGCTCCAGCCAAAGAAAATAAACCTTAGGAGG
Nrf1-2    ACACTCTGACCCAAGACGAAAGGCCTGTAGCTCCAGCCAAAGAAAATAAACCTTAGGAGG
          ************************************************************

Nrf1-1    GAGAAGGAAAAAAAAAATCCATCAGCTGTTCCTGAGAACAGCCTGCATTGGAATCTACAG
Nrf1-3    GAGAAGGAAAAAAAAAATCCATCAGCTGTTCCTGAGAACAGCCTGCATTGGAATCTACAG
Nrf1-2    GAGAAGGAAAAAAAAAATCCATCAGCTGTTCCTGAGAACAGCCTGCATTGGAATCTACAG
          ************************************************************

Nrf1-1    AGAGGACAACTAATGTGAGTGAGGAAGTGACTGTATGTGGACTGTGGAGAAAGTAAGTCA
Nrf1-3    AGAGGACAACTAATGTGAGTGAGGAAGTGACTGTATGTGGACTGTGGAGAAAGTAAGTCA
Nrf1-2    AGAGGACAACTAATGTGAGTGAGGAAGTGACTGTATGTGGACTGTGGAGAAAGTAAGTCA
          ************************************************************

Nrf1-1    CGTGGGCCCTTGAGGACCTGGACTGGGTTAGGAACAGTTGTACTTTCAGAGGTGAGGTGT
Nrf1-3    CGTGGGCCCTTGAGGACCTGGACTGGGTTAGGAACAGTTGTACTTTCAGAGGTGAGGTGT
Nrf1-2    CGTGGGCCCTTGAGGACCTGGACTGGGTTAGGAACAGTTGTACTTTCAGAGGTGAGGTGT
          ************************************************************

Nrf1-1    CGAGAAGGGAAAGTGAATGTGGTCTGGAGTGTGTCCTTGGCCTTGGCTCCACAGGGTGTG
Nrf1-3    CGAGAAGGGAAAGTGAATGTGGTCTGGAGTGTGTCCTTGGCCTTGGCTCCACAGGGTGTG
Nrf1-2    CGAGAAGGGAAAGTGAATGTGGTCTGGAGTGTGTCCTTGGCCTTGGCTCCACAGGGTGTG
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Nrf1-1    CTTTCCTCTGGGGCCGTCAGGGAGCTCATCCCTTGTGTTCTGCCAGGGTGGGGTACGGGG
Nrf1-3    CTTTCCTCTGGGGCCGTCAGGGAGCTCATCCCTTGTGTTCTGCCAGGGTGGGGTACGGGG
Nrf1-2    CTTTCCTCTGGGGCCGTCAGGGAGCTCATCCCTTGTGTTCTGCCAGGGTGGGGTACGGGG
          ************************************************************

Nrf1-1    TTTGACACTGAGGAGGGTAACCTGCTGGCTGGAGCGGCAGAGCAGTGGCCTTGATTTGTC
Nrf1-3    TTTGACACTGAGGAGGGTAACCTGCTGGCTGGAGCGGCAGAGCAGTGGCCTTGATTTGTC
Nrf1-2    TTTGACACTGAGGAGGGTAACCTGCTGGCTGGAGCGGCAGAGCAGTGGCCTTGATTTGTC
          ************************************************************

Nrf1-1    TTTTGGAAGATTTTAAAAACCAAAAAGCATAAACATTCTGGTCCTTCAGCAATGCTTTCT
Nrf1-3    TTTTGGAAGATTTTAAAAACCAAAAAGCATAAACATTCTGGTCCTTCAGCAATGCTTTCT
Nrf1-2    TTTTGGAAGATTTTAAAAACCAAAAAGCATAAACATTCTGGTCCTTCAGCAATGCTTTCT
          ************************************************************

Nrf1-1    CTGAAGAAATACTTAACGGAAGGACTTCTCCAGTTCACCATTCTGCTGAGTTTGATTGGG
Nrf1-3    CTGAAGAAATACTTAACGGAAGGACTTCTCCAGTTCACCATTCTGCTGAGTTTGATTGGG
Nrf1-2    CTGAAGAAATACTTAACGGAAGGACTTCTCCAGTTCACCATTCTGCTGAGTTTGATTGGG
          ************************************************************

Nrf1-1    GTACGGGTGGACGTGGATACTTACCTGACCTCACAGCTTCCCCCACTCCGGGAGATCATC
Nrf1-3    GTACGGGTGGACGTGGATACTTACCTGACCTCACAGCTTCCCCCACTCCGGGAGATCATC
Nrf1-2    GTACGGGTGGACGTGGATACTTACCTGACCTCACAGCTTCCCCCACTCCGGGAGATCATC
          ************************************************************
                                                sh-Nrf1-5
Nrf1-1    CTGGGGCCCAGTTCTGCCTATACTCAGACCCAGTTCCACAACCTGAGGAATACCTTGGAT
Nrf1-3    CTGGGGCCCAGTTCTGCCTATACTCAGACCCAGTTCCACAACCTGAGGAATACCTTGGAT
Nrf1-2    CTGGGGCCCAGTTCTGCCTATACTCAGACCCAGTTCCACAACCTGAGGAATACCTTGGAT
          ************************************************************

Nrf1-1    GGCTATGGTATCCACCCCAAGAGCATAGACCTGGACAATTACTTCACTGCCCGGCGGCTC
Nrf1-3    GGCTATGGTATCCACCCCAAGAGCATAGACCTGGACAATTACTTCACTGCCCGGCGGCTC
Nrf1-2    GGCTATGGTATCCACCCCAAGAGCATAGACCTGGACAATTACTTCACTGCCCGGCGGCTC
          ************************************************************

Nrf1-1    CTCAGTCAGGTGAGGGCCCTGGACAGGTTCCAGGTGCCAACCACTGAGGTAAATGCCTGG
Nrf1-3    CTCAGTCAGGTGAGGGCCCTGGACAGGTTCCAGGTGCCAACCACTGAGGTAAATGCCTGG
Nrf1-2    CTCAGTCAGGTGAGGGCCCTGGACAGGTTCCAGGTGCCAACCACTGAGGTAAATGCCTGG
          ************************************************************

Nrf1-1    CTGGTTCACCGAGACCCAGAGGGGTCTGTCTCTGGCAGTCAGCCCAACTCAGGCCTCGCC
Nrf1-3    CTGGTTCACCGAGACCCAGAGGGGTCTGTCTCTGGCAGTCAGCCCAACTCAGGCCTCGCC
Nrf1-2    CTGGTTCACCGAGACCCAGAGGGGTCTGTCTCTGGCAGTCAGCCCAACTCAGGCCTCGCC
          ************************************************************

Nrf1-1    CTCGAGAGTTCCAGTGGCCTCCAAGATGTGACAGGCCCAGACAACGGGGTGCGAGAAAGC
Nrf1-3    CTCGAGAGTTCCAGTGGCCTCCAAGATGTGACAGGCCCAGACAACGGGGTGCGAGAAAGC
Nrf1-2    CTCGAGAGTTCCAGTGGCCTCCAAGATGTGACAGGCCCAGACAACGGGGTGCGAGAAAGC
          ************************************************************
                                 sh-Nrf1-2
Nrf1-1    GAAACGGAGCAGGGATTCGGTGAAGATTTGGAGGATTTGGGGGCTGTAGCCCCCCCAGTC
Nrf1-3    GAAACGGAGCAGGGATTCGGTGAAGATTTGGAGGATTTGGGGGCTGTAGCCCCCCCAGTC
Nrf1-2    GAAACGGAGCAGGGATTCGGTGAAGATTTGGAGGATTTGGGGGCTGTAGCCCCCCCAGTC
          ************************************************************
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Nrf1-1    AGTGGAGACTTAACCAAAGAGGACATAGATCTGATTGACATCCTTTGGCGACAGGATATT
Nrf1-3    AGTGGAGACTTAACCAAAGAGGACATAGATCTGATTGACATCCTTTGGCGACAGGATATT
Nrf1-2    AGTGGAGACTTAACCAAAGAGGACATAGATCTGATTGACATCCTTTGGCGACAGGATATT
          ************************************************************

Nrf1-1    GATCTGGGGGCTGGGCGTGAGGTTTTTGACTATAGTCACCGCCAGAAGGAGCAGGATGTG
Nrf1-3    GATCTGGGGGCTGGGCGTGAGGTTTTTGACTATAGTCACCGCCAGAAGGAGCAGGATGTG
Nrf1-2    GATCTGGGGGCTGGGCGTGAGGTTTTTGACTATAGTCACCGCCAGAAGGAGCAGGATGTG
          ************************************************************

Nrf1-1    GAGAAGGAGCTGCGAGATGGAGGCGAGCAGGACACCTGGGCAGGCGAGGGCGCGGAAGCT
Nrf1-3    GAGAAGGAGCTGCGAGATGGAGGCGAGCAGGACACCTGGGCAGGCGAGGGCGCGGAAGCT
Nrf1-2    GAGAAGGAGCTGCGAGATGGAGGCGAGCAGGACACCTGGGCAGGCGAGGGCGCGGAAGCT
          ************************************************************

Nrf1-1    CTGGCACGGAACCTGCTAGTGGATGGAGAGACTGGGGAGAGCTTCCCTGCACAG------
Nrf1-3    CTGGCACGGAACCTGCTAGTGGATGGAGAGACTGGGGAGAGCTTCCCTGCACAGGTGCCT
Nrf1-2    CTGGCACGGAACCTGCTAGTGGATGGAGAGACTGGGGAGAGCTTCCCTGCACAGGTGCCT
          ******************************************************

Nrf1-1    ------------------------------------------------------------
Nrf1-3    AGTGGGGAGGACCAGACGGCCCTGTCCCTGGAAGAGTGCCTTAGGCTGCTGGAAGCCACC
Nrf1-2    AGTGGGGAGGACCAGACGGCCCTGTCCCTGGAAGAGTGCCTTAGGCTGCTGGAAGCCACC

                                                        sh-Nrf1-3
Nrf1-1    ------------------------TTTCCAGCAGACATTTCCAGCATAACAGAAGCAGTG
Nrf1-3    TGCCCCTTTGGGGAGAATGCTGAGTTTCCAGCAGACATTTCCAGCATAACAGAAGCAGTG
Nrf1-2    TGCCCCTTTGGGGAGAATGCTGAGTTTCCAGCAGACATTTCCAGCATAACAGAAGCAGTG
                                     ************************************

Nrf1-1    CCTAGTGAGAGTGAGCCCCCTGCTCTTCAAAACAACCTCTTGTCTCCTCTTCTGACCGGG
Nrf1-3    CCTAGTGAGAGTGAGCCCCCTGCTCTTCAAAACAACCTCTTGTCTCCTCTTCTGACCGGG
Nrf1-2    CCTAGTGAGAGTGAGCCCCCTGCTCTTCAAAACAACCTCTTGTCTCCTCTTCTGACCGGG
          ************************************************************

Nrf1-1    ACAGAGTCACCATTTGATTTGGAACAGCAGTGGCAAGATCTCATGTCCATCATGGAAATG
Nrf1-3    ACAGAGTCACCATTTGATTTGGAACAGCAGTGGCAAGATCTCATGTCCATCATGGAAATG
Nrf1-2    ACAGAGTCACCATTTGATTTGGAACAGCAGTGGCAAGATCTCATGTCCATCATGGAAATG
          ************************************************************

Nrf1-1    CAGGCCATGGAAGTGAACACATCAGCAAGTGAAATCCTGTACAGTGCCCCTCCTGGAGAC
Nrf1-3    CAGGCCATGGAAGTGAACACATCAGCAAGTGAAATCCTGTACAGTGCCCCTCCTGGAGAC
Nrf1-2    CAGGCCATGGAAGTGAACACATCAGCAAGTGAAATCCTGTACAGTGCCCCTCCTGGAGAC
          ************************************************************

Nrf1-1    CCACTGAGCACCAACTACAGCCTTGCCCCCAACACTCCCATCAATCAGAATGTCAGCCTG
Nrf1-3    CCACTGAGCACCAACTACAGCCTTGCCCCCAACACTCCCATCAATCAGAATGTCAGCCTG
Nrf1-2    CCACTGAGCACCAACTACAGCCTTGCCCCCAACACTCCCATCAATCAGAATGTCAGCCTG
          ************************************************************

Nrf1-1    CATCAGGCGTCCCTGGGGGGCTGCAGCCAGGACTTCTTACTCTTCAGCCCCGAGGTGGAA
Nrf1-3    CATCAGGCGTCCCTGGGGGGCTGCAGCCAGGACTTCTTACTCTTCAGCCCCGAGGTGGAA
Nrf1-2    CATCAGGCGTCCCTGGGGGGCTGCAGCCAGGACTTCTTACTCTTCAGCCCCGAGGTGGAA
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Nrf1-1    AGCCTGCCTGTGGCCAGTAGCTCCACGCTGCTCCCGTTGGCCCCCAGCAATTCTACCAGC
Nrf1-3    AGCCTGCCTGTGGCCAGTAGCTCCACGCTGCTCCCGTTGGCCCCCAGCAATTCTACCAGC
Nrf1-2    AGCCTGCCTGTGGCCAGTAGCTCCACGCTGCTCCCGTTGGCCCCCAGCAATTCTACCAGC
          ************************************************************

Nrf1-1    CTCAACTCCACCTTCGGCTCCACCAACCTGACAGGGCTCTTCTTTCCACCCCAGCTCAAT
Nrf1-3    CTCAACTCCACCTTCGGCTCCACCAACCTGACAGGGCTCTTCTTTCCACCCCAGCTCAAT
Nrf1-2    CTCAACTCCACCTTCGGCTCCACCAACCTGACAGGGCTCTTCTTTCCACCCCAGCTCAAT
          ************************************************************

Nrf1-1    GGCACAGCCAATGACACAGCAGGCCCAGAGCTGCCTGACCCTTTGGGGGGTCTGTTAGAT
Nrf1-3    GGCACAGCCAATGACACAGCAGGCCCAGAGCTGCCTGACCCTTTGGGGGGTCTGTTAGAT
Nrf1-2    GGCACAGCCAATGACACAGCAGGCCCAGAGCTGCCTGACCCTTTGGGGGGTCTGTTAGAT
          ************************************************************

Nrf1-1    GAAGCTATGTTGGATGAGATCAGCCTTATGGACCTGGCCATTGAAGAAGGCTTTAACCCT
Nrf1-3    GAAGCTATGTTGGATGAGATCAGCCTTATGGACCTGGCCATTGAAGAAGGCTTTAACCCT
Nrf1-2    GAAGCTATGTTGGATGAGATCAGCCTTATGGACCTGGCCATTGAAGAAGGCTTTAACCCT
          ************************************************************

Nrf1-1    GTGCAGGCCTCCCAGCTGGAGGAGGAATTTGACTCTGACTCAGGCCTTTCCTTAGACTCG
Nrf1-3    GTGCAGGCCTCCCAGCTGGAGGAGGAATTTGACTCTGACTCAGGCCTTTCCTTAGACTCG
Nrf1-2    GTGCAGGCCTCCCAGCTGGAGGAGGAATTTGACTCTGACTCAGGCCTTTCCTTAGACTCG
          ************************************************************

Nrf1-1    AGCCATAGCCCTTCTTCCCTAAGCAGCTCTGAAGGCAGTTCTTCCTCTTCTTCCTCCTCC
Nrf1-3    AGCCATAGCCCTTCTTCCCTAAGCAGCTCTGAAGGCAGTTCTTCCTCTTCTTCCTCCTCC
Nrf1-2    AGCCATAGCCCTTCTTCCCTAAGCAGCTCTGAAGGCAGTTCTTCCTCTTCTTCCTCCTCC
          ************************************************************

Nrf1-1    TCTTCCTCTTCTTCCTCTGCTTCTTCCTCTGCCTCTTCCTCCTTTTCTGAGGAAGGTGCG
Nrf1-3    TCTTCCTCTTCTTCCTCTGCTTCTTCCTCTGCCTCTTCCTCCTTTTCTGAGGAAGGTGCG
Nrf1-2    TCTTCCTCTTCTTCCTCTGCTTCTTCCTCTGCCTCTTCCTCCTTTTCTGAGGAAGGTGCG
          ************************************************************

Nrf1-1    GTTGGCTACAGCTCTGACTCTGAGACCCTGGATCTGGAAGAGGCCGAGGGTGCTGTGGGC
Nrf1-3    GTTGGCTACAGCTCTGACTCTGAGACCCTGGATCTGGAAGAGGCCGAGGGTGCTGTGGGC
Nrf1-2    GTTGGCTACAGCTCTGACTCTGAGACCCTGGATCTGGAAGAGGCCGAGGGTGCTGTGGGC
          ************************************************************
                   sh-Nrf1-4
Nrf1-1    TACCAGCCTGAGTATTCCAAGTTCTGCCGCATGAGCTACCAGGATCCAGCTCAGCTCTCA
Nrf1-3    TACCAGCCTGAGTATTCCAAGTTCTGCCGCATGAGCTACCAGGATCCAGCTCAGCTCTCA
Nrf1-2    TACCAGCCTGAGTATTCCAAGTTCTGCCGCATGAGCTACCAGGATCCAGCTCAGCTCTCA
          ************************************************************

Nrf1-1    TGCCTGCCCTACCTGGAGCACGTGGGCCACAACCACACATACAACATGGCACCCAGTGCC
Nrf1-3    TGCCTGCCCTACCTGGAGCACGTGGGCCACAACCACACATACAACATGGCACCCAGTGCC
Nrf1-2    TGCCTGCCCTACCTGGAGCACGTGGGCCACAACCACACATACAACATGGCACCCAGTGCC
          ************************************************************

Nrf1-1    CTGGACTCAGCCGACCTGCCACCACCCAGTGCCCTCAAGAAAGGCAGCAAGGAGAAGCAG
Nrf1-3    CTGGACTCAGCCGACCTGCCACCACCCAGTGCCCTCAAGAAAGGCAGCAAGGAGAAGCAG
Nrf1-2    CTGGACTCAGCCGACCTGCCACCACCCAGTGCCCTCAAGAAAGGCAGCAAGGAGAAGCAG
          ************************************************************
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Nrf1-1    GCTGACTTCCTGGACAAGCAGATGAGCCGGGATGAGCACCGAGCCCGAGCCATGAAGATC
Nrf1-3    GCTGACTTCCTGGACAAGCAGATGAGCCGGGATGAGCACCGAGCCCGAGCCATGAAGATC
Nrf1-2    GCTGACTTCCTGGACAAGCAGATGAGCCGGGATGAGCACCGAGCCCGAGCCATGAAGATC
          ************************************************************

Nrf1-1    CCTTTCACCAATGACAAAATCATCAACCTGCCTGTGGAGGAGTTCAATGAACTGCTGTCC
Nrf1-3    CCTTTCACCAATGACAAAATCATCAACCTGCCTGTGGAGGAGTTCAATGAACTGCTGTCC
Nrf1-2    CCTTTCACCAATGACAAAATCATCAACCTGCCTGTGGAGGAGTTCAATGAACTGCTGTCC
          ************************************************************

Nrf1-1    AAATACCAGTTGAGTGAAGCCCAGCTGAGCCTCATCCGAGACATCCGGCGCCGGGGCAAG
Nrf1-3    AAATACCAGTTGAGTGAAGCCCAGCTGAGCCTCATCCGAGACATCCGGCGCCGGGGCAAG
Nrf1-2    AAATACCAGTTGAGTGAAGCCCAGCTGAGCCTCATCCGAGACATCCGGCGCCGGGGCAAG
          ************************************************************

Nrf1-1    AACAAGATGGCGGCGCAGAACTGCCGCAAGCGCAAGCTGGACACCATCCTGAATCTGGAG
Nrf1-3    AACAAGATGGCGGCGCAGAACTGCCGCAAGCGCAAGCTGGACACCATCCTGAATCTGGAG
Nrf1-2    AACAAGATGGCGGCGCAGAACTGCCGCAAGCGCAAGCTGGACACCATCCTGAATCTGGAG
          ************************************************************

Nrf1-1    CGTGATGTGGAGGACCTGCAGCGTGACAAAGCCCGGCTGCTGCGGGAGAAAGTGGAGTTC
Nrf1-3    CGTGATGTGGAGGACCTGCAGCGTGACAAAGCCCGGCTGCTGCGGGAGAAAGTGGAGTTC
Nrf1-2    CGTGATGTGGAGGACCTGCAGCGTGACAAAGCCCGGCTGCTGCGGGAGAAAGTGGAGTTC
          ************************************************************

Nrf1-1    CTGCGCTCCCTGCGACAGATGAAGCAGAAGGTCCAGAGCCTGTACCAGGAGGTGTTTGGG
Nrf1-3    CTGCGCTCCCTGCGACAGATGAAGCAGAAGGTCCAGAGCCTGTACCAGGAGGTGTTTGGG
Nrf1-2    CTGCGCTCCCTGCGACAGATGAAGCAGAAGGTCCAGAGCCTGTACCAGGAGGTGTTTGGG
          ************************************************************

Nrf1-1    CGGCTGCGAGATGAGAACGGACGACCCTACTCGCCCAGTCAGTATGCGCTCCAGTACGCC
Nrf1-3    CGGCTGCGAGATGAGAACGGACGACCCTACTCGCCCAGTCAGTATGCGCTCCAGTACGCC
Nrf1-2    CGGCTGCGAGATGAGAACGGACGACCCTACTCGCCCAGTCAGTATGCGCTCCAGTACGCC
          ************************************************************

Nrf1-1    GGGGACGGCAGTGTCCTCCTCATCCCCCGCACGATGGCCGACCAGCAGGCCCGGCGGCAG
Nrf1-3    GGGGACGGCAGTGTCCTCCTCATCCCCCGCACGATGGCCGACCAGCAGGCCCGGCGGCAG
Nrf1-2    GGGGACGGCAGTGTCCTCCTCATCCCCCGCACGATGGCCGACCAGCAGGCCCGGCGGCAG
          ************************************************************

Nrf1-1    GAGAGGAAGCCAAAGGACCGGAGAAAGTGAGCCTGGGGAAGAAGGGGGTTTGAAGCCCAC
Nrf1-3    GAGAGGAAGCCAAAGGACCGGAGAAAGTGAGCCTGGGGAAGAAGGGGGTTTGAAGCCCAC
Nrf1-2    GAGAGGAAGCCAAAGGACCGGAGAAAGTGAGCCTGGGGAAGAAGGGGGTTTGAAGCCCAC
          ************************************************************

Nrf1-1    CAAGACCGAAACTGGAGAAGGGCTGGACCTGGACCTGGACCTGGACCTACAGCGGGGACT
Nrf1-3    CAAGACCGAAACTGGAGAAGGGCTGGACCTGGACCTGGACCTGGACCTACAGCGGGGACT
Nrf1-2    CAAGACCGAAACTGGAGAAGGGCTGGACCTGGACCTGGACCTGGACCTACAGCGGGGACT
          ************************************************************

Nrf1-1    TAAATGCCTTCTTATCCAATATATCTTCTCAGATGGGATGACTGCGGGTCAGTGTACAGG
Nrf1-3    TAAATGCCTTCTTATCCAATATATCTTCTCAGATGGGATGACTGCGGGTCAGTGTACAGG
Nrf1-2    TAAATGCCTTCTTATCCAATATATCTTCTCAGATGGGATGACTGCGGGTCAGTGTACAGG
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Nrf1-1    AAGAGGCAGGCACTGGCTGGCTCAGCTCCACTCGGGTGGAGTGGAAGTGGCCAGACCATT
Nrf1-3    AAGAGGCAGGCACTGGCTGGCTCAGCTCCACTCGGGTGGAGTGGAAGTGGCCAGACCATT
Nrf1-2    AAGAGGCAGGCACTGGCTGGCTCAGCTCCACTCGGGTGGAGTGGAAGTGGCCAGACCATT
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Nrf1-1    TAGACGGACAGGGTCCTCACCCTACCCCTTTCCTGTGAGGCAGGGGTGGTGGTGGAGTTG
Nrf1-3    TAGACGGACAGGGTCCTCACCCTACCCCTTTCCTGTGAGGCAGGGGTGGTGGTGGAGTTG
Nrf1-2    TAGACGGACAGGGTCCTCACCCTACCCCTTTCCTGTGAGGCAGGGGTGGTGGTGGAGTTG
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Nrf1-1    CTGGAGGTAGAGGAGCTATGTGGAGCAAAGGCCGACAGAGGGGAAGGAATGGACCTGTGA
Nrf1-3    CTGGAGGTAGAGGAGCTATGTGGAGCAAAGGCCGACAGAGGGGAAGGAATGGACCTGTGA
Nrf1-2    CTGGAGGTAGAGGAGCTATGTGGAGCAAAGGCCGACAGAGGGGAAGGAATGGACCTGTGA
          ************************************************************

Nrf1-1    GAGGAAGGGAAGGTGGCAGAAAGTCTCATTTCAGGAAGGAGGGATAGAAGGAAGGAAGGA
Nrf1-3    GAGGAAGGGAAGGTGGCAGAAAGTCTCATTTCAGGAAGGAGGGATAGAAGGAAGGAAGGA
Nrf1-2    GAGGAAGGGAAGGTGGCAGAAAGTCTCATTTCAGGAAGGAGGGATAGAAGGAAGGAAGGA
          ************************************************************

Nrf1-1    AGGAACCCCCCCCCCCCCGAAAAAAAAATCAAAGCGGGAAGAAAATCAGAGGGAAGGTTA
Nrf1-3    AGGAACCCCCCCCCCCCCGAAAAAAAAATCAAAGCGGGAAGAAAATCAGAGGGAAGGTTA
Nrf1-2    AGGAACCCCCCCCCCCCCGAAAAAAAAATCAAAGCGGGAAGAAAATCAGAGGGAAGGTTA
          ************************************************************

Nrf1-1    AGGTTGGCTCTGGCCAGGATTCCAGGCAGCAGGTTGGAGTGACTGGTGGGCCTAGATCAC
Nrf1-3    AGGTTGGCTCTGGCCAGGATTCCAGGCAGCAGGTTGGAGTGACTGGTGGGCCTAGATCAC
Nrf1-2    AGGTTGGCTCTGGCCAGGATTCCAGGCAGCAGGTTGGAGTGACTGGTGGGCCTAGATCAC
          ************************************************************

Nrf1-1    TGGTGTGATAAACCCCAATTTTCACCCCGGGGGGGGTGGGGTACACAGACACAGGGTGGG
Nrf1-3    TGGTGTGATAAACCCCAATTTTCACCCCGGGGGGGGTGGGGTACACAGACACAGGGTGGG
Nrf1-2    TGGTGTGATAAACCCCAATTTTCACCCCGGGGGGGGTGGGGTACACAGACACAGGGTGGG
          ************************************************************

Nrf1-1    GGTGGGGAGGGACGGTGTTAACTCTTTCTGCTCCTTGCATTTTGACATCCCTGAAGGGGA
Nrf1-3    GGTGGGGAGGGACGGTGTTAACTCTTTCTGCTCCTTGCATTTTGACATCCCTGAAGGGGA
Nrf1-2    GGTGGGGAGGGACGGTGTTAACTCTTTCTGCTCCTTGCATTTTGACATCCCTGAAGGGGA
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Nrf1-1    GCTCTTGGATATCATTGGCCATGTTTCAATCGAATGGAGCCACTGGGCCCCAACACTGGC
Nrf1-3    GCTCTTGGATATCATTGGCCATGTTTCAATCGAATGGAGCCACTGGGCCCCAACACTGGC
Nrf1-2    GCTCTTGGATATCATTGGCCATGTTTCAATCGAATGGAGCCACTGGGCCCCAACACTGGC
          ************************************************************
                 sh-Nrf1-1
Nrf1-1    TTTGAGATTTAGAGTCAAAGGGTAGAGTGAACAGGAAAGGGTCACGTGGTCCCATGTTGC
Nrf1-3    TTTGAGATTTAGAGTCAAAGGGTAGAGTGAACAGGAAAGGGTCACGTGGTCCCATGTTGC
Nrf1-2    TTTGAGATTTAGAGTCAAAGGGTAGAGTGAACAGGAAAGGGTCACGTGGTCCCATGTTGC
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Nrf1-1    AACAGCCCCAACATCACGCATGTCATTCACTGCCTTGCCACTCCATCTCCCTCCGTGCTC
Nrf1-3    AACAGCCCCAACATCACGCATGTCATTCACTGCCTTGCCACTCCATCTCCCTCCGTGCTC
Nrf1-2    AACAGCCCCAACATCACGCATGTCATTCACTGCCTTGCCACTCCATCTCCCTCCGTGCTC
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Nrf1-1    CAGCCACCCCTGAGCTGAGGCTCCCATTGTCTCCATCAGAGCCTGCATGTGTATGCCGTC
Nrf1-3    CAGCCACCCCTGAGCTGAGGCTCCCATTGTCTCCATCAGAGCCTGCATGTGTATGCCGTC
Nrf1-2    CAGCCACCCCTGAGCTGAGGCTCCCATTGTCTCCATCAGAGCCTGCATGTGTATGCCGTC
          ************************************************************

Nrf1-1    CTCCCCTGGTCCGGTGTTTGTGTTCCCCACCCCTCACAGACTGCCTGAGCTCTTCTGTAA
Nrf1-3    CTCCCCTGGTCCGGTGTTTGTGTTCCCCACCCCTCACAGACTGCCTGAGCTCTTCTGTAA
Nrf1-2    CTCCCCTGGTCCGGTGTTTGTGTTCCCCACCCCTCACAGACTGCCTGAGCTCTTCTGTAA
          ************************************************************

Nrf1-1    GCTGGGGTAGGGTGATGGCAGTGCTCCGGGAACTGGGCCTGCAGCCTTCCTCTTCTGGGA
Nrf1-3    GCTGGGGTAGGGTGATGGCAGTGCTCCGGGAACTGGGCCTGCAGCCTTCCTCTTCTGGGA
Nrf1-2    GCTGGGGTAGGGTGATGGCAGTGCTCCGGGAACTGGGCCTGCAGCCTTCCTCTTCTGGGA
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Nrf1-1    CTGCTGTGAGGCAGAGGAATGATGGAGAATCTAGTGTAGCAGCCTCCAGGCAGGATTCAG
Nrf1-3    CTGCTGTGAGGCAGAGGAATGATGGAGAATCTAGTGTAGCAGCCTCCAGGCAGGATTCAG
Nrf1-2    CTGCTGTGAGGCAGAGGAATGATGGAGAATCTAGTGTAGCAGCCTCCAGGCAGGATTCAG
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Nrf1-1    CACAACACTGGGGAGTCACCCTTCCCTCGGGCCTCTGCCTACCAACAACTGGGCTTATCA
Nrf1-3    CACAACACTGGGGAGTCACCCTTCCCTCGGGCCTCTGCCTACCAACAACTGGGCTTATCA
Nrf1-2    CACAACACTGGGGAGTCACCCTTCCCTCGGGCCTCTGCCTACCAACAACTGGGCTTATCA
          ************************************************************

Nrf1-1    CTGGGAAAACACAAAAAATTACACAACCCAGCAACAACAAAAGAACTAGTCCTCTTAGAA
Nrf1-3    CTGGGAAAACACAAAAAATTACACAACCCAGCAACAACAAAAGAACTAGTCCTCTTAGAA
Nrf1-2    CTGGGAAAACACAAAAAATTACACAACCCAGCAACAACAAAAGAACTAGTCCTCTTAGAA
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Nrf1-1    TTTCTTGCGCTTTGATTTTTTTAGGGCTTGTGCCCTGTTTCACTTATAGGGTCTAGAATG
Nrf1-3    TTTCTTGCGCTTTGATTTTTTTAGGGCTTGTGCCCTGTTTCACTTATAGGGTCTAGAATG
Nrf1-2    TTTCTTGCGCTTTGATTTTTTTAGGGCTTGTGCCCTGTTTCACTTATAGGGTCTAGAATG
          ************************************************************

Nrf1-1    CTTGTGTTGAGTAAAAAGGAGATGCCCAATATTCAAAGCTGCTAAATGTTCTCTTTGCCA
Nrf1-3    CTTGTGTTGAGTAAAAAGGAGATGCCCAATATTCAAAGCTGCTAAATGTTCTCTTTGCCA
Nrf1-2    CTTGTGTTGAGTAAAAAGGAGATGCCCAATATTCAAAGCTGCTAAATGTTCTCTTTGCCA
          ************************************************************

Nrf1-1    TAAAGACTCCGTGTAACTGTGTGAACACTTGGGATTTTTCTCCTCTGTCCCGAGGTCGTC
Nrf1-3    TAAAGACTCCGTGTAACTGTGTGAACACTTGGGATTTTTCTCCTCTGTCCCGAGGTCGTC
Nrf1-2    TAAAGACTCCGTGTAACTGTGTGAACACTTGGGATTTTTCTCCTCTGTCCCGAGGTCGTC
          ************************************************************

Nrf1-1    GTCTGCTTTCTTTTTTGGGTTTCTTTCTAGAAGATTGAGAAGTGCATATGACAGGCTGAG
Nrf1-3    GTCTGCTTTCTTTTTTGGGTTTCTTTCTAGAAGATTGAGAAGTGCATATGACAGGCTGAG
Nrf1-2    GTCTGCTTTCTTTTTTGGGTTTCTTTCTAGAAGATTGAGAAGTGCATATGACAGGCTGAG
          ************************************************************

Nrf1-1    AGCACCTCCCCAAACACACAAGCTCTCAGCCACAGGCAGCTTCTCCACAGCCCCAGCTTC
Nrf1-3    AGCACCTCCCCAAACACACAAGCTCTCAGCCACAGGCAGCTTCTCCACAGCCCCAGCTTC
Nrf1-2    AGCACCTCCCCAAACACACAAGCTCTCAGCCACAGGCAGCTTCTCCACAGCCCCAGCTTC
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Nrf1-1     GCACAGGCTCCTGGAGGGCTGCCTGGGGGAGGCAGACATGGGAGTGCCAAGGTGGCCAGA
Nrf1-3     GCACAGGCTCCTGGAGGGCTGCCTGGGGGAGGCAGACATGGGAGTGCCAAGGTGGCCAGA
Nrf1-2     GCACAGGCTCCTGGAGGGCTGCCTGGGGGAGGCAGACATGGGAGTGCCAAGGTGGCCAGA
           ************************************************************

Nrf1-1     TGGTTCCAGGACTACAATGTCTTTATTTTTAACTGTTTGCCACTGCTGCCCTCACCCCTG
Nrf1-3     TGGTTCCAGGACTACAATGTCTTTATTTTTAACTGTTTGCCACTGCTGCCCTCACCCCTG
Nrf1-2     TGGTTCCAGGACTACAATGTCTTTATTTTTAACTGTTTGCCACTGCTGCCCTCACCCCTG
           ************************************************************

Nrf1-1     CCCGGCTCTGGAGTACCGTCTGCCCCAGACAAGTGGGAGTGAAATGGGGGTGGGGGGAAG
Nrf1-3     CCCGGCTCTGGAGTACCGTCTGCCCCAGACAAGTGGGAGTGAAATGGGGGTGGGGGGAAG
Nrf1-2     CCCGGCTCTGGAGTACCGTCTGCCCCAGACAAGTGGGAGTGAAATGGGGGTGGGGGGAAG
           ************************************************************

Nrf1-1     CACTGATTCCCAGTTAGGGGGTGCCTAACTGAGCAGTAGGGATAGAAGGTGTGAACCTGG
Nrf1-3     CACTGATTCCCAGTTAGGGGGTGCCTAACTGAGCAGTAGGGATAGAAGGTGTGAACCTGG
Nrf1-2     CACTGATTCCCAGTTAGGGGGTGCCTAACTGAGCAGTAGGGATAGAAGGTGTGAACCTGG
           ************************************************************

Nrf1-1     GAGTGCTTTTATAAATTATTTTCCTTGTAGATTTTATTTTTAATTTATCTCTGTGACCTG
Nrf1-3     GAGTGCTTTTATAAATTATTTTCCTTGTAGATTTTATTTTTAATTTATCTCTGTGACCTG
Nrf1-2     GAGTGCTTTTATAAATTATTTTCCTTGTAGATTTTATTTTTAATTTATCTCTGTGACCTG
           ************************************************************

Nrf1-1     CCAGGGAGAGGGGAGAGAGAGAGAGATGCTGTTGAGCACATGACAAAATAAAATAAAATG
Nrf1-3     CCAGGGAGAGGGGAGAGAGAGAGAGATGCTGTTGAGCACATGACAAAATAAAATAAAATG
Nrf1-2     CCAGGGAGAGGGGAGAGAGAGAGAGATGCTGTTGAGCACATGACAAAATAAAATAAAATG
           ************************************************************

Nrf1-1     GATGATTCATTCTTAAGTGCACTTTTTCCCCACTTTGAATTTAAATTGAGAATAAAGGAA
Nrf1-3     GATGATTCATTCTTAAGTGCACTTTTTCCCCACTTTGAATTTAAATTGAGAATAAAGGAA
Nrf1-2     GATGATTCATTCTTAAGTGCACTTTTTCCCCACTTTGAATTTAAATTGAGAATAAAGGAA
           ************************************************************

Nrf1-1     ATGGACTCATTGT
Nrf1-3     ATGGACTCATTGT
Nrf1-2     ATGGACTCATTGT
           *************
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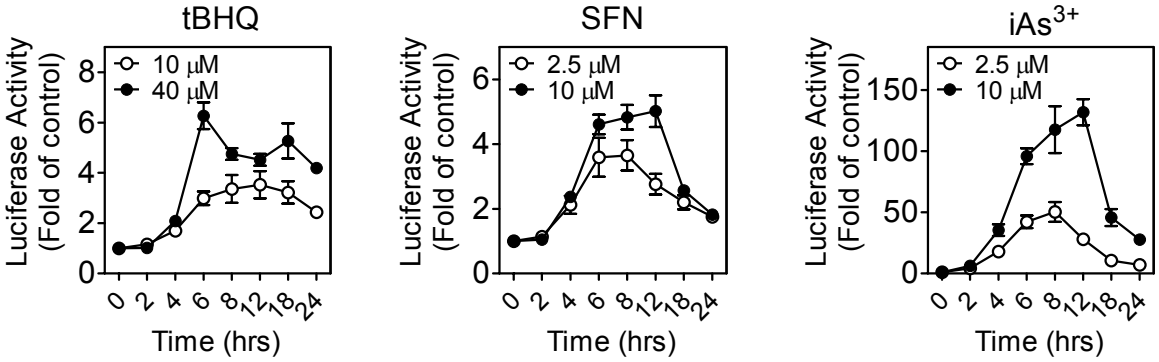
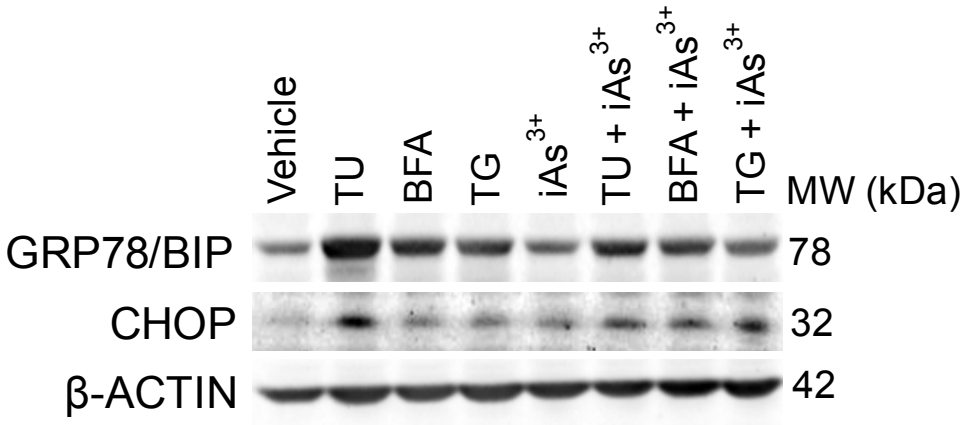
Supplemental Material, Figure 1:



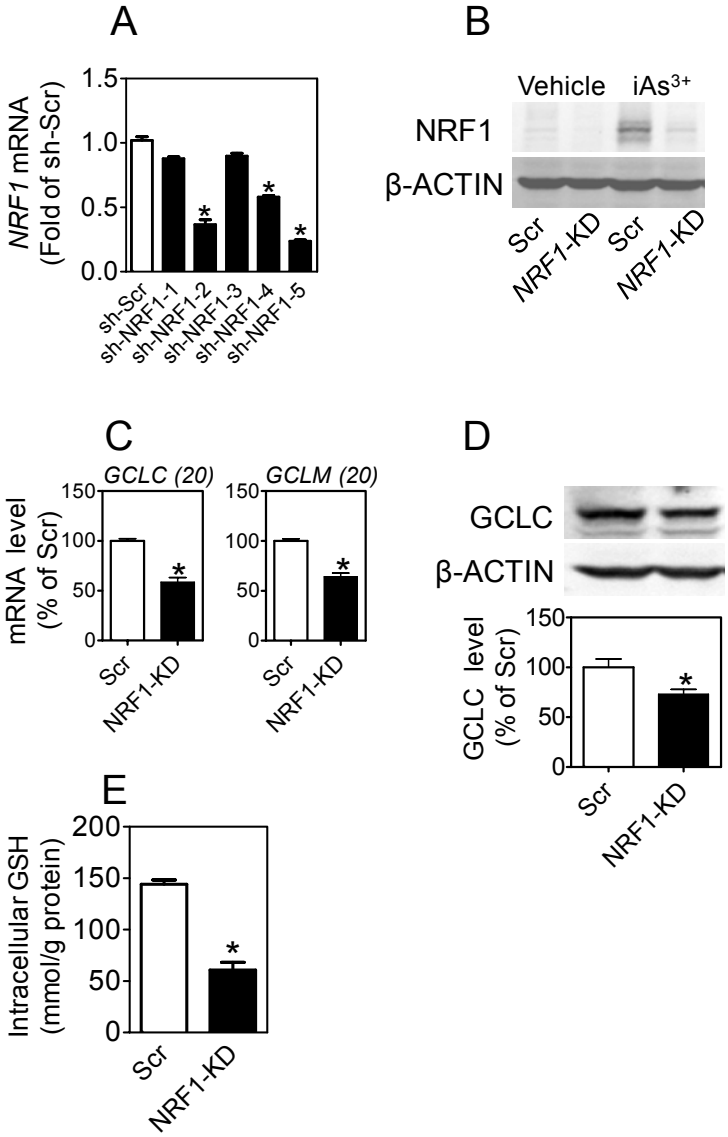
ARE-luciferase reporter in HaCaT cells is responsive to NRF2 and NRF1 activators.

Supplemental Material, Figure 2:



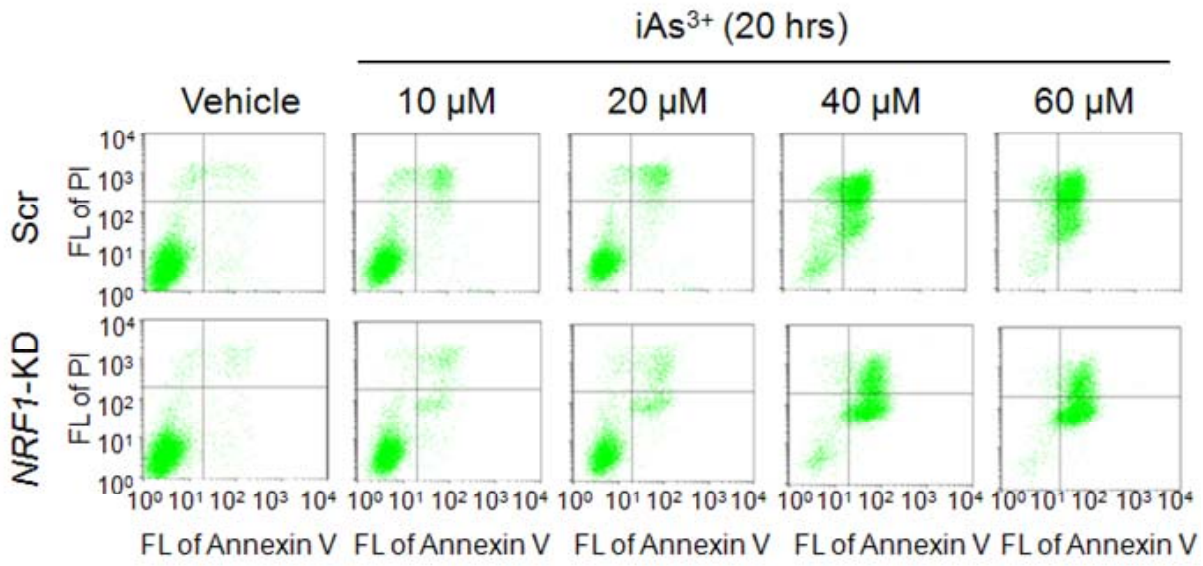
TU, BFA and TG induce ER stress in HaCaT cells. The cells were treated with Vehicle (0.5 % DMSO), TU (2 µg/ml tunicamycin), BFA (1 µg/ml brefeldin A), TG (2 µM thapsigargin) with or without 10 µM of iAs^{3+} for 6 hrs and whole cell lysates were used for Western blot. GRP78/BIP and CHOP are downstream protein markers for ER stress.

Supplemental Material, Figure 3:



Stable knockdown of *NRF1* decreases the expression of GCL and intracellular glutathione (GSH) content. (*A*) Expression of *NRF1* in HaCaT cells transduced with shRNA lentivirus targeted against human *NRF1*. n = 3. *, $p < 0.05$ *vs.* sh-Scr. (*B*) Silencing effect of a selected sh-RNA (sh-NRF1-5) on NRF1 protein expression induced by iAs^{3+}. (*C*) Decreased gene expression of *GCLC* and *GCLM* in *NRF1*-KD cells. n = 3. *, $p < 0.05$ *vs.* Scr. The number in brackets following each gene name is the Ct value of that gene in Scr cells. (*D*) Decreased GCLC protein expression in *NRF1*-KD cells. (*E*) Lack of *NRF1* results in decreased intracellular GSH content. n = 6. *, $p < 0.05$ *vs.* Scr.

Supplemental Material, Figure 4:



Representative images of apoptosis measurements by flow cytometry. HaCaT cells stained with Annexin V and propidium iodide (PI) before being analyzed. FL, fluorescence.