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Appendix A: Vector maps

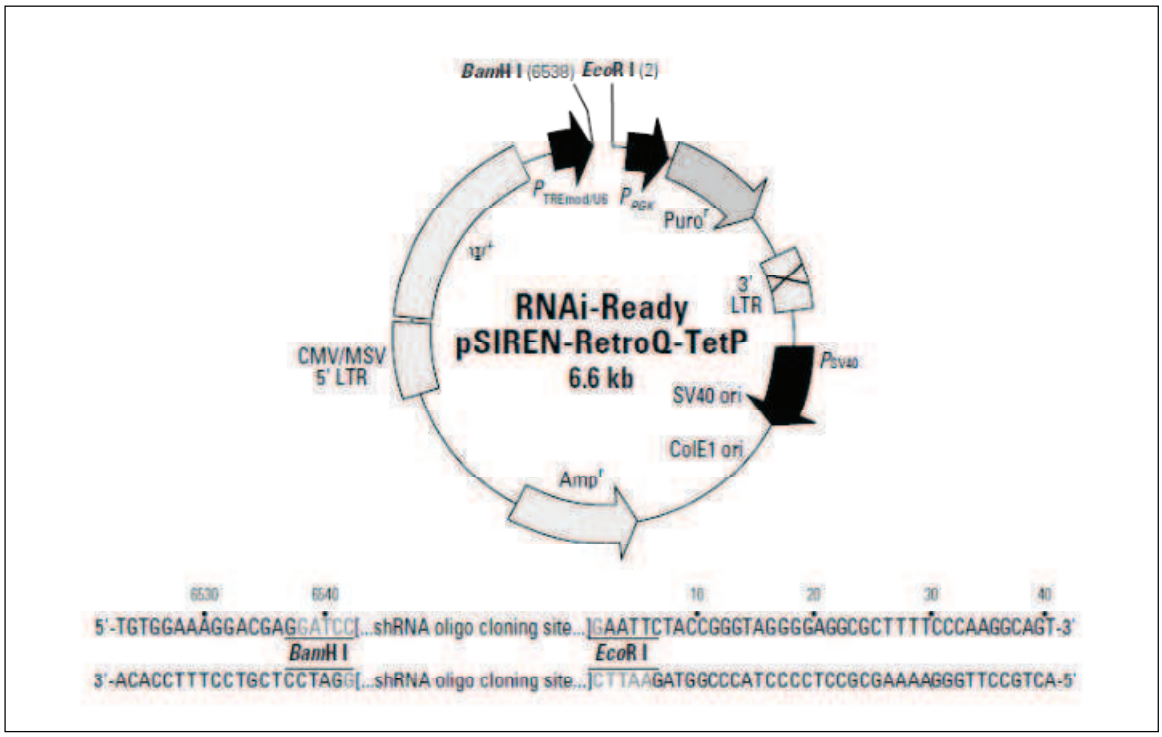


Figure A-1. RNAi-Ready pSIREN-RetroQ-TetP vector map.

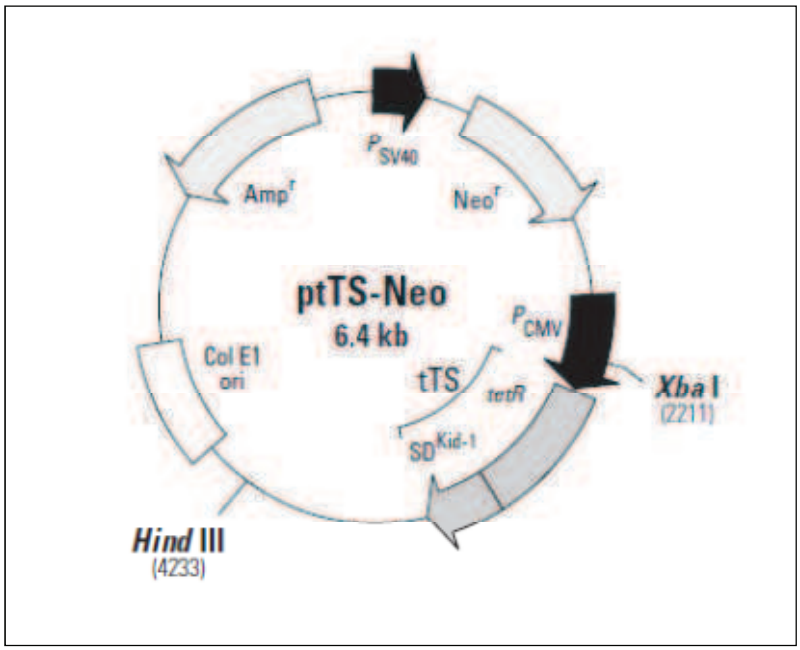


Figure A-2. ptTS-Neo vector map.

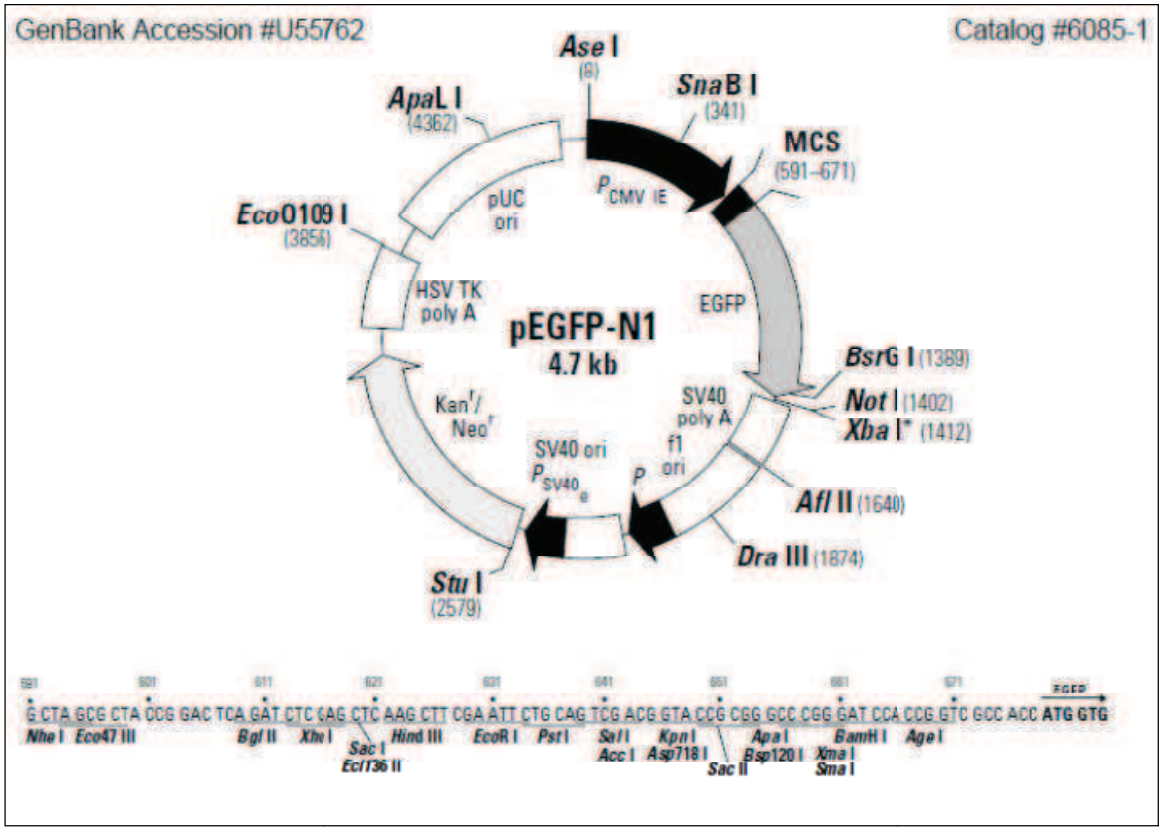


Figure A-3. pEGFP-N1 vector map.

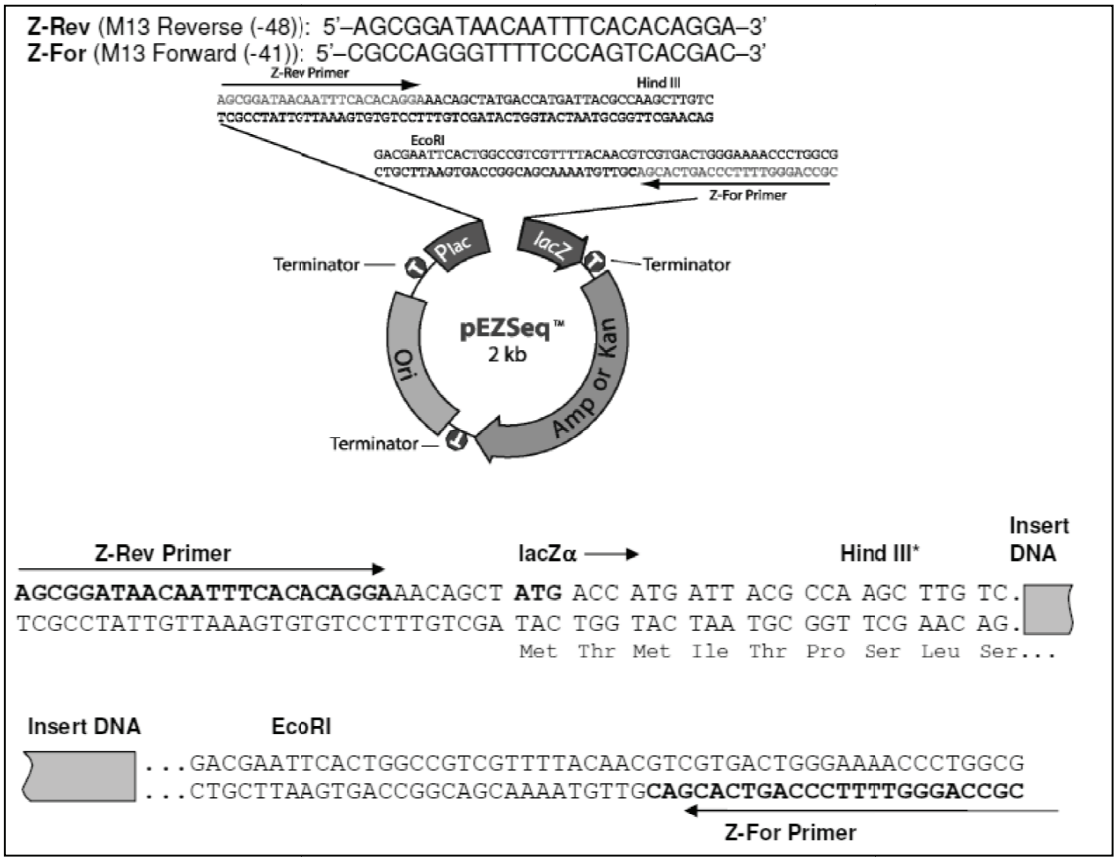
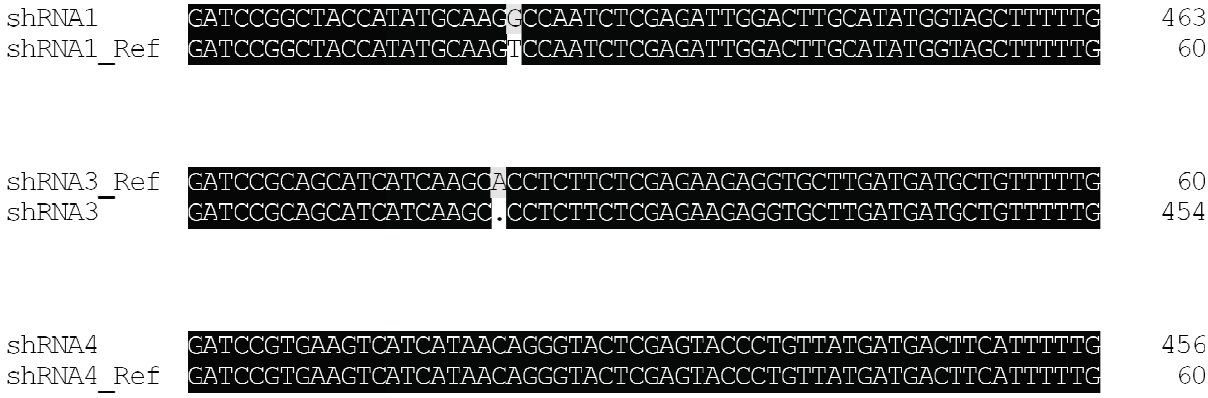


Figure A-4. pEZSeq vector map.

Appendix B


shRNA1 GATCCGGCTACCATATGCAAGGCCAATCTCGAGATTGGACTTGCATATGGTAGCTTTTTG 463
shRNA1_Ref GATCCGGCTACCATATGCAAGTCCAATCTCGAGATTGGACTTGCATATGGTAGCTTTTTG 60
shRNA3_Ref GATCCGCAGCATCATCAAGCACCTCTTCTCGAGAAGAGGTGCTTGATGATGCTGTTTTTG 60
shRNA3 GATCCGCAGCATCATCAAGC.CCTCTTCTCGAGAAGAGGTGCTTGATGATGCTGTTTTTG 454
shRNA4 GATCCGTGAAGTCATCATAACAGGGTACTCGAGTACCCTGTTATGATGACTTCATTTTTG 456
shRNA4_Ref GATCCGTGAAGTCATCATAACAGGGTACTCGAGTACCCTGTTATGATGACTTCATTTTTG 60

Appendix C

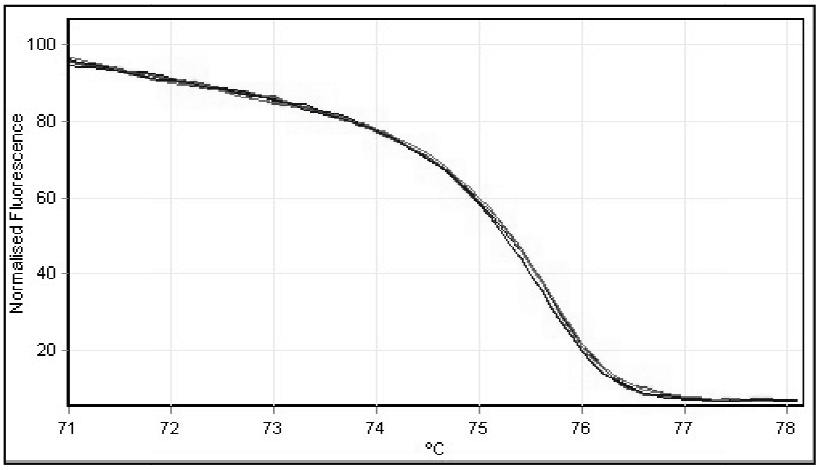


Figure C-1. HRM results from HPP1 fragment of mouse *hprt1*.

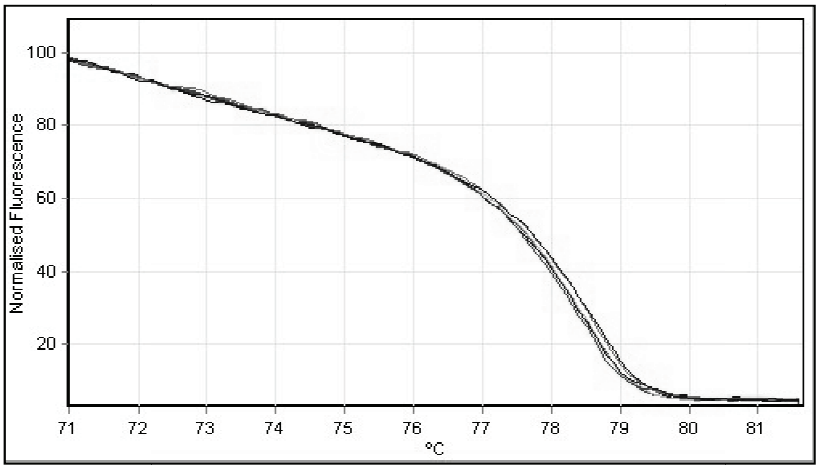


Figure C-2. HRM results from HPP5 fragment of mouse *hprt1*.

Appendix D

(In alphabetical order)

Ampicillin (1000X):

Ampicillin:.....100 mg
ddH_2O:..... 1 ml

Electrophoresis buffer:

NaOH [0.6M]:..... 500 ml
EDTA [0.05M]:..... 20 ml
ddH_2O:..... Up to 1 L

1% HMPA:

High melting point agarose:..... 0.4 g
EDTA [0.1 M]:..... 40 ml

p-Hydroxyphenylpyruvic acid [5 mM]:

4-Hydroxyphenylpyruvic acid:..... 9.008 g
ddH_2O:..... Up to 10 ml
Adjust pH by adding 75 µl [1 M] NaOH

0.5% LMPA:

Low melting point agarose: ..... 0.25 g
EDTA [0.1 M]:..... 50 ml

Lyses buffer:

NaCl [5M]:..... 500 ml
EDTA [0.4M] (pH 7-8):..... 250 ml
Triton X-100:..... 10 ml
DMSO [10%]:..... 100 ml
ddH_2O:..... Up to 1 L

Neutralising buffer:

Tris-HCl:..... 63.04 g
ddH_2O:..... Up to 500 ml
Adjust pH to 7.5 after 1 h in fridge with [0.6M] NaOH
ddH_2O:..... Up to 1 L

SOC Broth:

Tryptone:..... 5 g
Yeast extract:..... 1.25 g

NaCl:..... 0.125 g
ddH_2O:..... Up to 200 ml
Adjust pH to 7 with [5 M] NaOH
KCl [250 mM]:..... 2.5 ml
ddH_2O:..... Up to 250 ml
Autoclave
Filtered glucose [1 M]:..... 5 ml

Staining buffer:

Ethidium Bromide: ..... 0.005 g
ddH_2O: ..... 1000 ml
Store in fridge (4˚C)

Succinylacetone [5 mM]:

4,6-Dioxoheptanoic acid:..... 7.9 g
ddH_2O:..... Up to 10 ml

TAE buffer:

Tris-base:..... 242 g
Glacial acetic acid:..... 57.1 ml
EDTA [0.5 M]:..... 100 ml
ddH_2O:..... Up to 1 L

YT-Agar plates:

Tryptone:..... 4 g
Yeast extract:..... 2.5 g
NaCl:..... 2.5 g
Agar:..... 7.5 g
ddH_2O:..... Up to 500 ml
Adjust pH to 7 with [5 M] NaOH
Autoclave

Appendix E: Conference Abstract

Abstract of the poster presented at the South African Society for Human Genetics conference in Stellenbosch in April 2009.

EFFECT OF HT1 METABOLITES ON NER AND/OR BER REPAIR OF DNA DAMAGE

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OBJECTIVES

Hereditary Tyrosinemia Type 1 (HT1) is an autosomal recessive disorder of tyrosine catabolism caused by a defective fumarylacetoacetate hydrolase enzyme. We previously suggested that the main effect of one of the minor accumulating metabolites, *p*-hydroxyphenylpyruvic acid (pHPPA), is the long term impairment of the DNA repair machinery. In this study we investigated the effect of pHPPA and succinylacetone (SA) on the excision repair pathways in HepG2 cells.

METHODS

The comet assay (single cell gel electrophoresis) has been modified to measure the ability of a sub-cellular extract of HepG2 cells to carry out the initial incision step of DNA repair (BER and NER). Gel embedded nucleoids from HepG2 cells pre-exposed to MMS or Benzo[a]pyrene were incubated with cell extracts from HepG2 cells exposed for 24 h to SA or pHPPA. The repair capacity of the extracts is derived from the rate at which incisions are introduced and the subsequent increase in tail DNA.

RESULTS

MMS pre-treated nucleoids exposed to cell extract from pHPPA treated HepG2 cells showed a significant ($p<0.05$) decrease in tail DNA compared to untreated HepG2 cell extract, whereas Benzo[a]pyrene treated nucleoids showed no significant difference compared to controls. Also, no significant difference in tail DNA was seen in MMS or Benzo[a]pyrene nucleoids exposed to SA treated HepG2 cell extracts.

CONCLUSIONS

Exposure of HepG2 cells to SA seems to have no effect on DNA repair via base or nucleotide excision repair. However, exposure to pHPPA appears to affect the repair enzymes of BER but not NER.