INTRODUCTION

Cancer relapse or recurrence is defined as the return of cancer or its signs/symptoms after a period of improvement. Surgery may not remove all cancer cells and leave behind a few which cannot be detected by scans or other tests. It is also possible that some tumor cells are resistant to chemotherapy or radiation. Although many cancer cells are killed by these treatments, there may exist a few which contain a different genetic makeup which allows them to survive. These hypermalignant cancer cells, or cancer stem cells (CSCs), have been associated with causing cancer relapse. It has also been predicted that these CSCs are created through the adaptation of normal cancer cells (NCCs) to high amounts of the free radical nitric oxide (HNO). In the present study, we looked at the mechanisms by which normal squamous cell carcinomas become cancer stem cells via HNO adaptation.

METHODS

HYPOTHESIS/OBJECTIVE

Adaptation to HNO in five human head and neck cell lines will result in the specific dysregulation of certain genes. Such a study will elucidate the mechanisms by which cancer cells become cancer stem cells.

RESULTS

Down-Regulated Gene Data

PDHA1 | AC093509.1
FAM129A | GLO1
RHDAM1 | SHCBP1
DHX9 | CENPN
SSR1 | KIAA0907
SKP2

RBMX | AC109456.1
Clorf48 | IMPAD1
CD2AP | TK1
MOS1 | KIAA1984
NDUF52 | STAMBPL1
MFS52

RP1-159A1.2 | AC100793.8
RP11-51G2.4 | ANLN
TPX2 | SMCC
NCCAP2 | GLUD1
WAR2 | AIFM1
NRF1

RP11-25N24.3 | TRMT5
PRIM1 | PIK3C2G
TSCC1 | IMPDH2
CDK7 | GLUD2
GSR1 | AT1F
MTHFS

RP11-2023E.1 | GINS2
USP14 | ECT2
SORL1 | MRPS36
CDK2 | SNTB1
CLPB
LAMA3

SLCA5A21 | HNRPA2B1
RSRC1 | MRPS15
MBNL1 | MNAT1
PCCB | PRKAR1B
SNRPA
KIAA0101
RFC4

Up-Regulated Gene Data

CORO1B | FOS
AC138872.1 | COMMD6
PSAP | CD63
WIP1 | ACO06534.6
SERINC1 | RPS24

COX7C | LCN2
KNU | NRB2
MVD | HLA-F
RPL30 | ACO22431.1
NPC2 | Clorf10

PSMA7 | CYP1A1
CTSC | RPL37AP1
STARID10 | OPTN
RP11-64105.1 | RPL26P12
TTP1 | SERF2

GPMBN | S100P
RPL37 | RPL37A
CB1 | EXOC3
RPL22 | ARPC2
GRN | RPL15

Down-Regulated Pathways from DAVID Analysis – Cell Cycle Pathways

Up-Regulated Pathways from DAVID Analysis – Ribosomal Pathway

CONCLUSION

Adaptation to HNO results in the up-regulation of ribosomal proteins in human H&N cell lines (SCC-016, SCC-040, SCC-056, SCC-114, SCC-116). This up-regulation is understandable, as HNO-adapted / CSCs are very aggressive and thus, produce more proteins in a given amount of time, compared to normal cells. HNO-adaptation also causes the down-regulation of critical genes involved in the cell cycle and DNA replication. This down-regulation perhaps causes genomic instability, which in turn drives the creation of CSCs and thus recurrence of the disease in patients. The pathways can potentially be targeted (inhibited or augmented) to inhibit the conversion of cancer cells to CSCs.

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