様　式　Ｃ－１９、Ｆ－１９－１、Ｚ－１９　（共通）

科学研究費助成事業　　研究成果報告書

令和　元 年　 ６ 月　 ６ 日現在

機関番号：１６１０１
研究種目：基盤研究(C)（一般）
研究期間：2016～2018
課題番号：１６Ｋ０９３１４

研究課題名（和文）mRNAプロセシングを介したがんのヘテロジェナイティの新規メカニズムの解明

研究課題名（英文）Mechanism of tumour heterogeneity mediated by mRNA processing

研究代表者
西田　憲生（NISHIDA, Kensei）

徳島大学・大学院医歯薬学研究部（医学域）・准教授

研究者番号：１０６２４０３３

交付決定額（研究期間全体）：（直接経費）　　3,600,000円

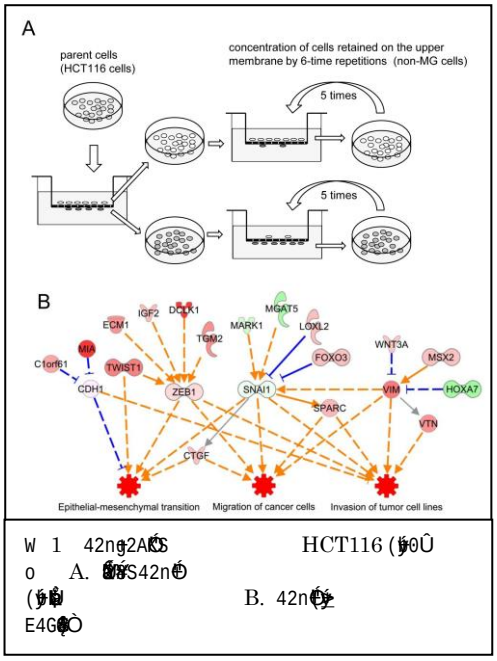
研究成果の概要（和文）：独自に樹立した細胞遊走能の高いヒト大腸がん細胞株HCT116細胞を用いて、遊走能獲得形質に関わる新規因子の同定を試みた。その結果、(1)遊走能獲得過程においてプロモーター領域DNAメチル化が亢進し、遺伝子発現が低下する35遺伝子の同定に成功した。（２）遊走能獲得形質過程において、発現が亢進するマイクロRNAクラスターの同定に成功した。

研究成果の学術的意義や社会的意義
がんの遊走能獲得は、浸潤・転移などのがんの悪性形質獲得における重要な形質となる。本研究で同定に成功した、（１）遊走能獲得過程でDNAメチル化を介して発現が制御される遺伝子、ならびに（２）発現が上昇するmicroRNAクラスターは、大腸がんの進展・悪性化を制御する分子生物学的メカニズムの解明ならびに、治療ターゲットの開発に役立つ可能性が示唆された。

研究成果の概要（英文）：We purified a subpopulation of cells from the colon cancer cell line HCT116, which had high migration capacity. Using this subpopulation, we investigated novel factors involved in migrating capacity. We had following findings: (1) identifiation of 35 up-regulated genes in mRNA expression, whose promoter region were hypermethylated and (2) identification of a microRNA cluster, which is upregulated in gene expression, in acquiring increased migratory capabilities in colon cancer cells.

研究分野：RNAバイオロジー

キーワード：ヘテロジェナイティ　大腸がん　上皮間葉移行　RNAプロセシング　DNAメチル化


A
parent cells
(HCT116 cells)
concentration of cells retained on the upper
membrane by 6-time repetitions (non-MG cells)
5 times
5 times
B
IGF2
DDR1
MGAT5
ECM1
MARK1
LOXL2
TGM2
MIA
FOXO3
WNT3A
C1orf61
TWIST1
MSX2
CDH1
ZEB1
SNAI1
VIM
HOXA7
SPARC
VTN
CTGF
Epithelial-mesenchymal transition
Migration of cancer cells
Invasion of tumor cell lines

MG cells \ non-MG cells b DNA

(6) microRNA b

(2) microRNA b PCR

microRNA b

(1) MG non-MG MG non-MG

MG non-MG

1.5 4,178 4G

MG Cellular MovementG M4G b

4 Xb pc ZEB1 VIM 4G MG

CDH1 SNAIL 4G g

MG

(2) DNA 2n 2A 4G

MG DNA 5- M 2n+

DNA 42n

DNA 0 8 MG DNA

5- 4G M 35 4G

The Cancer Genome Atlas ZG 35 4G DNA

ZNF350 4G

(3) S0 *in vitro*

S0

ZNF350 c G)) Z

ZNF350 4G

ZNF350 A

HCT116 42n

ZNF350 A 2n+

MG

(4) DNA

ZNF350 DNA

5

b CpG DNA MG

ZNF350 b

K S) G CpG C

ZNF350 b M8 KS

WS

(5) 42n microRNA b

)Y MG

microRNA b

microRNA b

microRNA KS G}

b microRNA 4G

VKZ8GK

SI} MG 4G

4(microRNA b ($

s@KZ 4G 3

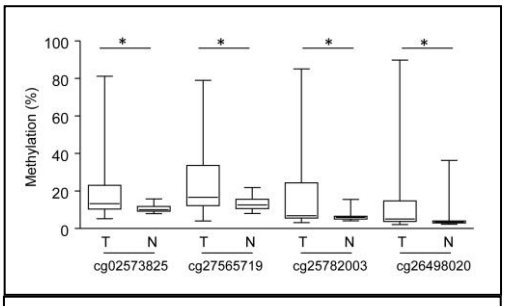
S a@GQS

7_ 5C RACE /838a

KS b38ajQ

bDI 8Z,A)FA0 W

Z8 (W 3)

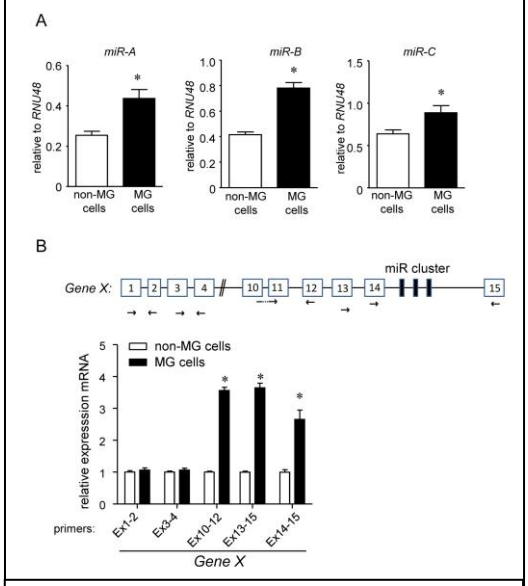


W ZNF350 MethHC

ZNF350

(W 2)

2018 *Oncotarget* 11 V



W 3 9 2n M(KZ8

microRNA G

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3. [illegible] RNA TRA2 4 b[illegible] 2018 ″
4. [illegible] microRNA23b/27b/24 cluster [illegible] 2017 ″
5. [illegible] HOXA5 [illegible] 2017 ″
6. [illegible] TRA2 4 b RNA [illegible] 2017 ″
7. [illegible] hnRNP family [illegible] TRA2 4RNA b[illegible] 2017 ″

8. [illegible] 0Y# [illegible] 0Y | S5 [illegible] M¸ [illegible]
[illegible] DNA [illegible] 40 G¥[illegible]
" 2017 "

9. [illegible] Serine/arginine-rich [illegible]
SRSF [illegible]
[illegible] 39 G¥[illegible] " 2016 "

10. [illegible] /[illegible])1æ 0Y# [illegible]
[illegible] M¸ Ultraconserved region [illegible] 75$ [illegible]
[illegible] 39 G¥[illegible] 2016 "

11. [illegible]
SRSF7 [illegible] 39 G¥[illegible] 2016 "

12. [illegible] /[illegible] 0Y# [illegible] [illegible] 1¡(#)1[illegible] 4)S5 [illegible]
([illegible] M[illegible] DNA [illegible] 2016
"

[illegible]

(1)[illegible] *
[illegible] (TANAKA, Hiroki)

[illegible] S5 [illegible]
(KUWANO, Yuki)

[illegible] M¸
(ROKUTAN, Kazuhito)

[illegible]