Lung Adenocarcinoma Literature Presentation

Lilly Jiang, Kaining Feng, Alex Zhang, Riddhee Mehta

-Omics

Review Article | Published: 12 August 2019

Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy

Ferdinandos Skoulidis & John V. Heymach

Nature Reviews Cancer **19**, 495–509 (2019) | Cite this article

23k Accesses | **354** Citations | **345** Altmetric | Metrics

Omics:

- Genomics.

Article | Open Access | Published: 16 January 2020

circRNA-002178 act as a ceRNA to promote PDL1/PD1 expression in lung adenocarcinoma

JunFeng Wang, XuHai Zhao, YanBo Wang, FengHai Ren, DaWei Sun, YuBo Yan, XiangLong Kong, JianLong Bu, MengFeng Liu & ShiDong Xu

Cell Death & Disease **11**, Article number: 32 (2020) | Cite this article

5490 Accesses | **166** Citations | Metrics

Omics:

- Genomics, transcriptomics.

Review Paper

Review > Nat Rev Cancer. 2019 Sep;19(9):495-509. doi: 10.1038/s41568-019-0179-8.
Epub 2019 Aug 12.

Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy

Ferdinandos Skoulidis [1], John V Heymach [2]

Affiliations + expand

PMID: 31406302 PMCID: PMC7043073 DOI: 10.1038/s41568-019-0179-8
Free PMC article

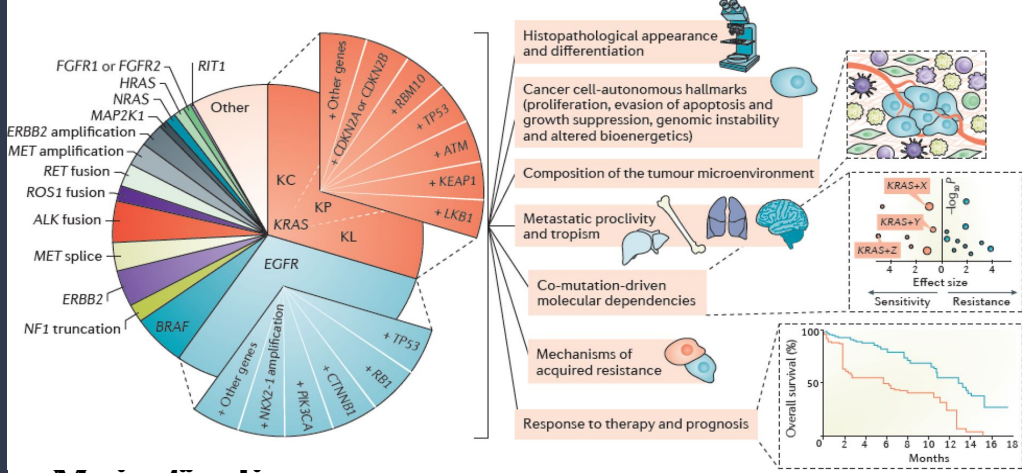
Goals:

- Discuss the impact of co-occurring genomic alterations on non-small-cell lung cancer
- Assess the challenges/opportunities they present for personalized anti-cancer therapy & precision immunotherapy

Methodology:

- Pathogenesis
- Biology
- Microenvironmental interactions
- Therapeutic vulnerabilities

Review Paper



Main findings:

- Co-occurring genomic alterations in oncogenic drivers and tumor suppressor genes significantly make up the molecular diversity of NSCLC
- Proposal of a new model for the molecular classification of NSCLC that encompasses these factors
- Development of improved clinical response prediction algorithms and personalized therapeutic approaches

Research Paper

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Hypothesis:

- circRNA-002178 could act as a ceRNA to promote PDL1/PD1 expression in lung adenocarcinoma.

Goals

- To compare the circRNA expression profiles of LUAD tissue with that of non-cancerous tissue.
- To study the effects of circRNA on PDL1/PDL expression in LUAD.

Methodology

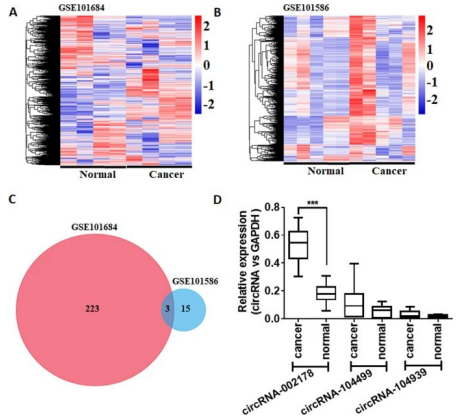
- The serum samples from 30 healthy volunteers and 120 LUAD patients without any treatment were collected at the Harbin Medical University Cancer Hospital

Research Paper

Methodology continued

- circRNA expression profile data obtained from GEO database.
- Cultured the cell, isolate the exosome from serum, and incubate exosomes with CD8+ T cells
- RNA extraction using TRIzol reagent and manipulation
- Expression and statistical analysis: The Mann–Whitney U-test was used to compare significant differences in exosomal circRNA expression between the LUAD patients and healthy volunteers; Receiver operating characteristic curve (ROC) analysis was utilized to estimate the diagnostic value of exosomal circRNA (significant: $P<0.005$)

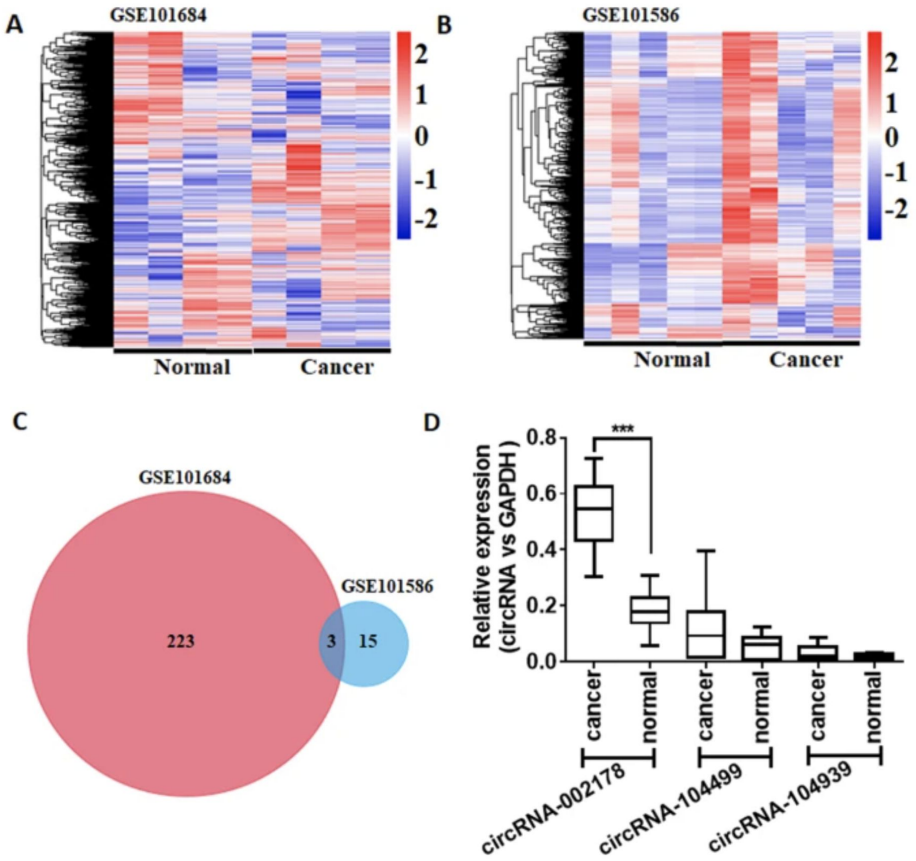
Research Paper



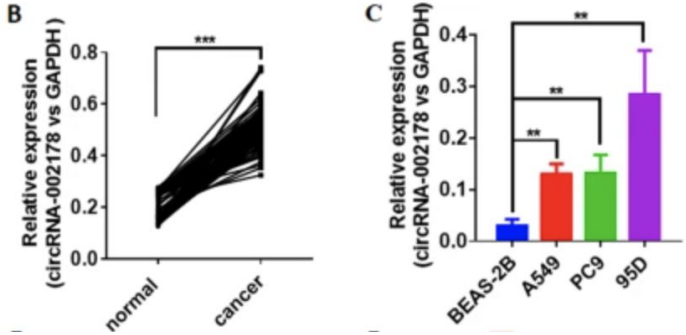
Main findings:

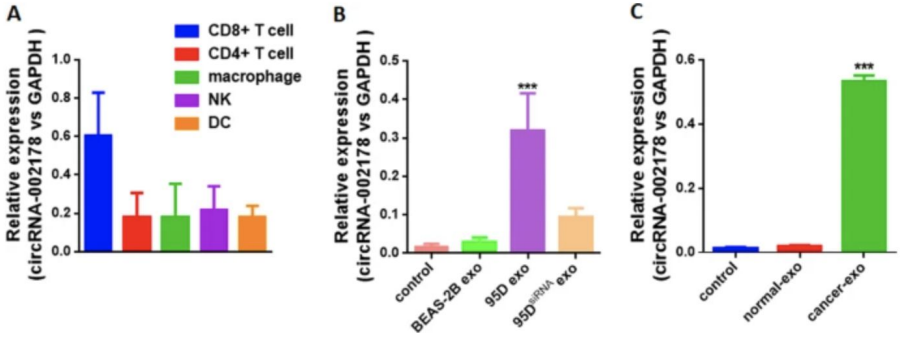
- circRNA-002178 was highly expressed in LUAD tissues.
- circRNA-002178 enhanced PDL1 expression through the absorption of miR-34a.
- Enhanced PD1 expression by absorption of miR-28-5p in CD8+ T cells.
- The exosomal circRNA-002178 significantly upregulated in the serum from LUAD patients.
- circRNA-002178 also exist in exosomes and can be used as a new diagnosis biomarker for LUAD.

Figures


A
GSE101684
2
1
0
-1
-2
Normal
Cancer
B
GSE101586
2
1
0
-1
-2
Normal
Cancer
C
GSE101684
GSE101586
223
3
15
D
Relative expression (circRNA vs GAPDH)
0.8
0.6
0.4
0.2
0.0
***
cancer
normal
cancer
normal
cancer
normal
circRNA-002178
circRNA-104499
circRNA-104939

Figures


B
Relative expression (circRNA-002178 vs GAPDH)
0.8
0.6
0.4
0.2
0.0
***
normal
cancer
C
Relative expression (circRNA-002178 vs GAPDH)
0.4
0.3
0.2
0.1
0.0
**
**
**
BEAS-2B
A549
PC9
95D


A
Relative expression (circRNA-002178 vs GAPDH)
1.0
0.8
0.6
0.4
0.2
0.0
CD8+ T cell
CD4+ T cell
macrophage
NK
DC
B
Relative expression (circRNA-002178 vs GAPDH)
0.5
0.4
0.3
0.2
0.1
0.0
***
control
BEAS-2B exo
95D exo
95D siRNA exo
C
Relative expression (circRNA-002178 vs GAPDH)
0.6
0.4
0.2
0.0
***
control
normal-exo
cancer-exo

Questions

1. What new model could be proposed that can more precisely target the effects of co-occurring genomic alterations on NSCLC?
2. What's the difference between RT-PCR and qRT-PCR?
3. Is there any limitation of circRNA-002178 as a potential non-invasive biomarker for the LUAD detection?

Citations

1. Skoulidis, F., Heymach, J.V. Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy. *Nat Rev Cancer* 19, 495–509 (2019). https://doi.org/10.1038/s41568-019-0179-8
2. Wang, J., Zhao, X., Wang, Y. *et al.* circRNA-002178 act as a ceRNA to promote PDL1/PD1 expression in lung adenocarcinoma. *Cell Death Dis* 11, 32 (2020). https://doi.org/10.1038/s41419-020-2230-9