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Editorial Open Access

The Disappeared Cancer Cell by SncRNAs: Application of DDMC Vector/SncRNAs Complex for Transformation of Cancer Cells into Non-cancerous Cells

Oxana V. Klimenko[1]* and Yasuhiko Onishi[2]

[1]SID ALEX GROUP, Ltd., Kyselova 1185/2, Prague, 182 00 Czech Republic
[2]Ryujyu Science Corporation, 39-4 Kosora-cho, Seto, Aichi 489-0842, Japan

Editorial

DDMC/sncRNAs (Diethylaminoethyl-Dextran-Methacrylic acid Methyl ester Copolymer/small non-coding RNAs) complex is a new tool for the anticancer treatment. It consists of DDMC polymer delivery system with sncRNAs as passengers. The main function of DDMC carrier is supporting of the entrance of sncRNAs in the nucleus/cytoplasm and protection them from rapid biodestruction by DNases and RNases in plasma and cellular matrix. After getting inside the nucleus, sncRNAs epigenetically induce and promote cancer cells genome modifications, and finally result in cancer cell transformation. In primary investigations were used complexes by DDMC/miRNAs (microribonucleic acid and piRNAs (piwi-interacting ribonucleic acid). Its slow velocity of biodegradation helps to prolong epigenetic regulation of cellular genome by sncRNAs, near 40 days in *in vitro* experiments.

DDMC carrier is very stable *in vivo* and has EPR (Enhanced permeation and retention) effect and avoiding RES (reticuloendothelial system). Mechanisms of protection activity of DDMC carrier for sncRNAs and supporting of low velocity of biodegradation are mainly owe to its stable properties. This may be due not only to the coulomb force between the phosphoric acid of RNA and the diethyl-amino-ethyl(DEAE) group of DDMC but also a force from the multi-inter-molecule hydrogen bond and a hydrophobic force from the hydrophobic domains of the graft poly(MMA) in DDMC. These lead us to conclude that DNA/RNA condensation by a coil-globule transition for DDMC, thus make it possible to obtain higher transfection efficiency in the cell and nucleus. The new type of polymer carrier have good RNA protection properties, high transfection efficiency index (11-30 days) and it's rate is 70-98% in different cell types, low toxicity of DDMC/sncRNAs complex after treatment *in vitro* and *in vivo* experiments [1]. After entrance into the cytosol, DDMC/sncRNAs complexes are partially biodegrade and small part of sncRNAs such as miRNAs can react with mRNA in cellular matrix. In cytosol, it is beginning primary effects after action of miRNAs, which were incorporated in complex DDMC/sncRNAs. These events result in modification of mRNA on the post-transcriptional level (Figure 1). MiRNAs trigger gene comes to silencing by the mean of RNA interference mechanisms. The functions of oncogenic miRNAs are suppressed after using of particular antago-miRs for oncogenic miRNAs, and vice versa, the action of anti-oncogenic miRNAs is promoted after treatment with anti-oncogenic miRNAs. In previous studies, were identified different miRNAs or antago-miRs, which regulated apoptotic program of cancer cells. For example, miR-15 and miR-16 expression modify the expression of Bcl2, miR-26 induced apoptosis in liver cancer cells, and miR-29b promote apoptotic program in AML cells. Treatment with antago-miR for miR-15, miR-16, and let-7 result in activation of apoptosis in cancer cells, treatment of cells with miR-195, miR-24-2 and miR-365 led to induction of apoptosis in breast cancer cells. MiR-34 is apoptosis inducer in liver cancer cells. Antago-miR-155 induces caspase 8/9 activity and miR-152 activates apoptosis and inhibits proliferation in lung cancer cells [2-11].

Full reprogramming of cancer cell genome achieved after entrance of DDMC/sncRNAs complex in the nucleus and complex biodegradation. In the nucleus, it begins action of miRNAs and piRNAs, which are slowly disengaging from the binding with DDMC. PiRNAs trigger deep re-construction of genetic program of cell. The main function of piRNAs is supporting of cellular genome stability. The main mechanisms of piRNAs action are mobile genomic transposable elements (TE) repression (LINE and SINE are natural pathogenic factors in cancers) [12]. PiRNAs suppress of NAHR non-allelic homologous recombination and they protect genome stability by expression H3K9me, and histone modification (suppression of position effect variegation) [13-15].

Besides, in the complex is included miRNAs, which trigger differentiation of cells. In previous investigations were confirmed the role of different miRNAs in cellular differentiation [16-23]. After releasing from the DDMC/sncRNAs complex, these miRNAs in co-operation with piRNAs switch-on complex mechanisms of full cellular transformation. Finally, cancer cells transform into physiologically non-cancerous cells.

Remarks

DDMC/SncRNAs helps to prolong epigenetic regulation of cellular genome by sncRNAs, near 40 days in *in vitro* experiments owing to disturb its biodegradation. In this periods, DDMC/SncRNAs as one body epigenetically will induce and promote cancer cells genome modifications. At this time, Gene control by DDMC/SncRNAs is shown by Hill Eq. and will take "Robustness feedback Control Systems" sustainably as bellows;

General form of Hill Eq. is

$$F(X) = \frac{\beta X^n}{K^n + X^n} \quad (1)$$

Here, $K_n < X_n$, β is active Allosteric factor. If X is inlet signal and Y is outlet signal in tumor microenvironment.

Then, $F(X) = \beta, F(X) = \alpha Y$, and $\Delta F(X) = dY/dt$ at α>0, β>0 in allosteric regulation in this tumor micro environment.

***Corresponding author:** Oxana V. Klimenko, SID ALEX GROUP, Ltd., Kyselova 1185/2, Prague, 182 00 Czech Republic, E-mail: O_klimenko@hotmail.com

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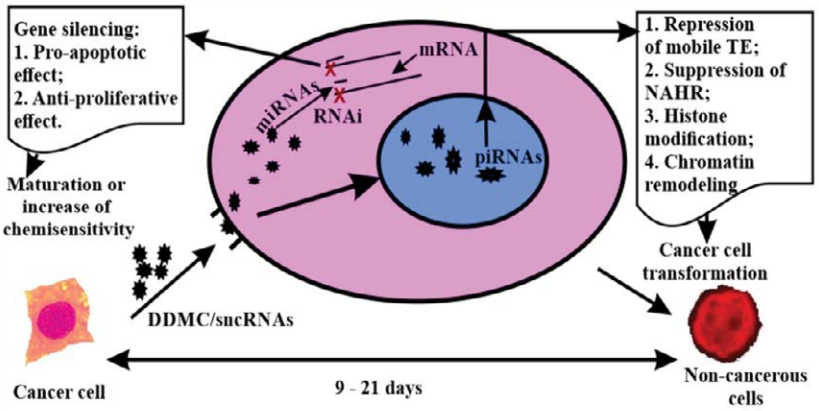

Figure 1: Mechanisms of cancer cell transformation after treatment with DDMC/sncRNAs complex.

The differential variation of $\Delta F(X) = \beta - \alpha Y$, then

$$dY/dt = \beta - \alpha Y \quad (2)$$

$$Y = (\beta/\alpha)(1 - \exp(-\alpha t)) \quad (3)$$

Outlet signal Y in Eq.(1) limits to β/α as α>0.

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