Trends in Cancer Research
Vol. 13, 2018

Short Communication

Cyclin E and FGF8 are downstream cell growth regulators in distinct tumor suppressor effects of ANXA7 in hormone-resistant cancer cells of breast versus prostate origin

A. Bera, X-M. Leighton, H. Pollard and M. Srivastava*

Department of Anatomy, Physiology and Genetics, and Institute for Molecular Medicine, Uniformed Services University of Health Sciences (USUHS) School of Medicine, Bethesda, MD 20814, USA.

ABSTRACT

Tumor suppressor function of Annexin-A7 (ANXA7) was demonstrated by cancer-prone phenotype in *Anxa7*(+/-) mice and ANXA7 profiling in human cancers including prostate and breast. Consistent with its more evident *in vivo* tumor suppressor role in prostate cancer, wild-type(wt)-ANXA7 *in vitro* induced similar G2-arrests, but reduced survival more drastically in prostate cancer cells compared to breast cancer cells (DU145 versus MDA-MB-231 and -435). In all three hormone-resistant cancer cell lines, wt-ANXA7 abolished the expression of the oncogenic low-molecular weight (LMW) cyclin E which was for the first time encountered in prostate cancer cells. Dominant-negative nMMM-ANXA7 (which lacks phosphatidylserine liposome aggregation properties) failed to abrogate LMW-cyclin E and simultaneously induced fibroblast growth factor 8 (FGF8) in DU145 that was consistent with the continuing cell cycle progression and reduced cell death. Adenoviral vector alone induced FGF8 in MDA-MB-231/435 cell lines, but not in DU145 cells. Our data indicated that the LMW-Cyclin E expressions in breast cancer and prostate cancer cell-lines were differentially regulated by wild-type and dominant-negative ANXA7 isoforms, demonstrating a different survival mechanism utilized by breast cancer cells. Conventional tumor suppressor p53 failed to completely abolish FGF8 and LMW-cyclin E in breast cancer cells, which were eventually translated into their survival. Thus, ANXA7 tumor suppression could modulate FGF8 and cyclin E expression, and control implying more specific associations with the annexin properties of ANXA7 in prostate tumorigenesis.

KEYWORDS: annexin A7, fibroblast growth factor 8 (FGF8), cyclin E, tumor suppression, prostate and breast cancer.

INTRODUCTION

Annexin-VII (ANXA7, or synexin) belongs to the Ca- and phospholipid-binding annexin family. First demonstrated in *Anxa7*(+/-) mice with cancer-prone phenotype [1], ANXA7 biomarker and tumor suppressor role was confirmed in numerous human cancers [2-7]. In prostate cancer, ANXA7 levels were specifically reduced after the development of hormone-refractory status, whereas high ANXA7 levels in breast cancer metastases were previously associated with poor survival [8]. The role of ANXA7 has been elucidated in gastric cancer as well [9]. However, our study elucidated a common pattern of ANXA7-loss in cancerous versus normal tissues, unequivocally confirming ANXA7 hormone-associated tumor suppressor role [3, 5]. In breast cancer metastases, the level of ANXA7 expressions between lymph node metastases from breast compared to primary breast cancer sites revealed ANXA7-loss in

*Corresponding author: meera.srivastava@usuhs.edu

metastatic breast cancer similar to other cancers [3, 5, 8]. ANXA7 associations with epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR)-negative status indicated a possible role of the hormone-associated and phospholipid-binding ANXA7 in aggressive basal-like breast cancer [5, 8, 10, 11]. This ANXA7-mediated cellular signaling particularly activates the phospholipid-relevant PI3K-Akt survival cascade including in particular cyclin E pathway [12].

Oscillating with each cell cycle, cyclin E controls genomic stability and, as a specific regulator of S-phase-entry through RB phosphorylation, couples signal transduction to the cell cycle control [13]. Cyclin E overexpression has been associated with different malignancies (in particular, breast cancer), supporting its role as a dominant oncoprotein. In prostate tumorigenesis, as a specific androgen receptor (AR) coactivator directly enhancing AR ligand-independent function, aberrantly expressed cyclin E may contribute to persistent AR activation [14].

Androgen-induced fibroblast growth factor FGF8, or AIGF, which is located next to the ANXA7-harboring TSG region, was affected in our *Anxa7*(+/-) murine model. Aberrant expression of FGF8, which is normally restricted to gonads in adult human tissues, can contribute to hormone-related prostate and breast tumorigenesis [15]. Originally isolated from the androgen-dependent mouse mammary Shionogi carcinoma cells, FGF8 is also associated with the AR and AR-regulated prostate-specific antigen in human breast carcinomas. An earlier study also indicated that the FGF8 and Cyclin E cooperated each other for cell-cycle maintenance [16].

Hence, in this present study, we evaluated protein expression of the cell growth regulators and potential oncogenes cyclin E and FGF8 in association with tumor suppressor effects of ANXA7. We also demonstrated the cooperative expression of cyclin E and FGF8 with the dominant- negative nMMM-ANXA7 and p53 in the ER/PR-negative breast cancer cells (MDA-MB-231 and -435) compared to the prostate cancer cells with abolished AR (DU145).

MATERIALS AND METHODS

Cell culturing and treatment

Androgen-insensitive DU145 prostatic cancer cells (ATCC, Manassas, VA) were cultured (18 hrs) after transfection with AdEasy-based vectors containing wt/nMMM-ANXA7 or p53 constructs as previously described [17]. Dominant-negative nMMM-ANXA7 construct contains triple mutations which affected the Ca/phospholipid binding sites in annexin repeats 2, 3 and 4 (E277→Q277, D360-E361→N360-Q361 and D435-D436→N435-N436, respectively).

Viability, cytotoxicity and programmed cell death (PCD) detection using cell cycle analysis

Cytotoxicity and viability were determined by LDH Cytotoxicity Detection Kit and XTT Cell Proliferation Kit II, respectively (both from Roche Applied Science, Indianapolis, IN). PCD was detected by Annexin V-PE and APO-BRDU Apoptosis Detection Kits (both from BD Pharmingen, San Jose, CA) using only single green fluorescence protein (GFP)-positive cells. Early (phosphatidylserine exposure) and late (membrane permeabilization) stages of PCD were analyzed by flow cytometry (EPICs XL-MCL, Beckman Coulter, Fullerton, CA) using Annexin V-PE assay. DNA fragmentation in the end-stage PCD was detected by flow cytometry (LSRII, BD Biosciences, San Jose, CA) with the use of exogenous terminal deoxynucleotidyl transferase (TdT), commonly defined as the TUNEL assay [18]. We bought the reagent APO-BrdU™ TUNEL Assay Kit, with Alexa Fluor™ 488 Anti-BrdU from ThermoFisher. Cell cycle analysis was based on propidium iodide staining after dsRNA removal by DNase-free RNase (Sigma-Aldrich, St. Louis, MO) in the cells fixed in 70% ethanol. ModFit LT (Verity Software House, Topsham, ME) was used for immediate flow cytometry analysis (EPICs XL-MCL, Beckman Coulter, Fullerton, CA). Statistical analysis was performed on replicates using Student's t-test for independent samples or two-tailed Z-test for proportions; p-values <0.05 (two-sided test) were considered statistically significant.

Western immuno-blotting

Cell extracts were prepared using the standard procedure and equal amounts of total protein were electrophoresed on 4-20% Tris/Glycine gels with MagicMark as protein standard (Invitrogen, Carlsbad, CA). Immuno-blotting was performed using antibodies specific for FGF8 (Sigma-Aldrich, St. Louis, MO) and cyclin E (HE12 from

Cell Signaling Technology, Danvers, MA) with housekeeping beta-actin as control.

cDNA microarray

Total RNA (3 µg per experiment) was isolated and processed using RNA extraction kit (Ambion, Austin, TX). FGF8 gene expression in DU145 cells transfected with wt- versus nMMM-ANXA7 was derived from cDNA microarray analysis (Atlas Human Cancer 1.2 Arrays and AtlasImage 2.01 software, Clontech, Palo Alto, CA). Adjusted intensities were calculated as spot intensities minus background values for spots, multiplied by global normalization coefficients. Ratio for FGF8 gene expression in the nMMM-ANXA7-array was compared to wt-ANXA7-array.

Ingenuity Pathways Analysis-based bioinfomatic data mining

Oncomine and Ingenuity Pathways Analysis (IPA) platforms and data mining were used to explore the interrelated network between ANXA7, cyclin E, and FGF8. FGF signaling pathway was used as a start point which was then superimposed with individually created 'my pathways' (MP) of ANXA7, FGF8, cyclin E, and AR as well as with common pathways (CP) of p53, PTEN, inositol phosphate metabolism, and IGF-1 signaling. Created custom pathway of the ANXA7-FGF8-cyclin E network was then used to overlay with a gene expression profile (red - upregulated; green - downregulated, as mentioned in Figure 3) corresponding to the prostate cancer subtype from available comparison analyses samples. In addition, developed ANXA7-FGF8-cyclin E network was analyzed using two tissue expression overlays: prostate and mammary gland with combination of the cDNA microarray data.

RESULTS

Wt (but not nMMM)-ANXA7 reduced cell proliferation and induced programmed cell death (PCD) in the hormone-resistant DU145 prostate cancer cells that was associated with distinct profiles of FGF8 and cyclin E

Wt-ANXA7 induced cytotoxicity and reduced the viability of DU145 cells, whereas the dominant-negative nMMM-ANXA7 decreased cell death and increased cell proliferation compared to the "empty"-vector control (Figure 1a). In particular, wt (but not the nMMM)-ANXA7 arrested DU145 cells in the G2-phase unlike the cell cycle regulator p53 which increased the number of cells in G1 (Figure 1b). Similar to p53, wt-ANXA7 eliminated DU145 cells by inducing PCD with DNA fragmentation and phosphatidylserine exposure (Figure 1c and 1d, respectively), whereas the nMMM-ANXA7 clearly lacked PCD-inducing effects.

Next, we juxtaposed the cell death/proliferation responses to wt/nMMM-ANXA7 and p53 to the corresponding cyclin E and FGF8 profiles (Figure 2). Regulation of cyclin E is complemented by proteasome degradation, and pioneering research by Keyomarsi group [13] showed an amplified oncogenic role of the LMW-cyclin E in breast cancer. Since cyclin E is limiting for the G1/S passage, S-phase progression is prolonged, but G1 is shortened by its excess activity. Western blotting showed that, similar to the cell cycle regulator p53, wt-ANXA7 abolished the 30 kDa-LMW-cyclin E expression (Figure 2a) which was initially induced in the DU145 cells transfected with "empty"-vector. Whereas the wt-ANXA7-caused G2-arrest was evidently mediated by additional factors, the nMMM-ANXA7 failed to reduce the LMW-cyclin E that was consistent with a prolonged S-phase and continuing cell proliferation in its response.

Moreover, the nMMM-ANXA7 induced FGF8 protein, which remained undetectable in response to wt-ANXA7 or p53 (Figure 2b). Additionally, cDNA microarray analysis indicated a >2-fold increase in FGF8 gene expression at the transcriptional level in response to the nMMM-ANXA7 compared to wt-ANXA7. Lack of FGF8 expression under wt-ANXA7, in particular, was consistent with the decrease in DU145 colony formation and tumorigenicity *in vivo* due to the FGF8 inhibition [15].

Thus, unequivocal tumor suppressor effects of the wt-ANXA7 versus a continuing cell growth progression in response to the nMMM-ANXA7 corresponded to distinct synexpression profiles of the two major cell survival regulators, cyclin E and FGF8.

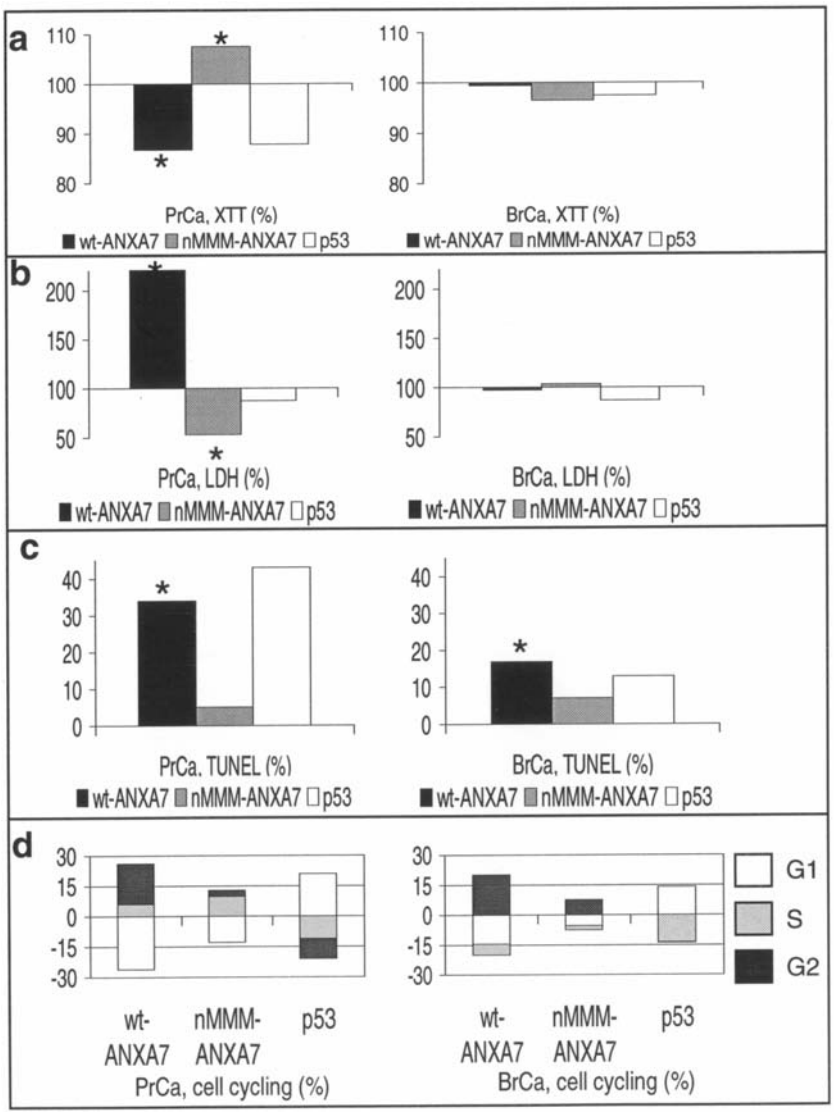

Figure 1. Cell death/proliferation in the androgen-resistant DU145 prostate cancer cells in response to wt/nMMM-ANXA7 and p53. (**a**) Average results from replicate experiments on cytotoxicity (LDH) and viability (XTT) represented levels relative to vector control (100%). Cell cycling (**b**) and APO-BRDU-derived PCD (**c**) data represented the differences (delta-%) compared to adenoviral vector control (TUNEL-based apoptotic rates and cell numbers in different cell cycle phases). Statistically significant p-values were designated by an asterisk (*). (**d**) Images and numbers were representative of ANXA V-PE-derived PCD with phosphatidylserine exposure and membrane permeabilization (bottom and top right quadrants, respectively) from replicates.

Ca/phospholipid-binding properties of ANXA7 involving the overlapping pathways of FGF8 and cyclin E can be responsible for ANXA7 tumor suppressor effects in hormone-resistant prostate cancer

Since ANXA7 can act as a Ca^{2+}-activated GTPase affecting exocytosis and phospholipid membrane fusion [19], its annexin family member properties (which can include phosphatidylserine exposure on dying cells) could contribute to ANXA7 control over DU145 cell survival. Dominant-negative nMMM-ANXA7 (which is known to inhibit the wt-ANXA7-mediated phosphatidylserine liposome aggregation) lacked tumor suppressor effects and, thereby, implicated ANXA7 Ca/phospholipid-binding properties in the FGF8 and cyclin E

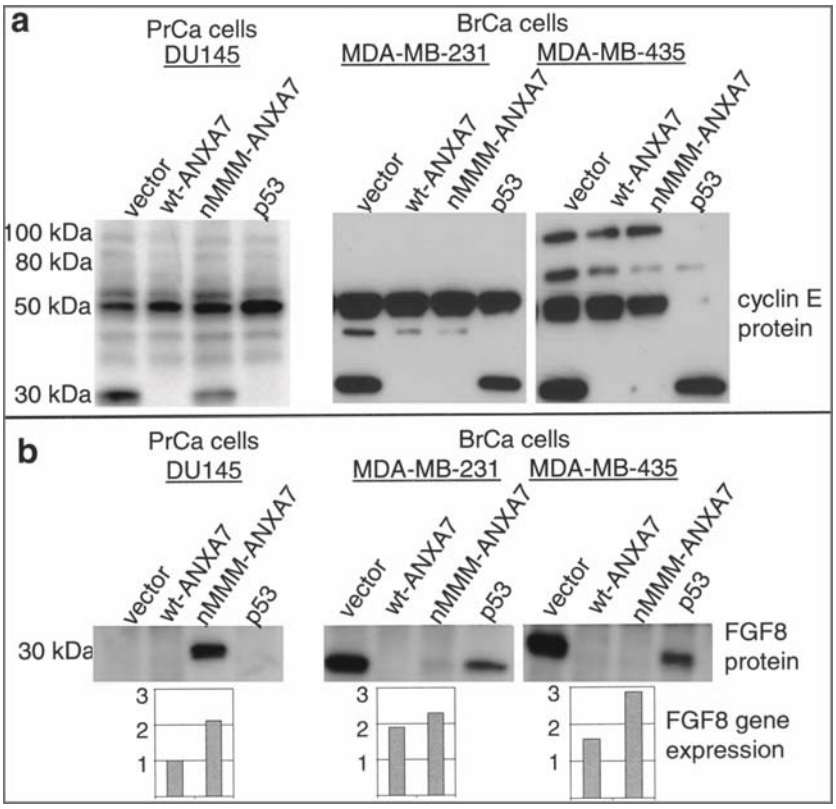

Figure 2. Syn-expression of FGF8 and cyclin E in the androgen-resistant DU145 prostate cancer cells in response to wt/nMMM-ANXA7 and p53. (**a, b**) Western immunoblotting was performed using antibodies specific for cyclin E (HE12 from Cell Signaling Technology, Danvers, MA) and FGF8 (Sigma-Aldrich, St. Louis, MO). FGF8 gene expression in response to wt- versus nMMM-ANXA7 (**b**) was derived from cDNA microarray analysis using RNAqueous-4PCR Kit (Ambion, An Applied Biosystems Business, Austin, TX) with Atlas Human Cancer 1.2 Arrays and AtlasImage 2.01 software (Clontech, Palo Alto, CA). Adjusted intensities were calculated as spot intensities minus background values and multiplied by the coefficients based on global normalization. Presented ratios were calculated based on adjusted spot intensities in two compared categories and normalized to a level (as 1) corresponding to wt-ANXA7.

signaling in prostate tumorigenesis. Remarkably, unsaturated fatty acids were required for a continuous FGF-stimulated proliferation [20].

Using Oncomine and Ingenuity Pathways platforms, we explored possible connections of the phospholipid-binding tumor suppressor ANXA7 to FGF8 and cyclin E, in addition to their interrelated pathways in prostate cancer (Figure 3). Among multiple signal transduction pathways including vascular endothelial growth factor (VEGF), the FGF (FGF8)-FGFR-signaling involves differential syn-expression (indicated by expression bars) of docking proteins SHP2-GRB2 and a scaffolding adaptor GAB1 in prostate cancer. Eventually, the PI3K-Akt 'survival' pathway is linked to the cyclin E-associated cellular signaling. Similar to tumor suppressors such as lipid phosphatase, phosphatase and tensin homolog (PTEN) or cell cycle regulator p53, ANXA7 could counterbalance an onocogenic potential of the FGF8 and cyclin E through the previously shown multiple links (Ca, ITPR3, PTEN, and IGF) to the core inositol phosphate (IP3) signaling [21, 22] including arachidonic acid (AA) cascade [17]. An intrinsic Ca-dependent membrane fusion activity of ANXA7 can be enhanced by the elevated expression of phosphatidylinositol hydrolysis diacylglycerol, DAG [23] or by the protein kinase C in combination with guanine nucleotide [24]. Remarkably, DAG- and Ca- regulated RAS-GRP1

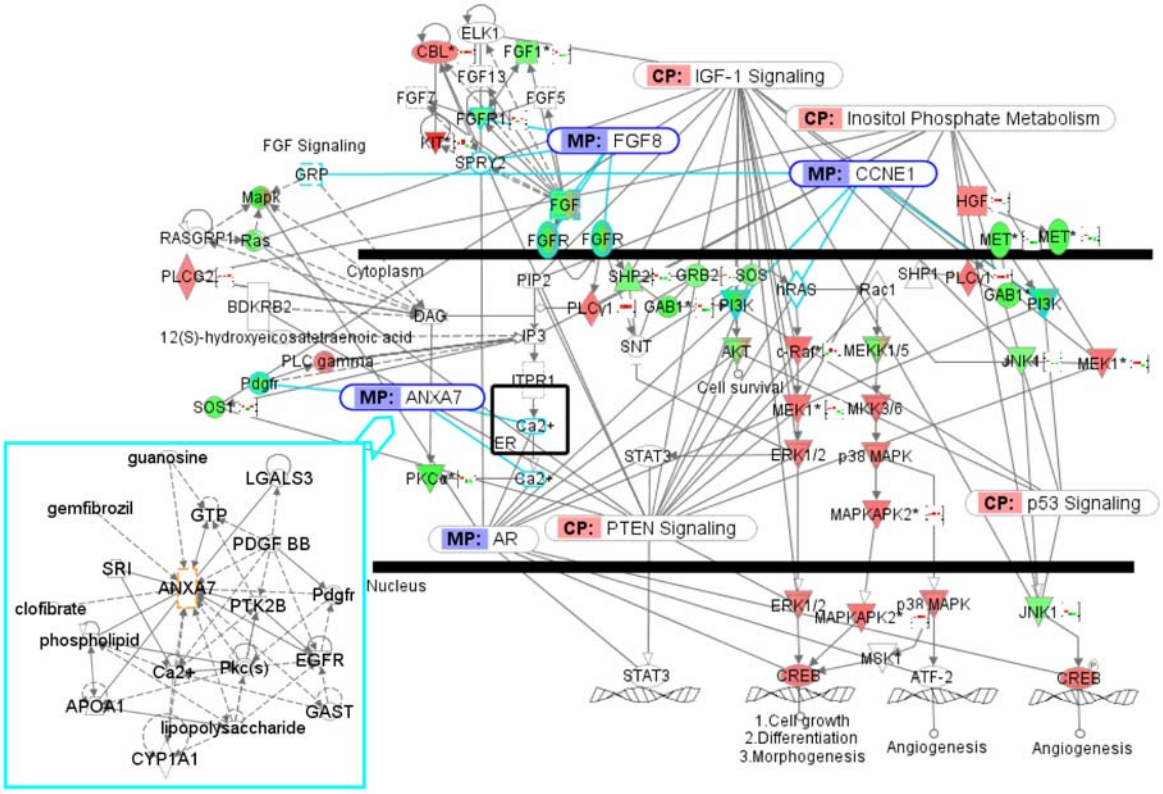

Figure 3. Phospholipid-binding tumor suppressor ANXA7 linked to the interrelated FGF8 and cyclin E pathways through Ca/phospholipid signaling in prostate cancer. Custom pathway of FGF-signaling with interrelated ANXA7, FGF8 and cyclin E links (all three highlighted in blue) was developed using the Ingenuity Pathways Analysis, IPA as described in 'Materials and Methods'. Additional ANXA7 links are presented on a small image in the left corner. Overlay with gene expression profile (red - upregulated, green - downregulated) corresponds to the prostate cancer subtype.

indicated a Ras connection for the phospholipid-binding ANXA7 which was shown to be affected by the oncogenic Ras [25]. On the other hand, negative Ras-MAPK regulators (possibly including ANXA7) can control FGF-signaling thereby limiting growth promotion [15]. In addition, ANXA7 effects could be modified by corresponding hormone-relevant profiles such as AR which is also involved in the Ca/phospholipid signaling in prostate cancer (as shown in Figure 3). Thus, bioinformatic data mining tied ANXA7 to the FGF8 and cyclin E pathways and emphasized a pivotal role for Ca/phospholipid signaling and hence, presenting its tumor suppressor activity.

DISCUSSION

Direct cell growth-related effects of ANXA7 were demonstrated [26, 27] in slime mold *Dictyostelium discoideum*, whose *Anxa7*-knockouts lost their properties related to growth/differentiation, motility, and chemotaxis, especially under the Ca^{2+}-limiting conditions. Current observations provided a convincing evidence for a direct inhibition of the cell growth-promoting factors and potential oncogenes, FGF8 and cyclin E, in ANXA7 tumor suppression.

By promoting S-phase, cyclin E opposes the p53-regulated checkpoints and apoptosis, while cyclin E oncogenic effects (especially overexpression of LMW-forms) intervene with the p53 control over cell death/proliferation [13, 28]. By incorporating regulation of the RB-E2F-relevant cyclin E whose aberrant activity causes genomic instability and increases tumorigenesis, ANXA7 tumor suppressor effects in DU145 implied a novel protection mechanism against cyclin E deregulation and

possible restoration of the p53-dependent checkpoints disabled by the cyclin E excess in cancer. In the meantime, we report for the first time, to our knowledge, LMW-cyclin E expression in DU145 cells representing an androgen-resistant prostate cancer model. However, in addition to the well-studied role in breast cancer [29], cyclin E amplification was reported in different human cancer cell lines as well as neoplasms (rhabdomyosarcoma and pheochromocytoma) and carcinomas involving the ovary, uterus, bladder and gastrointestinal tract [30]. Cyclin E overexpression is expected to function as a surrogate for the commonly mutated p53/RB-E2F pathways in different cancers. As a result, the list of potential oncogenic cyclin E implications and, subsequently, the cyclin E-associated tumor suppressor effects of ANXA7 could be extended beyond the prostate cancer. Hormone-relevant [3] ANXA7 control over the AR-coactivator cyclin E and the androgen-induced FGF8 could, in particular, lead to the restored AR tumor suppressor function in prostate and other hormonal cancers.

On the other hand, FGF8 signaling can be co-regulated by NF-κB with the FGF8 repression required for cell growth inhibition by TGF-beta [31, 32] or steroid-relevant VitD3 [15, 33], delineating additional regulatory pathways in the ANXA7 cell death/proliferation control.

Associations between closely located ANXA7 (10q21) and FGF8 (10q24) could specifically contribute to a genomic search for gatekeeper oncogene versus tumor suppressor on the 10q, a major chromosomal breakpoint in prostate cancer. While FGF8 could potentially contribute to the 10q-gains in prostate [34] and breast cancers [35], allelic loss of the ANXA7-harboring 10q.21 was shown in both hormonal cancers [2, 5]. Remarkably, PTEN (10q23.3) which is a major contributor to the 10q-loss in prostate cancer [36] is downregulated in Langerhans islets from *Anxa7*(+/-) mice [21] . In addition, a predominant allelic loss of ANXA7 was found in the ER/PR-negative tumors [4, 5] which can correspond to the basal-like breast cancer [10] with a commonly lost PTEN and ties to the PI3K-Akt survival cascade including cyclin E.

Additionally, the 10q-located FGF8 as well as FGFR2 and FGFBP3 could share a role in embryogenesis with ANXA7. ANXA7's capacity to affect FGF8 along with the lethal effect of *Anxa7*(-/-) status in mouse embryos [1] suggested that ANXA7 can be involved in the FGF8 facilitation of gastrulation, differentiation and organogenesis [15].

CONCLUSION

Thus, in a common hormone-resistant prostate cancer model, ANXA7 intervened in the cell survival controlled by "master" cyclin E and autocrine growth factor FGF8. More studies are needed to elucidate the intricate mechanisms of ANXA7 tumor suppression in different cancers. However, current data clearly implied anti-cancer therapeutic potential of ANXA7 which can overcome major oncogenic pathways intertwined with the phospholipid signaling.

ACKNOWLEDGEMENTS

This work was supported by the grant to Dr. Meera Srivastava (DOD, DAMD17-03-1-0107).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Srivastava, M., Montagna, C., Leighton, X., Glasman, M., Naga, S., Eidelman, O., Ried, T. and Pollard, H. B. 2003, Proc. Natl. Acad. Sci. USA, 100(24), 14287-92.
2. Srivastava, M., Bubendorf, L., Srikantan, V., Fossom, L., Nolan, L., Glasman, M., Leighton, X., Fehrle, W., Pittaluga, S., Raffeld, M., Koivisto, P., Willi, N., Gasser, T. C., Kononen, J., Sauter, G., Kallioniemi, O. P., Srivastava, S. and Pollard, H. B. 2001, Proc. Natl. Acad. Sci. USA, 98(8), 4575-80.
3. Srivastava, M., Torosyan, Y., Raffeld, M., Eidelman, O., Pollard, H. B. and Bubendorf, L. 2007, Int. J. Cancer, 121(12), 2628-36.
4. Leighton, X., Eidelman, O., Jozwik, C., Pollard, H. B. and Srivastava, M. 2017, Methods Mol. Biol., 1513, 23-35.
5. Leighton, X., Srikantan, V., Pollard, H. B., Sukumar, S. and Srivastava, M. 2004, Cancer Lett., 210(2), 239-44.

6. Xuan, H., Li, Z., Yan, H., Sang, Q., Wang, K., He, Q., Wang, Y. and Hu, F. 2014, Evid. Based Complement Alternat. Med., 2014, 280120.
7. Srivastava, M., Leighton, X., Starr, J., Eidelman, O. and Pollard, H. B. 2014, Biomed. Res. Int., 2014, 193635.
8. Srivastava, M., Bubendorf, L., Raffeld, M., Bucher, C., Torhorst, J., Sauter, G., Olsen, C., Kallioniemi, O. P., Eidelman, O. and Pollard, H. B. 2004, Clin. Cancer Res., 10(7), 2344-50.
9. Ye, W., Li, Y., Fan, L., Zhao, Q., Yuan, H., Tan, B. and Zhang, Z. 2017, Mol. Cell Biochem., 429(1-2), 33-43.
10. Yehiely, F., Moyano, J. V., Evans, J. R., Nielsen, T. O. and Cryns, V. L. 2006, Trends Mol. Med., 12(11), 537-44.
11. Srivastava, M., Eidelman, O., Zhang, J., Paweletz, C., Caohuy, H., Yang, Q., Jacobson, K. A., Heldman, E., Huang, W., Jozwik, C. and Pollard, H. B. 2004, Proc. Natl. Acad. Sci. USA, 101(20), 7693-8.
12. Chang, F., Lee, J. T., Navolanic, P. M., Steelman, L. S., Shelton, J. G., Blalock, W. L., Franklin, R. A. and McCubrey, J. 2003, eukemia, 17(3), 590-603.
13. Barton, M. C., Akli, S. and Keyomarsi, K. 2006, J. Cell Physiol., 209(3), 686-94.
14. Yamamoto, A., Hashimoto, Y., Kohri, K., Ogata, E., Kato, S., Ikeda, K. and Nakanishi, M. 2000, J. Cell Biol., 150(4), 873-80.
15. Mattila, M. M. and Harkonen, P. L. 2007, Cytokine Growth Factor Rev., 18(3-4), 257-66.
16. Kolupaeva, V. and Basilico, C. 2012, Cell Cycle, 11(13), 2557-66.
17. Torosyan, Y., Dobi, A., Naga, S., Mezhevaya, K., Glasman, M., Norris, C., Jiang, G., Mueller, G., Pollard, H. and Srivastava, M. 2006, Cancer Res., 66(19), 9609-16.
18. Gleyzer, N. and Scarpulla, R. C. 2013, J. Biol. Chem., 288(12), 8004-15.
19. Pollard, H. B., Burns, A. L. and Rojas, E. 1988, J. Exp. Biol., 139, 267-86.
20. Kasayama, S., Koga, M., Kouhara, H., Sumitani, S., Wada, K., Kishimoto, T. and Sato, B. 1994, Cancer Res., 54(24), 6441-5.
21. Srivastava, M., Eidelman, O., Leighton, X., Glasman, M., Goping, G. and Pollard, H. B. 2002, Mol. Med., 8(12), 781-97.
22. Watson, W. D., Srivastava, M., Leighton, X., Glasman, M., Faraday, M., Fossam, L. H., Pollard, H. B. and Verma, A. 2004, Biochim. Biophys. Acta., 1742(1-3), 151-60.
23. Chander, A., Chen, X. L. and Naidu, D. G. 2007, Biochim. Biophys. Acta., 1771(10), 1308-18.
24. Caohuy, H. and Pollard, H. B. 2002, J. Biol. Chem., 277(28), 25217-25.
25. Ji, H., Moritz, R. L., Kim, Y. S., Zhu, H. J. and Simpson, R. J. 2007, Electrophoresis, 28(12), 1997-2008.
26. Doring, V., Veretout, F., Albrecht, R., Muhlbauer, B., Schlatterer, C., Schleicher, M. and Noegel, A. A. 1995, J. Cell Sci., 108(5), 2065-76.
27. Bonfils, C., Greenwood, M. and Tsang, A. 1994, Mol. Cell Biochem., 139(2), 159-66.
28. Minella, A. C., Grim, J. E., Welcker, M. and Clurman, B. E. 2007, Oncogene., 26(48), 6948-53.
29. Akli, S. and Keyomarsi, K. 2003, Cancer Biol. Ther., 2(4 Suppl 1), S38-47.
30. Hwang, H. C. and Clurman, B. E. 2005, Oncogene., 24(17), 2776-86.
31. Takayashiki, N., Kawata, H., Kamiakito, T. and Tanaka, A. 2005, J. Steroid Biochem. Mol. Biol., 96(1), 1-12.
32. Bera, A., Zhao, S., Cao, L., Chiao, P. J. and Freeman, J. W. 2013, PLoS One, 8(12), e82282.
33. Ahn, J., Park, S., Zuniga, B., Bera, A., Song, C. S. and Chatterjee, B. 2016, Vitam. Horm., 100, 321-55.
34. Pan, Y., Lui, W. O., Nupponen, N., Larsson, C., Isola, J., Visakorpi, T., Bergerheim, U. S. and Kytola, S. 2001, Genes. Chromosomes Cancer, 30(2), 187-95.
35. Aubele, M. M., Cummings, M. C., Mattis, A. E., Zitzelsberger, H. F., Walch, A. K., Kremer, M., Hofler, H. and Werner, M. 2000, Diagn. Mol. Pathol., 9(1), 14-9.
36. Saramaki, O. and Visakorpi, T. 2007, Front Biosci., 12, 3287-301.