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Letter to the Editor

Prostate cancer cell both microRNA aberrant expression-mediated autophagy and radiation therapy resistance with short cross-reference to epigenetic/genetic mechanism implications

Dear Editor,

Two here recently published very interesting articles, respectively by Guo et al[1] and Wang et al[2], concerning both correlative prostate cancer cell autophagy and chemo-radiation therapy resistance under influence of different micro-ribonucleic acids (miRNAs or miRs), have significantly catched my attention.

With reference to Guo et al work, it has been properly pointed out that hypoxia-induced upregulation of miR-301a and miR-301b can contribute to enhance prostate cancer cell autophagic prosurvival mechanism – meanwhile with significant decrease in chemo/radiation inducible cancer cell apoptosis – by downregulation of tumor suppressive NDRG2 (N-myc downstream-regulated gene 2), so it leading to prostate tumor more high Gleason score and staging progression. It is here reported that the miR-301a expression might be promoted, under hypoxia, by pre-adipocytes as basic components of the cancer cell microenvironment.

Regarding Wang et al article, the miR-205, unlike miR-301a/b, can suppress – by targeting TP53INP1(tumor protein p53-inducible nuclear protein 1 gene) whose overexpression is predictive of prostate tumor relapse – stress condition (hypoxia, chemo-radiation therapy) induced cancer cell autophagy meanwhile, instead, enhancing apoptosis together with tumor radiosensitivity. Low prostate cancer cell miR-205 levels lead, on the other hand, to occurrence of tumor chemo-radiation therapy resistance. Therefore, miR-205 has been recently highlighted as cancer radiosensitizer as it moreover targeting – with relevance to what quoted by the authors – various components of MAPK (mitogen-activated protein kinase) besides androgen receptor signaling pathways.

Even by just last year here published intriguing article of Liu et al[3], it has been pointed out the leading role of miR-150 to increase prostate cancer stem cell development, hence the tumor progression and recurrence promotion together with chemo-radiation therapy resistance, via suppressing p27 Kip1 as cell-cicle inhitory protein in G1 given its interaction with cyclin-CDK2/CDK4.

As it is clear, on the basis of thorough articles above taken into consideration, various miRNAs may be assessed as key elements, in different ways, of autophagy, let alone linked with cancer chemo-radiation therapy resistance. Indeed it's well known that in many prostate cancer stem cells, multiple tumor-suppressor miRNAs – such as miR-141, miR-106a, miR-34a, let-7b) – are downregulated while others (miR-182, miR 452 besides above reported miR-301) are significantly overexpressed[4].

The knowledges on miRNA different roles, correlatively pertinent to prostate cancer cell autophagy together with chemo-radiation therapy resistance, could be properly combined, in my opinion, with data concerning – in addition to genetic abnormalities – also epigenetic alterations through DNA-cytosine methylation and histone

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modifications (particularly lysine acetylation) as important conditions on gene imprinting/transcription[5-7]. From such cognitive combination it should follow that an association of specific miRNA modulator agents with epigenetic-driven new therapeutic candidates such as either DNA-methylation- or histone deacetylase inhibitors, could result successful against prostate tumor progression by effectively avoiding cancer cell autophagy and chemo-radiation therapy resistance.

Conflict of Interest

The Author declares that he has no conflict of interests.

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