



Potential Role of Magnesium in Cancer Initiation and Progression

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Dear Editor,

Magnesium (Mg) has multiple physiological functions including energy metabolism, maintaining membrane stability, synthesis of proteins, activation of the cytoskeleton, functioning as an anti-oxidant, replication of DNA. In relation to cancer, physiological levels of Mg aids in DNA repair, and maintaining the overall genomic stability [1, 2]. Loss of Mg homeostasis could result in either increased or decreased intracellular Mg, either of which has been implicated in carcinogenesis [3, 4]. The present manuscript focusses on the potential role of loss of Mg homeostasis on cancer initiation and progression.

Reduced intracellular Mg levels: As mentioned above, Mg aids in maintaining the genomic stability, by reducing oxidative stress and aiding in the repair of potential DNA damage [1, 2]. Thus, reduction in the intracellular Mg levels would predispose the affected cells to develop oxidative stress-induced genomic instability which when

augmented by lack of DNA repair could potentially lead to cancer initiation (Fig. 1) [3].

Increased intracellular Mg levels: Although Mg has several anti-carcinogenic properties, Mg also plays a major role in energy metabolism [4]. Thus, an increase in Mg intra-cellular levels could induce the involved cell to increase its metabolic activity increasing in size and proliferative potential (Fig. Fig. 1). Neoplastic cells have shown to increase the influx of Mg enabling them to increase their carcinogenic properties allowing tumor progression [2, 4]. The excess Mg influx into the tumor cells are from non-neoplastic cells, and blood, which is reflected in the reduced blood Mg levels noted in breast cancer patients [1, 5].

Mg mediated carcinogenic pathways: A recent study on breast cancer has revealed an Mg induced carcinogenic pathway wherein the excess intra-cellular Mg has shown to inactivate p53 leading to cancer progression. The excess Mg influx inactivated p53 either directly through hypo-phosphorylation or through inactivation of p38MPK pathway. In addition to inducing p53 inactivation, the Mg induced inactivation of the p38MPK can also lead to loss of cell differentiation resulting in tumor progression (Fig. Fig. 1) [6–10].

Similar to breast cancer, a p53 protein inactivation is a common event in oral cancer. Recent studies have also shown reduced Mg levels in the blood and saliva of oral squamous cell carcinoma cases [11, 12]. Although intra-cellular neoplastic levels of Mg in oral cancer cells were not determined, it can be hypothesized that similar to breast cancer, the reduced salivary and blood Mg levels in oral cancer patients are a result of excess Mg influx into the oral neoplastic cells. Thus, it is

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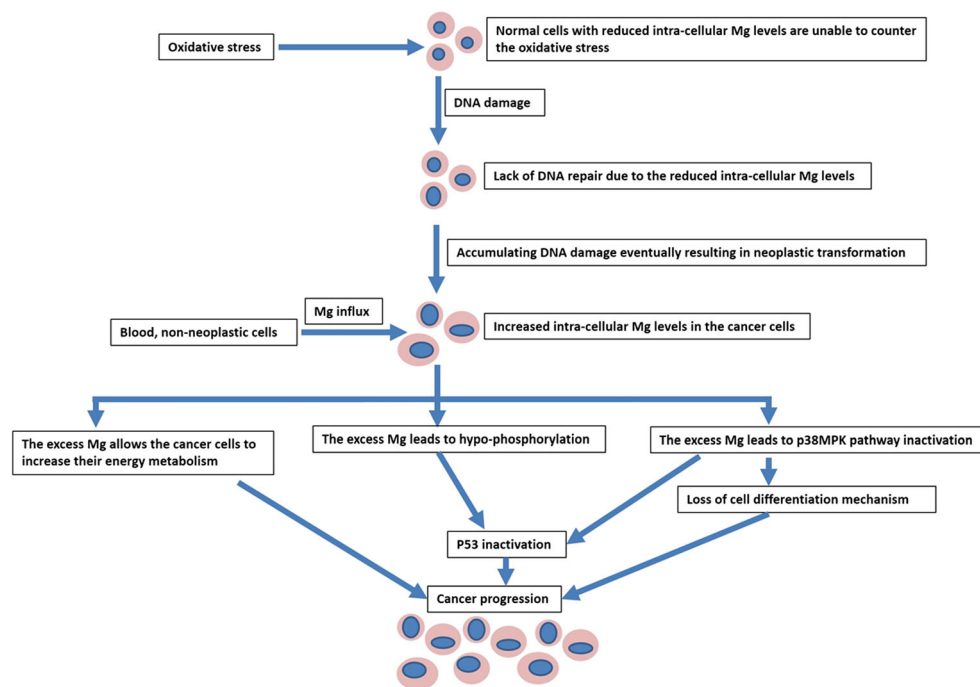
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Fig. 1 Potential pathways of Mg mediated cancer initiation and progression



possible that like breast cancer, Mg mediated oral cancer progression could be potentially mediated through p38MPK/p53 pathway. Further given the close proximity of saliva with oral cancer tissue, estimation of salivary Mg levels in oral cancer patients could be a sensitive non-invasive prognostic tool for monitoring disease progression.

Compliance with Ethical Standards

Conflict of Interest None.

References

- Grober U, Schmidt J, Kisters K (2015) Magnesium in prevention and therapy. *Nutrients* 7(9):8199–8226
- Hosthor SS, Mahesh P, Priya SM, Sharada P, Jyotsna M, Chitra S (2014) Quantitative analysis of serum levels of trace elements in patients with oral submucous fibrosis and oral squamous cell carcinoma: a randomized cross – sectional study. *J Oral Maxillofac Pathol* 18:46–51
- Mendes PMV, Bezerra DLC, Santos LRD, Santos LDO, Melo SRDS, Morais JBS et al (2018) Magnesium in breast Cancer: what is its influence on the progression of this disease? *Biol Trace Elem Res* 184(2):334–339
- Bertinato J, Xiao CW, Ratnayake WM et al (2015) Lower serum magnesium concentration is associated with diabetes, insulin resistance, and obesity in south Asian and white Canadian women but not men. *Food Nutr Res* 59(1):25974
- Abdelgawad IA, El-Mously RH, Saber MM, Mansour OA, Shouman SA (2015) Significance of serum levels of vitamin D and some related minerals in breast cancer patients. *Int J Clin Exp Pathol* 8(4):4074–4082
- Anastassopoulou J, Theophanides T (2015) Magnesium-DNA interactions and the possible relation of magnesium to carcinogenesis. Irradiation and free radicals. *Crit Rev Oncol Hematol* 42(1):79–91
- Karki K, Pande D, Negi R, Khanna S, Khanna RS, Khanna HD (2015) Association between biomarkers of oxidative stress, trace elements, and cell proliferation index in patients with benign and malignant breast diseases. *J Environ Pathol Toxicol Oncol* 34(1):1–10
- Karki K, Pande D, Negi R, Khanna S, Khanna RS, Khanna HD (2015) Correlation of serum toll like receptor 9 and trace elements with lipid peroxidation in the patients of breast diseases. *J Trace Elem Med Biol* 30:11–16
- Castiglioni S, Maier JA (2011) Magnesium and cancer : adangerous liason. *Magnes Res* 24(3):92–100
- Yu E, Ahn YS, Jang SJ, Kim MJ, Yoon HS, Gong G, Choi J (2007) Overexpression of the wip1 gene abrogates the p38 MAPK/p53/Wip1 pathway and silences p16 expression in human breast cancers. *Breast Cancer Res Treat* 101(3):269–278
- Bagulkar BB, Chaudhary M, Gawande M, Patil S, Gadail A, Bagulkar S (2013) Colorimetric determination of magnesium in blood and saliva in Oral squamous cell carcinoma and potentially malignant disorders by titan yellow method. *J Orofac Res* 3(4):240–244
- Aziz NZ, Arathi K, Prasad BG, Desai D, Shetty SJ, Shahid M (2018) Evaluation of magnesium levels in blood and saliva of oral squamous cell carcinoma and potentially malignant disorders by xylydyl blue method. *J Oral Maxillofac Pathol* 22(1):147–162

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