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Magnesium homeostasis goes awry in chemoresistance -TRPM6, TRPM7 and MagT1 in colon carcinoma LoVo cells

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Chemoresistance is one of the most significant factors impeding the progress of cancer therapy (1). It is known that neoplastic cells accumulate magnesium and frequently upregulate one of its transporters, i.e.TRPM7 (2). We have investigated magnesium homeostasis in a model of chemoresistance i.e. colon carcinoma LoVo cells sensitive (LoVo-S) or resistant to doxorubicin (LoVo-R). We observed that LoVo-R have higher amount of total intracellular magnesium than LoVo-S. We studied the expression of some magnesium transporter (TRPM6, TRPM7 and MagT1) by Real Time PCR and Western Blot and found that TRPM6 and 7 are overexpressed in LoVo-S, while MagT1 is upregulated in LoVo-R. In LoVo-S, silencing TRPM7 retards cell growth and shifts the phenotype to one more similar to resistant cells. On the other hand, calpeptin, a calpain inhibitor, upregulates TRPM7, stimulated proliferation and enhances the sensitivity to doxorubicin of LoVo-R. Silencing MagT1 in LoVo-R markedly inhibited cell growth without affecting the response to doxorubicin. We conclude that alterations of magnesium homeostasis play a role in drug resistance.

References

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Keywords
Magnesium; drug resistance; colon carcinoma; magnesium transporters.