Targeted Osmotic Lysis of Metastatic Carcinomas by Blockade of Sodium Pumps and Stimulation of Sodium Channels

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ABSTRACT – 2447

Inflammatory mediators contribute to a dramatic up-regulation of voltage-gated sodium channels, particularly the Na\textsubscript{v} 1.7 subtype, in neurons of DRG associated with the site of inflammation (Figure 1, Gould et al., 100, 104). There is also a compensatory increase in Na\textsubscript{K} -ATPase (Figure 2). We tested the hypothesis that if the channels and the pumps were functional, then pharmacological blockade of the pumps with cardiac glycoside, ouabain, and physiological stimulation of the inflamed paw should result in the osmotic lysis of the affected neurons (Figure 3). The discovery that many forms of malignant, epithelially-derived carcinomas overexpress VGSCs as much as 1400 times that of normal cells (Orical & Djamgoz, '05) led us to postulate that this concomitant pharmacological blockade of Na\textsubscript{K} -ATPase and electrical stimulation of VGSCs would cause invasive carcinomas to lyse, whereas normal tissue would not. We tested this hypothesis using the highly metastatic breast cancer cell line, MDA-MB-231.

**HISTOLOGICAL VERIFICATION**

Photomicrographs of malignant breast cancer xenografts that received no treatment, drug treatment alone and drug treatment with and without concomitant osmotic lysis which produces significant tumour destruction.

**CONCLUSIONS**

These results are evidence that simultaneous blockade of sodium pumps and electrical stimulation can be an effective treatment of MCs that overexpress VGSCs.

**REFERENCES**


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