Author's response to reviews

Title: Cimetidine Inhibits Salivary Gland Tumor Cell Adhesion to Neural Cells and Induces Apoptosis by Blocking NCAM Expression

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Version: 2 Date: 13 August 2008

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I am sending herewith the illustrations and the manuscripts entitled "**Cimetidine Inhibits Salivary Gland Tumor Cell Adhesion to Neural Cells and Induces Apoptosis by Blocking NCAM Expression**" by Masakatsu Fukuda *et al.*, which I should like to submit for publication in the BMC Cancer. The manuscript has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium. Acknowledgment that all authors have contributed significantly, and that all authors are in agreement with the content of the manuscript. This article has been written by using microssoft word 2008 Macintosh Edition and summary of this article is as follows:

Cimetidine, a histamine type-2 receptor (H2R) antagonist, inhibits the growth of glandular tumors such as colorectal cancer, however, the effects of cimetidine on salivary gland tumors are unknown. We demonstrated previously that human salivary gland tumor (HSG) cells spontaneously express neural cell adhesion molecule (NCAM), that HSG cell proliferation may be controlled via a homophilic (NCAM-NCAM) binding mechanism and that NCAM may be associated with perineural invasion by malignant salivary gland tumors. In this study, we investigated the effects of cimetidine on salivary gland tumor growth and neural invasion. We demonstrated for the first time that cimetidine can block the adhesion of salivary gland tumor cells to neural cell monolayers and that it can also induce significant apoptosis to tumor mass in a nude mouse model. We also demonstrated that these apoptotic effects of cimetidine involve down-regulation of the cell surface expression of NCAM on HSG cells. We further found that cimetidine-mediated down-regulation of NCAM involved suppression of the nuclear translocation of NF-κB, a transcriptional activator of NCAM gene expression. These findings suggest that growth and neural invasion of salivary gland tumors can be blocked by administration of cimetidine, a process that involves induction of apoptosis and in which NCAM plays a role.

With best regards,

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