Author's response to reviews

Title: Mechanisms of tumor-promoting activities of nicotine

Authors:

Alex I Chernyavsky (sgrando@uci.edu)
Igor B Shchepotin (sgrando@uci.edu)
Valentin Galitovkiy (sgrando@uci.edu)
Sergei A Grando (sgrando@uci.edu)

Version: 3 Date: 15 November 2014

Author's response to reviews: see over
Dear Editor,

I am glad to submit for your consideration our new manuscript titled "MECHANISMS OF TUMOR-PROMOTING ACTIVITIES OF NICOTINE."

This study elaborates on the novel concept linking nicotinic receptors expressed on the cell membrane to growth promotion of lung cancer cells through modification of growth factor signaling, and mitochondrial nicotinic receptors — to inhibition of intrinsic apoptosis. We demonstrated for the first time that the nicotinic receptor-mediated growth-promoting effects of nicotine synergize with those of EGF, IGF-I and VEGF. We also demonstrated for the first time that the quantity of mitochondrial nicotinic receptors coupled to inhibition of apoptosis increases upon malignant transformation of lung cells. Altogether, our results indicate that the biological sum of effects resulting from simultaneous activation of nicotinic receptors on the cell membrane and the mitochondrial membrane produces a combination of growth-promoting and anti-apoptotic signals that implement the tumor-promoting action of nicotine. Therefore, elucidation of this novel mechanism of tumor promoting action of nicotine should pinpoint the lung nicotinic receptors that may become a promising molecular target to prevent, reverse, or retard lung cancer progression by receptor inhibitors.

Based on the novelty of the concept elaborated in our study, the technical excellence of the experimental work, the breakthrough nature of research findings and their significance to both clinical and fundamental aspects of modern biomedical science, we sincerely believe that our manuscript deserves publication in your highly esteemed journal.

Expert reviewers include:

Kent E. Pinkerton (kepinkerton@ucdavis.edu)
Professor and Director
Center for Health and the Environment
University of California, Davis CA
(Expert in the tobacco-related lung cancers)

Eliot R Spindel (spindele@ohsu.edu)
Division of Neuroscience,
Oregon National Primate Research Center,
Oregon Health and Science University, Beaverton, OR
(Expert in the nicotinergic pharmacology of lung cancer)

Andrzej Slominski (aslomins@uthsc.edu)
Department of Pathology
The University of Tennessee, Memphis, TN
(Expert in experimental oncology and tumor cell biology)

Due to the conflict of interest we ask that Dr. H. M. Schuller will be excluded from the review.
Thank you for considering this manuscript.

On behalf of the authors.
Sincerely,

Sergei A. Grando, MD, PhD, DSc
Professor,
Departments of Dermatology and Biological Chemistry
Cancer Center & Research Institute