Erythropoietin and Ovarian Cancer – Response

We have read with interest the letter of Swift et al. that criticizes certain technical aspects of our article entitled “Erythropoietin inhibits apoptosis induced by photodynamic therapy in ovarian cancer cells” (1) and offer the following reply.

Our conclusion was not, as Swift et al. state, “based on tumor immunohistochemistry (IHC) data generated with anti-EpoR antibodies...” Indeed, one could eliminate all data generated using anti-EpoR antibodies from the article and the conclusion would still stand. Arguments regarding the “true” size of the EpoR determined by SDS-PAGE and Western blotting fail to take into consideration the inherent variation of this technique as well as the well-known effect of differential glycosylation on the estimated size of any glycoprotein. Because different cell types impart different, and sometimes unpredictable, glycan structures to glycoproteins, it is reasonable to expect that the same glycoprotein will exhibit differing apparent molecular weights on SDS-PAGE depending on its cellular source. This is exemplified by recombinant human Epo itself (epoetin alfa), which is produced in Chinese hamster ovary cells and has a higher apparent molecular weight on SDS-PAGE than does human urinary Epo.

Interestingly, other studies have shown EpoR on the same A2780 and SKOV3 cells using a different antibody (2, 3). Furthermore, the study of Paragh et al. (3) has revealed that specific inhibition of EpoR expression using a short hairpin RNA expression plasmid resulted in markedly reduced proliferation and invasiveness of ovarian cancer cells in vitro and led to abrogated growth of these cells with decreased EpoR signaling in vivo. Analogous results have been shown by one of our groups for human prostate cancer cells, which also express a functional EpoR and exhibit Epo-induced signal transduction and Epo-dependent phenotypic properties (4).

What is really at issue is whether nonhematopoietic cells express functional EpoR, a question that Swift et al. routinely answer in the negative because they fail to detect nonhematopoietic EpoR with their antibody. Yet the literature is replete with examples which show that functional EpoR are widely expressed by many tissues, including cancer cells (several reviews are available, including refs. 5, 6) and that Epo has widespread antiapoptotic activity. One need only refer to the recent abstracts from Professor Jelkmann’s “8th Int. Luebeck Conference: Pathophysiology and pharmacology of erythropoietin and other hemopoietic growth factors,” many of which describe the action of Epo on such nonhematopoietic tissues as brain, neural progenitors, heart and cardiomyocytes, skeletal muscle, mammary cells, hair follicles, endothelial cells, liver, adipose, prostate cancer, and lung microvasculature, to name a few (7). To imply that all of these scientists are wrong and that only one group, which finds no functional extra-hematopoietic EpoR, is correct is a position that cannot be sustained upon a review of the literature. It is also a position that can result in adverse consequences clinically (8).

Peter Solár
Ján Koval
Jaromír Mikeš
Ján Kleban
Zuzana Solárová
Ján Lazúr
Ingrid Hodorová
Peter Fedoročko
P.J. Šafárik University, Košice, Slovak Republic

Arthur J. Sytkowski
Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

Molecular Cancer Therapeutics

Erythropoietin and Ovarian Cancer – Response

Peter Solár, Ján Koval, Jaromír Mikes, et al.


Updated version  Access the most recent version of this article at:
doi:10.1158/1535-7163.MCT-09-1217

Cited articles  This article cites 5 articles, 2 of which you can access for free at:
http://mct.aacrjournals.org/content/9/4/1071.full#ref-list-1

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.