REPLY TO COMMENTS

We thank Drs. S. Davidson and D. Yellon for their review of our published data and are pleased to respond to their comments. In regards to the distinction between cell growth and proliferation, we are aware of the ample menu of definitions offered in the literature – particularly in the field of oncology – regarding the terms growth, proliferation and proliferation rate. As we stated in Varma et al. (2005) any difference in cell numbers may be due to either a reduced proliferation rate or increased cell death. Therefore, we submit that our original interpretation and their comments are both tenable. We determined cell count/well as a function of time for a set of experiments as shown on Fig 1 (Varma et al, 2005), but all subsequent data (Akt phosphorylation, etc) were obtained on day 8 (mid-log phase) of exposure to different concentrations of glucose. Thus, while we know the slope of a particular data set, we did not evaluate changes in total and phosphorylated akt, etc. as a function of time.

Because the timing of the initiation of apoptosis and the rate at which it persisted in each cell division cycle are unknown, as is the extent of the contribution of necrosis to loss of cells, the occurrence of the hypothetical situation described in Drs. Davidson and Yellon’s Fig 1, is unclear but possible. Regardless of whether Akt works preferentially via proliferation or via apoptosis, it is clear that this kinase plays a major role in glucose-induced endothelial dysfunction. As we demonstrated (Varma et al, 2005), transfection of Akt+/+ rescues these cells from the deleterious effects of 20 and 40 mM glucose.

We appreciate the interest expressed by Drs. Davidson and Yellon in our work.

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