

### Instructor's Response(s) to Discussion Question(s) - Module 4

Briefly describe/explain the role of phospholamban in smooth muscle relaxation. Please **post your response to the discussion board by 9:00 PM of day 4 of this module.**

This Discussion Question is different from the ones you have seen so far in that to address it you had to go to the literature – there is nothing specific in your text books(s) that speaks to the role of phospholamban in smooth muscle relaxation. You will learn something about the role of phospholamban in cardiac muscle in Module 5, but that information does not necessarily carry over to smooth muscle. So ...

There is evidence that phospholamban (PLB) is found, associated with the sarcoplasmic reticulum (SR), in some types of smooth muscle<sup>1</sup>, and that PLB plays a role in relaxation of (some types of) smooth muscle<sup>2</sup>. **To actually address the question asked: PLB is associated with SR SERCA. PLB, when not phosphorylated, inhibits SERCA function; that is, it reduces the rate at which SERCA pumps  $\text{Ca}^{2+}$  into SR from the myofilament space. If PLB is phosphorylated it (phosphorylated PLB) no longer inhibits SERCA function, thus increasing the rate of uptake of  $\text{Ca}^{2+}$  into SR from the myofilament space. This increased uptake of  $\text{Ca}^{2+}$  into SR potentiates smooth muscle relaxation<sup>3</sup>.** If you wish to explore this matter in more detail see, for example, the reviews by Sanders<sup>4</sup> and/or by Wray and Burdyga<sup>5</sup>.

**Please note** that (1) the description/explanation I've given here is minimal; the situation is actually more complex – it is not the intention of this course to go down that path, and (2) the literature cited here is minimal; there is more where that came from. I did NOT intend that in answering this question you would do a massive literature search, only that you would realize that to answer the question it was necessary that you examined some material from the literature.

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<sup>1</sup> Ferguson DG et al., Localization of Phospholamban in Smooth Muscle Using Immunogold Electron Microscopy, J Cell Biol 1988 107:555-562.

<sup>2</sup> Kim M et al., Phospholamban Knockout Increases CaM Kinase II Activity and Intracellular  $\text{Ca}^{2+}$  Wave Activity and Alters Contractile Responses of Murine Gastric Antrum, Am J Physiol Cell Physiol 2008 294:C432-C441.

<sup>3</sup> Kim M et al., CaM Kinase II Activation and Phospholamban Phosphorylation by SNP in Murine Gastric Antrum Smooth Muscles, Am J Physiol Gastrointest Liver Physiol 2007 292: G1045-G1054.

<sup>4</sup> Sanders KM, Invited Review: Mechanisms of Calcium Handling in Smooth Muscle, J Appl Physiol 2001 91: 1438-1449.

<sup>5</sup> Wray S and T Burdyga, Sarcoplasmic Reticulum Function in Smooth Muscle, Physiol Rev 2010 90: 113-178.

Rev 0, 8/17/17 - copied from Rev 2 of Spring 2016, adapted for Pages

Rev 1, 9/25/17 - format changes; no content changes

Rev 2, 7/13/18 - from Spring 2018, up-dated for 601; no content changes

Rev 3, 9/23/18 - revise (improve?) explanation

Rev 4, 9/10/19 - change time due from 6:00 PM to 9:00 PM