

# My Dog is Broken! A Case Study in Cell Signaling

by

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**T-dog:** Melody it's me, Tessa. Are you at your computer?

**DrM:** Yeah, I just finished with my meeting, what's up?

**T-dog:** I'm feeling a little depressed lately. You know how much money I spent on my new champion Yorkshire terrier, Akira Edelweiss?

**DrM:** I still think you're crazy for spending that much on a dog!

**T-dog:** Well I bought him to father champion puppies with Emerald and he just won't "perform," if you know what I mean. I think he might have erectile dysfunction (ED). My freaking dog has ED!!! What on earth should I do???

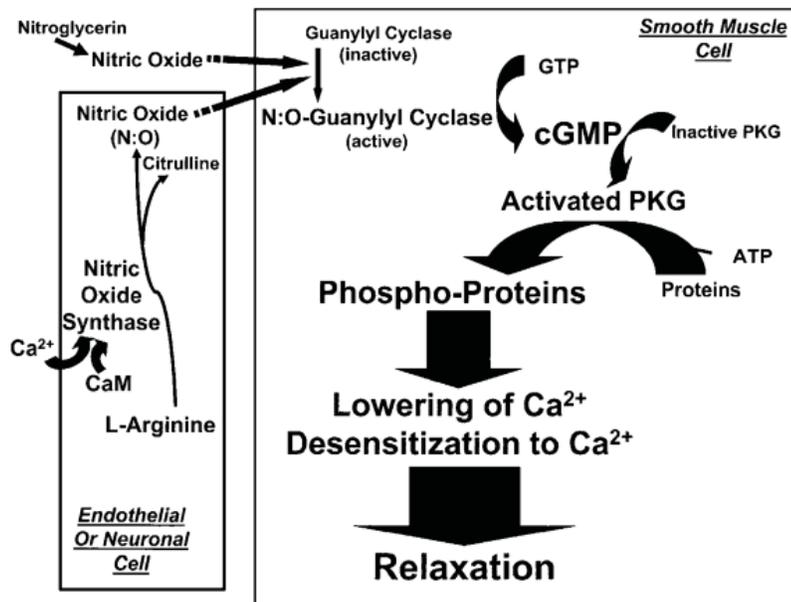
**DrM:** = ) Tess, I'm sorry but that's really funny!

**T-dog:** Mel! Really, I expect you, as a doctor, to take this more seriously. Who else can I turn to if not to you...?!

**DrM:** Ok, ok. There's actually a lot of research on other organisms and enhancing "performance." Erection is controlled via a cell signaling pathway (like everything else!). Here, let me email you a picture that may be helpful.

## Email 1

**From:** Melody Mikelson <[mmikel@mhospital.com](mailto:mmikel@mhospital.com)>  
**Sent:** Wednesday, November 29, 2006 12:17 pm  
**To:** Tessa Wright <[T-dog@dogs.com](mailto:T-dog@dogs.com)>  
**Subject:** Cell signaling pathway



### Abbreviations:

N:O: nitric oxide  
GTP: guanosine triphosphate  
cGMP: cyclic guanosine monophosphate  
PKG: cGMP dependent protein kinase  
ATP: adenosine triphosphate



**T-dog:** Ok, so lots of proteins are involved in an erection and I care because....

**DrM:** Well there's probably something in that pathway or before that pathway that's broken and preventing the signal from getting through.

**T-dog:** Can I do something to fix it?

**DrM:** Actually, there are a bunch of different drugs that are well known to help with ED. In fact, we can actually narrow down where the problem is in your dog's signaling pathway by discovering which drug does the trick.

**T-dog:** Alright, so there is something I can do then?

**DrM:** Yep! I've got two things you could try. The first you are probably already familiar with, it's called Viagra and it works on phosphodiesterase (PDE). PDE acts on cyclic guanosine monophosphate (cGMP), breaking it down and deactivating it.

**T-dog:** Viagra, for my dog?

**DrM:** I bet the cell signaling pathway is the same in dogs as it is in mice and humans. There's a really good chance it will work.

**T-dog:** I'm willing to try anything!

**DrM:** The other chemical you might want to try is ginseng.

**T-dog:** Like the stuff in my tea?

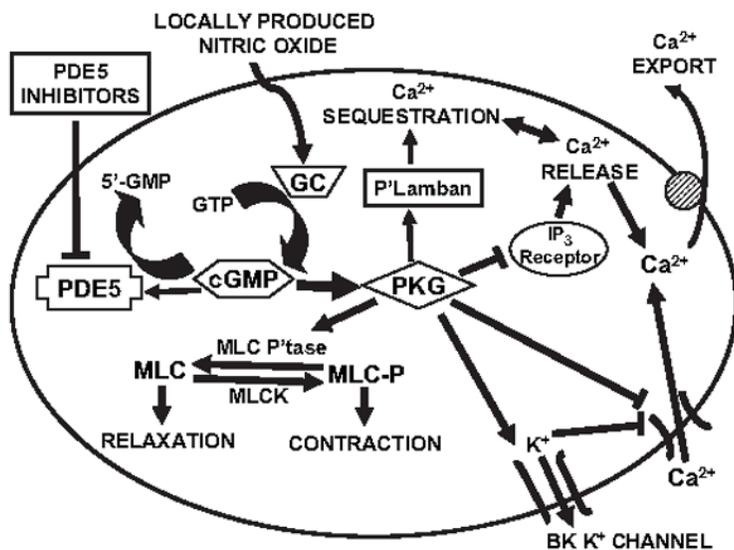
**DrM:** That would be the one.

**T-dog:** Are you serious?

**DrM:** Completely, there's lots of evidence out there that ginseng acts on the nitric oxide in the cell signaling pathway that leads to erection. Here, let me send you another picture that might help you to understand what I'm talking about.

## Email 2

**From:** Melody Mikelson <mmikel@mhospital.com>  
**Sent:** Wednesday, November 29, 2006 12:31 pm  
**To:** Tessa Wright <T-dog@dogs.com>  
**Subject:** More detailed pathway



### Abbreviations:

PDE5: phosphodiesterase  
GC: guanylyl cyclase  
GTP: guanosine triphosphate (inactive form)  
cGMP: cyclic guanosine monophosphate (active form)  
5'-GMP: hydrolyzed guanosine monophosphate (inactive form)  
PKG: cGMP dependent protein kinase  
MLC: myosin light chain  
MLC-P: phosphorylated myosin light chain  
MLC P'tase: myosin light chain phosphatase  
MLCK: myosin light chain kinase  
IP<sub>3</sub> Receptor: inositol triphosphate receptor  
Ca<sup>2+</sup>: calcium ions  
P-Lamban: phospholamban

DrM: So Tess, I guess the real question is, do you really want to propagate those genes?

### **Assignment 1**

Review Email 1 and then write an email to Tess identifying the first messenger that starts the signal transduction in the smooth muscle cell, the likely second messenger, and finally the cellular response caused by the cell signaling cascade. Explain why the arrows go from small to bigger. Also identify whether the receptor that starts the cell signaling pathway is in the plasma membrane or intracellular.

### **Assignment 2**

Review Email 2 and then answer the following questions:

1. Melody said that ginseng enhances erection. What effect would you expect ginseng to have on nitric oxide? Why?
2. Knowing that Melody said Viagra also enhances erection, what effect would you expect it to have on PDE<sub>5</sub>? Why?
3. If neither chemical works what protein(s) would you suspect is “broken”?

Credits: Illustrations of the cell signalling pathways have been reprinted from *Urologic Clinics of North America*, 32, S.H. Francis and J.D. Corbin, “Phosphodiesterase-5 inhibition: The molecular biology of erectile function and dysfunction,” 419–429, Copyright (2005), with permission from Elsevier. Dog photograph was licensed and adapted from an original by © Mariola Kraczowska (Agency: Dreamstime.com).

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