

A Story for Ken Storey

by Julia Sharma, 4th year student,
Department of Biology, McGill University, 2004.

Herbert the frog was a happy frog. He was a small wood frog, even for his young age. He lived in the woods near Carleton University with the rest of his family and friends. He had lived in those lush forests for a few months now, and had been blown away by the beauty that surrounded him. Each change of season seemed to him more beautiful than the next.

First, there had been spring. He had hatched in the little pond by the big spruce tree with all the other tadpoles. There, they had played without a care in the world, until one day, Herbert's friend Olivia's tail disappeared.

"No, it didn't just disappear, it's been getting shorter for some time now," Olivia explained.

Herbert kept staring at her with a blank face.

"You know, metamorphosis and all that. Haven't your parents explained this to you yet?" Olivia searched for some sign of understanding from Herbert. Finding only his bulging eyes staring at her in an even bulgier way than usual, she continued, "Well, my parents told ME all about it. You start to change: lose your tail, grow stronger arms, lose your gills, and just like that, you're a frog. It's part of growing up."

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Looking back, Herbert felt foolish about that day in the pond. Of course Olivia had been right. He had, like all the other tadpoles, gradually become more and more frog-like. Although he often missed his old pond, he was having such fun jumping around on his muscular legs that there was little time for nostalgia.

Soon, as spring turned into summer, tadpole life seemed no more than a dream. Food was plentiful, the trees were full of leaves, and the flowers were in full bloom. Herbert would spend hours hopping through the woods, just taking it all in. But around every corner was Olivia.

"Herbert...Herbert! HERBERT! Olivia screeched.

"What, what. I was just looking around. What's your problem?" Herbert answered after a long pause.

"Well, if I were you, I would be more concerned with building up my glycogen stores for this upcoming winter, than with looking around," Olivia fired back.

"What are you talking about? Glycogen stores? What?" Herbert was helplessly confused. She had done it again. How did she know all this?

"Okay, basically, it goes like this," Olivia began, "Glycogen is a polymer of glucose. When we start to freeze, like we're going to this winter, our cells shrink. When our cells shrink, our bodies respond by producing adrenaline. Adrenaline then binds to its receptor, which happens to be a G-protein coupled receptor, which activates adenylyl cyclase. Adenylyl cyclase then converts ATP to cAMP, which then activates a protein kinase cascade. The end result is that glycogen phosphorylase is activated, and your glycogen stores are broken down into small sugars, like glucose."

Herbert, in his state of total confusion, only managed to say softly, "We're going to freeze...?"

"Look, Herbert, it's not like anything bad is going to happen to us. The sugars act like cryoprotectants. They keep the ice out of our cells so they don't burst when everything freezes. They also increase the osmolarity of our cells to prevent cellular dehydration."

After a long pause and careful consideration, Herbert calmly replied, "Olivia, I don't believe you. You're just making all this up to scare me." And with that, he let out a loud croak, and hopped off into the forest.

Freezing cells! Ha! Glycogen phosphorylase! Did she really think he was so gullible? He was going eat just as much as he liked, no more, no less. It wasn't his fault he was a picky eater.

Weeks passed. Herbert had gotten good at avoiding Olivia. He would hear her coming and dart under a leaf, or hide next to a stone that looked particularly frog-like. Even so, sometimes she caught him unawares, and would start going on about glycogen stores, and cryoprotectants. Still, Herbert stubbornly refused to

listen. He continued to eat very little, being so absorbed in the beauty of the woods. Summer had turned into fall, and all the leaves were bright red and yellow. At night, it was getting cool, and the frogs started sleeping huddled together close to the roots of the big spruce. Herbert was beginning to get concerned, and Olivia wasn't helping.

"You're going to be in for it when the ice starts passing down your veins. Yup, all the way down to your muscles and heart. There's no escaping it now, Herbert." Olivia whispered one night after all the other frogs had fallen asleep.

Herbert was petrified. He was going to die. That night, he dreamt that the temperature had dropped dramatically, and he felt his whole body turn to ice.

"AAAAAAAAAAAAAAAAAAAAHHHHHHHHH!!!!!" Herbert woke up from his dream screaming. "Olivia. Olivia", He whispered.

"Yes," came Olivia's sleepy reply.

"You, know, I've been thinking about this freezing stuff", Herbert ventured, "And I was wondering if you might be able to help me out. You see, I want to survive."

Olivia looked into his bulgy eyes brimmed with tears, and had no choice but to agree. "Sure, Herbert, tomorrow I'll tell you about the p38 pathway."

The next morning, Olivia explained how the p38 pathway was activated in the heart, liver, and kidney in response to osmotic stress and freezing. She told Herbert about how the pathway inhibits most translation and puts the process in stasis, phosphorylates transcription factors, and activates heat shock proteins, like HS-p27 to prevent the cells from being squished. Olivia also told Herbert about two of the selective genes that were upregulated during freezing when most other genes were being shut off. She called these the "special freezing genes", and named them Fr10 and Li16. When asked about these names, she explained that she had made them up. Fr10 stood for frog #10 because she had been the tenth tadpole to hatch, and Li16 stood for Lily 16 because she loved lilies and there were 16 in her favorite patch.

Herbert had been listening attentively, but was starting to lose patience.

"Look, Olivia, this is all very interesting and all that, but how is it going to help me survive the winter?" Herbert asked.

"That's what I was just getting into." Olivia replied. "You see, this pathway acts independently of glucose. It will work in your system no matter how little you eat."

"So I'm going to be alright?"

"Of course, I was only teasing before. Although, it is true that some frogs don't survive the Big Freeze. I was just trying to give you a better chance at survival", Olivia explained.

"Well that was nice of you", Herbert replied sarcastically, "you almost scared me to death."

"That's it!" Olivia suddenly remarked, "I know how we can compensate for your low glycogen stores."

"What?" Herbert was confused again.

"We'll just have to scare you right before we freeze. This is such a good idea. I can't believe I hadn't thought of it before."

Herbert looked puzzled.

"If we scare you, we'll increase your adrenaline levels and upregulate all these pathways I've been telling you about. It's brilliant, Herbert, really!" Olivia explained excitedly.

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Days went by, and as the temperature continued to drop, Herbert started to get nervous. Despite all of Olivia's advice, he couldn't help but be scared of freezing. What if it didn't work? What if it was painful? If it did work, what if he didn't survive the thawing? A million questions and concerns raced through Herbert's head. He hardly slept anymore.

One night, when the chill in the air was especially biting, Herbert noticed that there were no frogs in the usual sleeping spot by the old spruce. "I guess everyone's having a late night", Herbert thought to himself and settled down by the old spruce. He was soon interrupted by the sound of Olivia falling from a branch overhead.

"Boo!" Olivia shrieked.

"Olivia, what are you doing?" Herbert exclaimed.

"Did I scare you?"

"No, did you hurt yourself?"

"A little", Olivia admitted.

"What's going on?" Herbert asked.

"Everyone has gone underground. There's talk that tonight's going to be the Big Freeze, so if I were you, I'd hurry up and start digging yourself a hole. I've already finished mine. Actually, I've been working on it for some time now. You know, picking the spot, making sure the earth is soft." Olivia said.

"Well, I..." Herbert trailed off. Tonight! So soon! He wasn't prepared in the least. He hadn't even been properly scared. "Olivia, I haven't been scared."

"Oh don't worry about it, just find some place to dig down", Olivia replied. And with that, she hopped off to find her hole. "See you in the spring!" She called back when she was nearly out of sight.

"Yeah, in the spring", Herbert answered meekly.

Herbert sat thinking for a few minutes, then sprang into action. He would give himself a few hours to try and scare himself before giving up and digging a hole. There was bound to be a predator nearby. He would simply get scared, and then run away and dig a hole. The night air was cold as Herbert hopped around looking for something big, something scary. After hopping around in the dark without seeing anything even the least bit frightening, he thought he heard heavy steps walking through the forest. Herbert froze, then fought the instinctual urge to run away. He waited until the human was only a few hops away before making his great escape.

Herbert dashed for the low shrubs by the pond, but soon found himself unable to move. He looked around and couldn't see any reason for his restricted movement. Then he noticed the thin mesh net and he felt himself being lifted into the air. Suddenly, he found himself staring at a huge face.

"Well hello there, little fellow, Dr. Storey sure will be happy to see you. And to think, I had almost thought that I had come out collecting too late."

Herbert was petrified. The last thing he remembered before blacking out was thinking of all the kinases which must be active right now in his cells. If only he could get into the ground.

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When Herbert regained consciousness, he was in a cage. The first thing he saw was Olivia.

"Are you okay Herbert?" She asked.

"Sure, I... Olivia? Where are we? How did we get here?"

"Shhhh. It's almost time. They're coming for us."

Suddenly, before Herbert could ask Olivia what she was talking about, they had been taken from their cages and were being transported across a white room with fluorescent lights. Herbert saw a white door open. Then suddenly, everything was dark, dark and cold.

"Olivia?" Herbert managed to say in between shivers. "Olivia, I'm scared."

"Me too", Olivia whimpered.

"So I guess we'll probably survive, right? With all this adrenaline." Herbert muttered before slipping into blackness.