UVic knowl**EDGE**

Sugar-coated fungi

Dutch elm fungus holds promise of new protein therapies

By Kristi Skebo

They're everywhere—on the ground after a rainfall, in the air you breathe and sometimes on the food you want to eat. "Fungi come in all shapes and sizes," explains UVic biologist Dr. Will Hintz, whose research on fungi may help to make more efficient drugs to treat human blood and immune system diseases. "They have unique genetic adaptations that allow them to live in so many different environments—marine, freshwater, terrestrial and even in your fridge."

Of particular interest to Hintz is *Ophiostoma novo-ulmi*, the fungus that causes Dutch elm disease. Transferred from tree to tree by bark beetles, the fungus clogs the water-conducting vessels within the tree, causing the leaves in the crown to wilt, curl, yellow and die.

Hintz studies the interactions between tree and fungus. Trees, like most other organisms, are able to identify foreign invaders such as fungi. Once a tree detects foreign organisms, it produces an arsenal of chemicals to rid itself of these invaders.

The outside of the fungus is covered in sugar-coated proteins produced by a process called glycosylation. The tree recognizes the fungal invader by this coating. By making the sugars more complex, the fungus is able to stay one step ahead of the host's defenses. "We're interested in the sugar-coating process," explains Hintz. "It determines the character of a protein, how it functions and how long it survives."

Hintz, along with his research associates Josh Eades and Paul de la Bastide, want to disrupt this sugar-coating process. "If we disrupt glycosylation, does the fungus become more vulnerable to the tree's natural defences?"

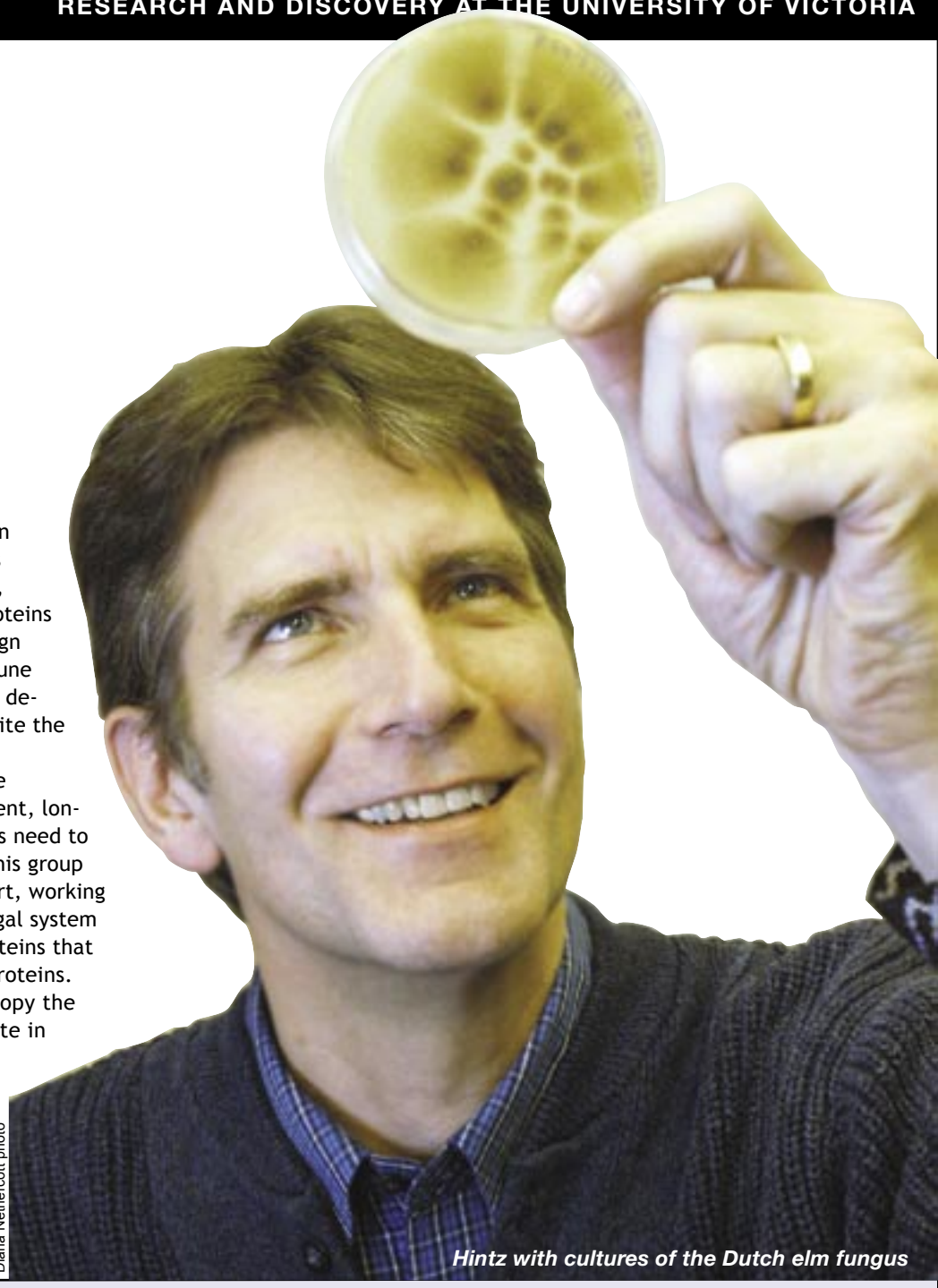
Their work in understanding glycosylation in *Ophiostoma* may turn out to be very useful for humans, particularly in the synthesis of effective protein therapies.

Glycosylation occurs in all eukaryotic organisms (organisms whose cell nuclei are surrounded by a membrane), and the human immune system identifies whether a foreign substance is friend or foe based on its protein coating. Certain illnesses, including some blood-clotting disorders and immune disorders, can be treated with protein pharmaceuticals, but these glycoproteins need to have the correct sugar coating to survive in the blood for relatively long periods of time and to avoid being recognized as foreign.

Currently, many protein therapy drugs are manufactured in fungi such as yeast, but the glycosylation process in yeast is different from that in humans. The specific types of sugars and the ways in which they are linked together differ between humans and yeast. This means that, in humans, these much-needed proteins are recognized as foreign particles, and the immune system will, over time, destroy the proteins despite the body's need for them.

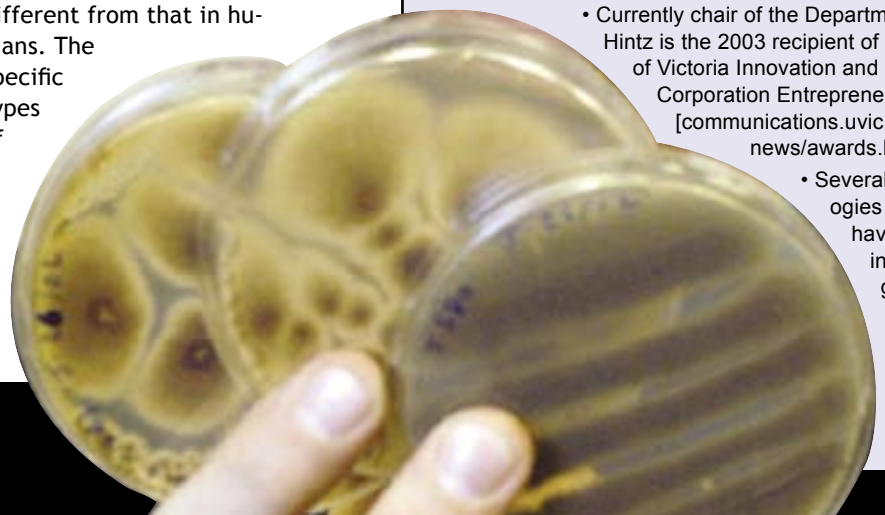
In order to make the treatments more efficient, longer-lasting therapeutics need to be created. Hintz and his group are helping in this effort, working towards creating a fungal system that produces glycoproteins that closely mimic human proteins.

"If we are able to copy the proteins that participate in the glycosylation process, we may be able to engineer therapeutic proteins that are more effective in treating these disorders," says Hintz.



Diana Nethercott photo

Hintz with cultures of the Dutch elm fungus



EDGEwise

- Currently chair of the Department of Biology, Hintz is the 2003 recipient of the University of Victoria Innovation and Development Corporation Entrepreneurship Award [communications.uvic.ca/ring/03nov06/news/awards.html].
- Several biological technologies developed by Hintz have been patented, including work with glycosylation-related systems.
- Hintz has been actively involved with the UVic Innovation and Development Corporation since 1994. The IDC works with UVic researchers to develop the economic potential of their work and make it available to the private sector. More information is available on the IDC Web site [web.uvic.ca/idc/]
- More information about Hintz and his research is available on his Web site [web.uvic.ca/biology/People/hintz/hintz.htm].

This article was written by Kristi Skebo, a student in the Faculty of Graduate Studies, as a participant in the UVic SPARK program (Students Promoting Awareness of Research Knowledge), supported by the Vice-President Academic and Provost and the Vice-President Research.