

Commandeering Cellular Machinery

Researchers manipulate recognition mechanism to detect small molecules.

Researchers have learned how to commandeer the complex machinery that cells use to recognize and respond to such important molecules as steroid hormones, thyroid hormones and vitamin D.

The development could provide a foundation for a new family of biologically based mechanisms able to detect common drugs, chemical weapons and other small molecules. By allowing manipulation of this cellular protein machinery — known as nuclear receptors — the technique could also lead to new methods for producing enzymes and important pharmaceutical compounds.

“We are hijacking these nuclear receptors for a new set of purposes,” explains Donald Doyle, an assistant professor in the School of Chemistry and Biochemistry at the Georgia Institute of Technology. “We want to change the nuclear receptors themselves so they don’t recognize what they normally recognize, and instead recognize the small molecules we want to detect. That would allow us to develop a new type of sensing mechanism.”

A paper published in the Sept. 27, 2004 issue of the journal *Proceedings of the National Academy of Sciences* describes how Doyle’s research team — which also included Lauren Schwimmer, Priyanka Rohatgi, Bahareh Azizi and Katherine Seley — modified one type of nuclear



PHOTOS BY GARY MEEK

LEFT: Georgia Tech Professor Donald Doyle and graduate student Lauren Schwimmer examine yeast colonies growing on a petri plate.

BELOW: Researchers are testing whether nuclear receptors engineered in yeast cells have the same function in mammalian cells.

receptor to bind a drug compound to which it previously did not respond. Based on this success, these researchers hope to demonstrate broader application with other small molecules.

The work was sponsored by the Research Corporation, the Seaver Foundation and the National Science Foundation.

“Now we have to see how far we can push this and how many small molecules we can accommodate with this technique,” Doyle says. “We are trying to generalize this approach to genetic selection. There is a lot of diversity we can work with in terms of different binding pockets and shapes, so this is only the first step.”

@ Read more at: gtresearchnews.gatech.edu/newsrelease/receptor.htm



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