

## Potential Problem with Using Embryonic Stem Cells to Cure Diabetes??

As reported by Joe Palca

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Scientists at Harvard University have uncovered a potential problem with using embryonic stem cells to treat diseases like diabetes. In theory, embryonic stem cells can turn into any cell type in the body, including the cells that make insulin. Two years ago, one team of scientists said that they'd succeeded in doing just that. But new research suggests that the cells aren't really producing insulin after all, and that means that they might not be useful for therapies

Joe Rajagopal is a scientist at Harvard. He and his colleagues are trying to make human embryonic stem cells turn into the kind of cells that make insulin. So when another team reported two years ago they managed to do that with mouse cells, Rajagopal called team leader Ron McKay and asked for details.

Dr. Rajagopal and his team were actually very eager to repeat their protocols because Dr. McKay's protocols were originally performed in mouse embryonic stem cells, and they actually were very grateful for their collaboration in attempting to do the same thing with human ES cells.

Rajagopal and his colleagues tried to follow McKay's protocols to the letter. They took ES cells, or embryonic stem cells, and coaxed them into differentiating, changing into cells that produce insulin. The only difference was they used human ES cells, not mouse. But there was a problem. There was plenty of evidence for insulin protein, but there wasn't as much evidence for the actual production of insulin in the cells.

Rajagopal says McKay's protocol called for growing the cells in a nutrient soup that contained insulin, and he thinks the cells were sucking up that insulin rather than producing their own. Rajagopal did the experiments again, this time using mouse embryonic stem cells, just as McKay did. It didn't matter. The results were the same. He and his colleagues reported their finding in the journal *Science*.

Ron McKay, who works at the National Institutes of Health in Bethesda, has seen Rajagopal's paper, and states "My own view is that our work still stands and that we have multiple lines of evidence that suggest that when we differentiated the cells they produced insulin. And what the current paper says is that you have to be careful about one of those pieces of evidence, which I kind of agree with.

Besides, McKay says his is not the only team that's been working with mouse embryonic stem cells to pursue treatments for diabetes. More than one group has now shown that you can take ES cells and differentiate them in a way that's similar to the way we did and produce cells that will secrete insulin. One of those groups is at Stanford University in Palo Alto.

Group leader Seung Kim says not only have he and his colleagues successfully repeated McKay's protocol, they've improved on it. What we found was by changing conditions we could produce more than 10 to 30 percent of cells producing insulin, we actually got over 95 percent.

Even though there are several ways of doing it, Kim says it's tricky to prove that the cells are really making insulin, not just storing it. In this sort of thing, if you change something slightly, even unknowingly, you may wind up with a completely different product than what was previously reported.

However back at Harvard, Jay Rajagopal says it's possible that there were some slight changes in the way he did the experiments that caused the results he observed. But it's also possible that researchers may be overanxious to see positive results from their studies. We just think that our finding is important in the sense that it will prevent people from chasing red herrings and that is important in a fast-moving field like embryonic stem cell research. In fact I have just seen

something else has just come online from a group in Germany; I knew that they were working in this area, but this is the first time I've seen the data. So really, since we talked, there's new evidence. Very exciting.

Exciting, indeed. But it's also possible doubts will be cast on that study as well. It's just the way science works.

This information from Joe Palca, NPR News, Washington.