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Fixing Pharma

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Stem cells could lead to better, safer drugs

Drug discovery is a cruel business. A hundred thousand people die every year because of adverse drug side effects. Millions die too young because drugs just aren't good enough.

The problem is that scientists invent medicines to treat people, but they have to use animal or tumor cells to do it. Heart cells, brain cells and liver cells all die when you try to keep them in a petri dish. So over decades researchers have come up with jury-rigged tests. They use preserved kidney cells extracted from a human fetus 30 years ago to see if an experimental drug will disrupt the rhythm of the heart. They use cells from a rat's digestive tract with human receptors stuck in. They force huge doses of every potential medicine down the throats of rodents. "The system is failing," says Gabriela Cezar, who left Pfizer (nyse: PFE - news - people) to study stem cells at the University of Wisconsin-Madison.

It's a testament to the ingenuity of pharmaceutical researchers that the system works at all. Nine out of ten drugs studied in humans turn out not to work or to be too toxic. Sanofi-Aventis (nyse: SNY - news - people), Pfizer and AstraZeneca (nyse: AZN - news - people) have all had promising compounds go up in flames because of dangerous side effects. One solution may be to use embryonic stem cells to test drugs for safety and efficacy. "You should be able to get rid of some of the nasty drugs before they even hit clinical trials," says uw-Madison stem cell pioneer James Thomson. "And we're able to do that today."

Two years ago Thomson founded Cellular Dynamics International, a biotech firm that uses embryonic stem cells to make beating human heart cells, something that's never before been available to drug companies. Thomson has avoided the business world as long as possible but now says it is time for his cells to go commercial. Roche (other-otc: RHHBY.PK - news - people) is the first announced customer. Earlier this year it began tests with Thomson's heart cells to catch cancer drugs that are toxic to the heart. A rival company, Sweden's Cellartis, is developing ways to test drugs for liver toxicity (with AstraZeneca) and for birth defects (Pfizer).

Even bigger, but further off, is the potential that being able to study neurons in a dish will allow researchers to understand what causes Parkinson's or Lou Gehrig's disease. It could be that in 20 years almost every medical researcher is going to use embryonic stem cells as basic tools. "That is going to profoundly change medicine," says Thomson.

Catapulting this work forward is the discovery of ways to create cells that act like embryonic stem cells but without ever using embryos. Last year Japan's Shinya Yamanaka and Thomson simultaneously showed that adult human cells could be transformed into embryolike stem cells by

activating only four genes using viruses. "That has galvanized the field," says Alexander Rod MacKenzie, head of basic research at Pfizer.

uc, San Diego researcher Lawrence Goldstein is using these so-called induced pluripotent stem cells to make neurons that are "genetically identical" to those of Alzheimer's patients. He is collecting 50 skin samples from Alzheimer's patients in order to hunt for new drugs.

Wisconsin's Cezar has started a biotech called Stemina that is using stem cells to get to the roots of autism. Autism appears in a tenth of the children born to mothers who take the epilepsy drug valproate. Valproate is known to injure neurons, so Cezar is converting embryonic stem cells into live neurons and adding valproate to the sample. The neurons gush chemicals that she is comparing to those found in brain cells of people with autism. If there's a match, Cezar could be on a path toward diagnostic tests or drugs. Stemina is using a similar strategy for a range of potential drugs. "[Autism] is an epidemic," she says, "and we have no idea about the cause.