Researchers find targeting rare form of cystic fibrosis earlier prevents organ damage in ferrets

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A team of researchers from the University of Iowa, University Medical Center Utrecht and Vertex Pharmaceuticals Incorporated, reports that

earlier administration of a drug already given to patients with a rare form of cystic fibrosis can prevent organ damage—at least in ferrets. In their paper published in the journal *Science Translational Medicine*, the group describes their study of the impact of the drug ivacaftor on ferret models and what they found. Thomas Ferkol with the Washington University School of Medicine has written a Focus piece on the work done by the team in the same issue.

Cystic fibrosis is a genetic disorder that notoriously leads to lung problems, but it also damages other organs such as the kidney, liver, pancreas and intestines. Prior research has shown that people with cystic fibrosis have problems with production of a protein called CFTR—the protein controls the behavior of charged atoms in cells that make fluids such as sweat, tears, saliva, mucus and digestive material. Prior research has shown that approximately 10 percent of cystic fibrosis patients have a G551D protein defect. Prior research has also found that the drug ivacaftor can reduce lung problems for people with the G551D protein defect. For most patients, treatment starts after the first year of life. Unfortunately, by that time, the disorder has already damaged organs in most G551D patients. In this new effort, the researchers found that administering ivacaftor to such patients can prevent much of that organ damage—at least in ferret models.

To learn more about the possible benefits of giving ivacaftor to patients earlier, the researchers engineered test ferret embryos with the rare form of cystic fibrosis. They administered the drug to the ferrets while they were still in the womb and continued to give it to them after they were born.

The researchers report that administering ivacaftor to the mouse models while they were still in the womb resulted in much less organ damage. More specifically, they report that it prevented male infertility and damage to the pancreas (which commonly leads to diabetes in people

with cystic fibrosis) and it also prevented damage to the lungs. They note that more testing will need to be done before doctors can begin prescribing ivacaftor earlier for patients.

More information: Sun et al. In utero and postnatal VX-770 administration rescues multiorgan disease in a ferret model of cystic fibrosis, *Science Translational Medicine* (2019). DOI: 10.1126/scitranslmed.aau7531

Thomas W. Ferkol. Prevention of cystic fibrosis: The beginning of the end?, *Science Translational Medicine* (2019). DOI: 10.1126/scitranslmed.aax2361 Xingshen