MedicalXpress

Unexpected discovery highlights new role for cell death regulator

June 14 2012

An unexpected discovery of how the body controls cell death has revealed a potential new therapeutic target.

A research team based at Cardiff University's School of Biosciences has already revealed the mechanism by which high alcohol intake can induce pancreatitis and its progression to pancreatic cancer. Now a new study, published in Current Biology, reveals a hitherto unknown interaction between two well known molecules, which has important implications for our understanding of inflammation and cancer in the pancreas as well as other organs.

The Cardiff team studied the protein Bcl-2, already known to be capable of inhibiting programmed cell death in all tissue types in the body. Cell death is vital to normal development, and under certain circumstances this protein can therefore promote tumour growth and cancer.

The Cardiff study of pancreas cells showed that removal of the Bcl-2 protein activated a molecule in the cell membrane which pumps calcium out of the cells. As the team expected, a lower level of Bcl-2 increased the level of programmed cell death. But they also found that the lack of Bcl-2 markedly protected against another much more dangerous form of cell death - necrosis, in which cells swell and burst, releasing their contents and causing severe inflammation. The team found the increased protection against necrosis was directly linked to increased activity of the calcium pump.

The team, led by Dr. Oleg Gerasimenko and MRC Professor Ole Petersen, believes that blocking the Bcl-2 effect on the calcium pump, so that the pump becomes more active, could be a beneficial therapy against necrosis and the subsequent dangerous inflammation. This is important because necrosis of the enzyme-secreting pancreatic cells, often the result of high alcohol consumption, markedly increases the risk of pancreatic cancer, the fourth leading cause of cancer deaths in both Europe and the US with a 5-year survival rate of only 4 per cent.

Professor Petersen, also Director of Cardiff's School of Biosciences, said: "The new findings come from studies of pancreatic cells. We have discovered an entirely unexpected link between two well known molecules and this link is a potentially attractive target for treatment of pancreatitis and the dangerous progression of pancreatitis to pancreatic cancer. However, our findings are also likely to be of more general importance. The inhibitor of programmed cell death, Bcl-2, and the calcium pump in the cell membrane are found in every type of cell in our body. The interaction between the two could well be important in deciding cell fates in many different organs and also the development of inflammation and different cancer types."

Provided by Cardiff University