



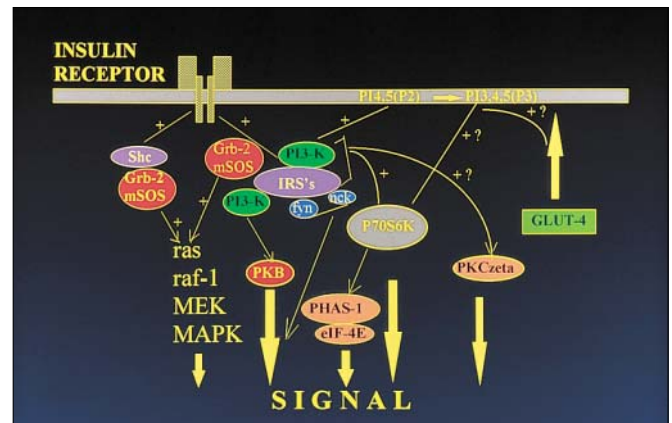
Research Update

Vanadium for diabetes

Vanadium, a common mineral used to strengthen steel and thought to have no use in humans, is now showing promise as a treatment for diabetes. Dr. John McNeill and colleagues in the University of British Columbia's Department of Pharmaceutical Sciences have discovered that vanadium salts stimulate the uptake of glucose in rats without raising insulin levels (*Science* 1985;227:1474-7). Now, McNeill and Dr. Chris Orvig, director of UBC's Medicinal Inorganic Chemistry Group, have received a \$700 000 research grant to continue their work.

A major challenge with the vanadium compounds was to improve absorption, so Orvig bound vanadium to maltol, a food additive that facilitates its entry into cells. The researchers believe that insulin activates a receptor that phosphorylates and activates kinases within the cell.

"We now know that there are at least 2 pathways leading to different events, 1 leading to metabolic events," explains McNeill. "Obviously, if you have a switch that turns things on, you also have to have a switch that turns things off. There is a group of enzymes that takes the phosphates off the proteins. That's where the vanadium is believed to work. So if your insulin levels were low, or the cells were not responding well to insulin, you could expect that if the phosphatase that brings about inactivation of the enzyme inside the cell is inhibited, then for a modest amount of insulin and receptor activation you should still get more bang for the buck later on down the pathway. That's the



Biochemical pathways affected by insulin. Vanadium prevents the dephosphorylation of the kinases that are phosphorylated by insulin.

conventional wisdom at the moment and there are some data that definitely support that concept."

A small number of recent US studies using vanadium compounds have shown positive results in lowering insulin levels in patients with diabetes. "What we have in the body, I think, is an insulin-enhancing effect," says McNeill. Now that the challenge of absorption has been overcome "the other challenge is convincing people that this is real and has potential for working in humans. Drug companies are very sceptical about metals." However, McNeill stresses that vanadium is a light metal. "This is in the ballpark of calcium and phosphorous, and nobody worries about them being toxic." — © Heather Kent

In the news . . .

Smoke gets in your genes

Secondhand smoking by pregnant mothers can cause genetic mutations that lead to some forms of cancer, a ground-breaking US study has revealed (*Nat Med* 1998;4:1144-51). The researchers looked at mutations in a reporter gene, *HPRT*, in cord blood T lymphocytes of newborns whose mothers were exposed to cigarette smoke, and compared the results with those from newborns whose mothers were not exposed to smoke. The newborns exposed to smoke in the womb had "illegitimate" genomic

deletions not seen in the unexposed newborns. These illegitimate deletions are associated with hematopoietic cancer in early childhood. The authors say that studies of mothers' exposure to cigarette smoke and childhood cancer need to be reinterpreted in light of this finding.

Successful treatment of acute promyelocytic leukemia

Remission of acute promyelocytic leukemia has been achieved with arsenic trioxide (*N Engl J Med* 1998; 339:1341-8). US researchers tried arsenic trioxide in 12 patients in whom earlier treatment had failed. Of these patients, 11 had a remission after 12

to 39 days of treatment, with only mild side effects. The treatment has been used with great success in China.

Fetal surgery for spina bifida

For the first time, a human fetus has undergone an operation in the womb to repair spina bifida (*Lancet* 1998;352[9141]). The baby was later delivered prematurely and appears to be developing normally except for a club foot. Previous in-utero repair of spina bifida in fetal sheep succeeded in stopping the spinal cord destruction that causes spina bifida and in "rescuing" neurologic function before birth.