Bench to Bedside

Polymer hints at new clotting agent

A molecule once studied exclusively in simple cellular organisms has been recently shown to play an important role in the ability of human platelets to clot. Polyphosphate, a polymer of inorganic phosphate, is widely found in nature and was discovered over a decade ago in bacteria, fungi and yeast, where it was found to be involved in virulence and stress responses.

In bacteria, polyphosphates are housed in acidocalcisomes. In humans, platelets were recently discovered to contain granules that strongly resemble acidocalcisomes and contain polyphosphate (*J Biol Chem* 2004;279:44250-7). Furthermore, people with defects in the dense granules of their platelets can display bleeding disorders, a discovery that led Stephanie Smith and colleagues to look into the role of polyphosphate in blood clotting. In a model using human plasma in vitro, they found that the addition of polyphosphate decreased clotting time from 25 minutes to less than 5 minutes, and extended the time until clots lysed (fibrinolysis) by over 20 minutes (*Proc Natl Acad Sci USA* 2006;103:903-8).

Polyphosphate appears able to enhance coagulation on several levels: It activates components involved in the clotting cascade and enhances the work of an inhibitor of fibrinolysis called thrombin-activatable fibrinolysis inhibitor (TAFI). Furthermore, platelets secrete polyphosphate upon activation, which Smith and colleagues suggest could be important after vascular injury, since it would accelerate blood clotting.

With this newly discovered function of polyphosphate, its interest broadens beyond its role in basic biology. Indeed, Smith and colleagues are already envisioning polyphosphate as an additive one day in topical agents that control bleeding.

National Cancer Institute

Imaging transplanted islet cells

Islet cell transplantation, a promising new way to treat type 1 diabetes, may someday obviate the need for exogenous insulin therapy. The ability to image transplanted cells would facilitate ongoing monitoring of both the cells and the patients who receive them.

Acquiring pictures of pancreatic β cells to assess their survival and improve transplant rates has been a focus in this field. Images of cells in islet grafts have successfully been made in the laboratory, for example by rendering the cells bioluminescent (*Transplantation* 2005;79:768-76). However, such techniques are not yet applicable in humans.

Natalia Evgenov and colleagues recently showed that it is possible to label transplanted islet cells with magnetic nanoparticles detectable by MRI (*Nature Med* 2006;12:144-8). They transplanted these tagged cells into mice and found that images of the cells could be made for up to 188 days afterward. The process did not alter the cell's insulin-secreting ability: normoglycemia was restored in the diabetic mice that received the transplanted cells.

The authors concluded that the tagging of islet cells could be useful in clinical practice to help evaluate graft survival and, during graft rejection, to monitor the response to therapies. — Compiled by David Secko, Vancouver

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