Improvement of liver stem cell engraftment by protein delivery

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Researchers at INSERM (France) have engineered a chimeric protein that increases cell survival, migration and proliferation to improve stem cell engraftment. The results, which appear in the September 2009 issue of *Experimental Biology and Medicine,* show that TAT-Tpr-Met, a cell permeable form of the hepatocyte growth factor receptor can increase the number of hepatic stem cells integrated into the liver of the mouse.

TAT-Tpr-Met is the result of the fusion of Tpr-Met, an autoactived tyrosine kinase, to the protein transduction domain from HIV-TAT that gives the potential of the whole protein to enter into cells. TAT-Tpr-Met enters into cells in just one hour, where it then remains stable and recapitulates several effects seen with the hepatocyte growth factor (HGF). As the activating signal induced by TAT-Tpr-Met comes from inside the cells, it is independent of the extracellular environment, and continues even if cells are placed in vivo. This property was used to transplant cells with an advantage that allows cells pretreated with TAT-Tpr-Met to engraft twice more than untreated cells.

The research team, Guillaume Kellermann, a graduate student in Biotechnology (University Paris VII), along with Lyes Boudechice, a veterinarian surgeon, Dr. Anne Weber and Dr. Michelle Hadchouel performed the studies in six week old mice. Dr. Kellermann noted that "previous work had already shown that cells engraft better with HGF, but contrary to other strategies, our method is virus and DNA free, so it may be safe for humans. However, before, considering clinical applications further studies need to be performed to check for the long

term effects".

In summary, stem cells have an enormous potential in cell therapy, however their ability to engraft in solid tissues remains low. Here, a chimeric protein was engineered that switches them to a state more favorable to engraftment by promoting their survival, migration and proliferation. After a few days the protein is completely degraded inside the cells, therefore our method is safer than other strategies using modified virus and may be compatible with clinical applications.

Dr. Steven R. Goodman, Editor-in-Chief of Experimental Biology and Medicine, said "The authors have reported a very clever approach, utilizing the fusion protein TAT-Tpr-Met, to increase hepatic stem cell engraftment into the liver. The fact that the approach does not require virus or DNA makes it a reasonable strategy for future clinical applications."

Source: Society for Experimental Biology and Medicine (news : web)