

Leukemia drug could save lives of stroke patients

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Studies in mice reveal why tPA may cause brain damage

The drug tPA is the most effective treatment currently available for stroke patients, but its safety is limited to use within the first three hours following the onset of symptoms. After that, tPA may cause dangerous bleeding in the brain. However, in a study published today in *Nature Medicine*, investigators from the Stockholm Branch of the Ludwig Institute for Cancer Research (LICR) and the University of Michigan Medical School show that these problems might be overcome if tPA is combined with the leukemia drug, imatinib (Gleevec®). The results demonstrate that imatinib greatly reduces the risk of tPA-associated bleeding in mice, even when tPA was given as late as five hours after the stroke had begun. The LICR team, in collaboration with the Karolinska University Hospital in Stockholm, is now planning a clinical trial with imatinib in stroke patients.

According to the World Health Organization (WHO), 80 percent of the 15 million strokes that occur each year are caused by the type of blood clots in the brain that tPA can dissolve. Today, less than 3% of patients with this type of stroke receive tPA because the narrow safety window has often passed by the time a stroke patient reaches a hospital and is diagnosed. If the planned clinical trial with stroke patients in Sweden confirms the findings of the present study, there is great promise that imatinib or similar drugs could be administered to stroke patients to increase the therapeutic window of tPA.

The basis for this novel proposal is the key growth factor PDGF-CC,

which has now been discovered to control the blood brain barrier (a structure that normally shields the brain from the blood). When tPA acts on PDGF-CC, the blood-brain barrier becomes porous and can start to leak. Imatinib inhibits the detrimental effect of PDGF-CC by binding to its receptor PDGFR alpha, seemingly without hindering tPA's therapeutic effect, which is to break down clots that have lodged in the brain's blood vessels.

"Ten years ago our research group identified the growth factor PDGF-CC, and we are now very excited having unraveled a mechanism in the brain involving this factor", says Professor Ulf Eriksson, who leads the LICR team. "This finding has indeed the potential to revolutionize the treatment of stroke."

Source: Ludwig Institute for Cancer Research

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