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Press release

Hibernating brown bears provide clues to protective mechanism against thrombosis

Immobilized acute patients could benefit

Brown bears do not develop thrombosis during hibernation despite weeks of rest. The protein hsp47 plays a central role in this. This finding should now help in the development of new therapies for immobilized acute patients. This cross-species mechanism is also found in pigs and mice. The international study, led by cardiologists from LMU University Hospital Munich in collaboration with researchers from Sweden, Denmark, Norway and England, has been published in the journal Science.

Translated with www.DeepL.com/Translator (free version)When people are bedridden for weeks, the risk of a blood clot forming in a vein, traveling through the circulatory system and clogging a blood vessel in the lungs is increasing. Immobility is actually one of the greatest risk factors for such venous thromboembolism, with its life-threatening consequences. But why can brown bears sleep almost motionless for months in winter without coming close to the risk of this condition? And why do paraplegic patients not have an increased risk of thrombosis after the acute phase of injury? Answers to this paradox have been found by an international team of researchers led by private lecturer Dr. Tobias Petzold from Department of Medicine I (Director: Prof. Dr. Steffen Massberg) at LMU Klinikum (LMU University Hospital Munich). The solution to the puzzle: Brown bears, like paraplegics, use a mechanism that reduces interactions between platelets and immune cells, thus preventing the formation of blood clots. The discovery is far-reaching and could open up new therapeutic options, as the highly renowned journal Science also found, which has now published the study results.

For the cardiovascular specialists at LMU University Hospital led by Tobias Petzold, this research project began with two trips to central Sweden – one in summer, one in winter. There, a whole flock of brown bears has been scientifically studied for more than ten years, among others by the Danish cardiologist Prof. Dr. Ole Frobert from the University Hospital in Örebro, Sweden, who suggested the new cooperation project to his Munich

colleagues.

The brown bears are wearing GPS transmitters marking their location and were sedated for a blood sample and immediately released back into the wild. In a mobile laboratory, cardiologist Petzold and his colleagues analyzed the samples within three to four hours. The question: Does the coagulation system of brown bears differ during hibernation and summer activity? The so-called plasmatic coagulation system normally plays a crucial role in the development of venous thrombosis. “But we didn't find a dramatic relevant difference there," says cardiologist Dr. Manuela Thienel, co-first author of the study.

The researchers took some of the blood samples to Munich, where they examined the platelets more closely in their laboratories. It turned out that, in the hibernating brown bear body, "the interaction between the blood platelets and inflammatory cells of the immune system is slowed down" as cardiologist Petzold says, "which explains the absence of venous thrombosis." The scientists then demonstrated exactly the same mechanisms in paraplegic patients – and in healthy volunteers who literally lay down in bed for three weeks as part of an experiment conducted by the European-German and American space agencies (DLR and NASA).

To track down the molecular mechanism behind the protective process, the physicians enlisted the expertise of Prof. Dr. Matthias Mann and Dr. Johannes Müller-Reif, also first author of the study, from the Max Planck Institute of Biochemistry in Martinsried. Using so-called mass spectroscopy-based proteomics, almost 2700 active proteins were quantified in the bears' blood platelets. Crucially, 71 proteins were upregulated and 80 downregulated during hibernation compared to summer activity. Johannes Müller-Reif: "The platelet protein with the greatest difference between hibernating and active bears was heat shock protein 47, which was downregulated 55-fold in hibernating bears." Notably, the researchers were able to show that downregulation of this HSP47 happens under long-term immobilization in different mammalian species (humans, brown bears, and pigs), making it an evolutionarily conserved mechanism for thrombosis prevention.

Low HSP47 protein levels reduce the interaction of platelets and inflammatory cells. In fact, says Tobias Petzold, "HSP47 alone is capable of activating inflammatory cells."

In biomedical terms, this means that if HSP47 could be blocked with a suitable molecule in immobilized acute patients, the risk of venous thrombosis could possibly be prevented. So-called small molecules that switch off HSP47 already exist for laboratory experiments. But they are not suitable for possible use in humans. "That's why", says Petzold, "we are now looking for promising substances."

Images are available on request.

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LMU Klinikum

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Outstanding facilities of the LMU University Hospital include the oncological center CCC M and Bavaria's largest transplant center TxM.

The LMU University Hospital is represented in all German centers of health research.

The Medical Faculty of Ludwig Maximilians-University Munich and the LMU University Hospital make a significant contribution to the excellence strategy of the Ludwig Maximilians University in Munich.

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