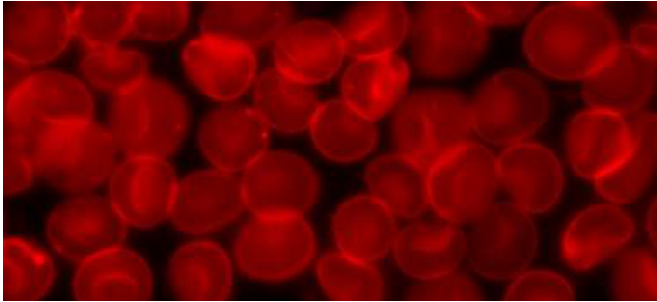


Health research discovers new link between hypoxia and blood clot risk

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Credit: Wikimedia Commons

Research led by Rinku Majumder, Ph.D., Associate Professor of Biochemistry at LSU Health New Orleans School of Medicine, has found how hypoxia (a low concentration of oxygen) decreases Protein S, a natural anticoagulant, resulting in an increased risk for the development of potentially life-threatening blood clots (thrombosis). Although hypoxia has been associated with an increased risk for thrombosis, this research showed for the first time a molecular cause. The work is published in the current issue of *Blood*.

"Hypoxia is common in many diseases including cancer, alcoholism, [sickle cell anemia](#), nonalcoholic fatty liver disease and more," notes Dr. Majumder. "Human Protein S (PS) is a natural blood anticoagulant. Although discovered 40 years ago, the exact mechanism of PS's anticoagulant action was deduced only in the last few years. Our earlier work found that PS inhibits a key clotting protein, Factor IXa. We knew that PS deficiency could occur in [hypoxia](#) but not why. With this study, our group identified the gene regulatory mechanism by which oxygen concentration controls PS production."

Because Protein S is primarily produced in the liver, the team of researchers cultured human

hepatocarcinoma cells at normal oxygen and also hypoxic conditions and then measured levels of the protein. They found that increasing hypoxia not only reduced PS but also significantly increased a protein that turns on the gene to produce hypoxia. This suggested that the [protein](#), hypoxia-inducing factor 1, might regulate Protein S, which the researchers confirmed through biochemical and genetic approaches in a mouse model.

The research is included in the journal's "Issue Highlights" featured on the cover and is accompanied by a [commentary](#) that calls the discovery "an important contribution to our understanding of the molecular basis of the augmentation of thrombosis by hypoxia."

"This study will open a new direction for targeting hypoxia-mediated thrombotic disorders," Majumder concludes.

More information: Vijaya S. Pilli et al, Hypoxia downregulates protein S expression, *Blood* (2018). DOI: [10.1182/blood-2018-04-841585](https://doi.org/10.1182/blood-2018-04-841585)

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