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Dr. Ashraf has focused his research that was of urgent need and challenge for nation and scientific community to elucidate the blood clotting problem inflicting our soldiers that are positioned at high altitude defending our borders. He remains a pioneer in the field of high altitude thrombosis and has done seminal work in resolving the mystery of blood clotting on exposure to hypoxia.

Amongst the major outcomes of his translational research, the landmark work was internationally recognized and published in prominent journal **'Blood'** in 2014, received accolade by an Editorial. The study revealed a novel cause for blood clot formation at altitudes and proposed 'Calpain' as a novel biomarker (IPO: 733/DEL/2014) for early diagnosis; thereby providing timely diagnosis to Indian Army Jawans posted at Siachen Glaciers defending our borders *(http://timesofindia.indiatimes.com/india/DRDO-lab-detects-reason-behindthrombosis/articleshow/40139095.cms)*.

Dr. Ashraf study has contributed enormously in understanding the etiopathology of clot formation at altitudes, for the development of possible drug targets. He elucidated previously unknown cause of thrombosis at altitudes is centrally regulated by a complex network of coagulatory and NLRP3-inflammasome mediated inflammatory responses. His research established (**PNAS, 2017)** that, hypoxia-inducible Factor-(HIF)-1α, a protein complex plays an integral role in the body's response to low-oxygen, activates an inflammatory complex inflammasome-NLRP3 and releases inflammatory cytokines like IL-18 and IL-1β, which eventually causes blood clotting. This novel finding was highly recognized worldwide and published in the **'PNAS'** in 2017; also proposed as potential therapy *(Nature India-doi:10.1038/nindia.2017.143)*. The Inflammation-Coagulation-Hypoxemia convolutions has also been observed in COVID-19 pathogenesis, low-molecular-weight heparin have shown encouraging results, therefore natural compound based anticoagulant are also being explore.

In a rare breakthrough, his lab developed a microRNAs mimic based therapy against thrombosis; for the first time the antithrombotic potential of microRNAs was established. These preclinical findings were validated in human patients, supporting the translational significance of miR-145 for development of a novel antithrombotics (IPO:1398/DEL/2015), which could be also tested against COVID-19 infection also. These findings were published in **EBiomedince (2017)**.

Chandigarh (Western command hospital, Chandimandir), Delhi (Army hospital R&R) and Pune (AFMC)to establish a distinct clinical, genetic, biochemical and molecular signature profiles for thrombosis at altitudes. The study was published in '**Blood Advances'** in 2019. The recommendation proposed by this study will be immensely useful for introduction of distinct diagnostic and treatment modalities for patients from altitudes and for the operational requirements of Indian Armed Forces.

Prof. Ashraf was the lead investigator of one of the biggest longitudinal prospective cohort study (comprising of 750 Indian soldiers). Not just they investigated the incidence and prevalence (along with genetic risk) of thrombotic event in soldiers stationed at extreme altitudes; they also corroborated the translational significance of his novel findings. His research collaborations with India Army have contributed to the people staying at high altitude regions **(Lancet Global Health South Asia: 2022**. Additionally, this observation has been considered for convincible recommendation in Indian Armed Forces during induction and operational deployments at extreme altitudes. *(https://www.tribuneindia.com/2014/20140813/nation.htm: DRDO to help Army fight thrombosis in Siachen).*

Dr. Ashraf's ability to translate his research findings for societal benefit has added new dimensions in the field of high altitude research. The high altitude research contributions were attested by his participation in International consortium for revision of Acute Mountain Sickness diagnosis guidelines.

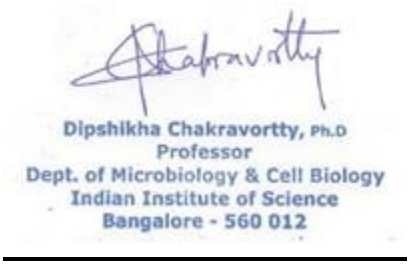
Lately, Dr. Ashraf had done very impressive work in the area of epigenetics, presenting the landscape of LncRNAs in disease progression. This pioneering study has successfully stratified HA-DVT patients from the high altitudes. The comprehensive analysis of identified lncRNA's transcriptional signature displays their functional prediction to be involved in thrombosis pathophysiology. As a result, lncRNAs may serve as novel mechanistic insight and with further in-depth study they could be used as diagnostic and therapeutic targets. These findings were published in the journal "**Thrombosis & Haemostasis**" with editorial commentary and also received prestigious "**Paul Dudley White International Scholar Award**" by American Heart Association.

In summary, Dr. Ashraf has established that hypoxia accelerates a prothrombotic milieu via calpain activation . Thrombus formation is critically regulated by activation of NLRP3-caspase-1-IL-1β -HIF-1α axis. The restoration of miR145 levels serves as promising antithrombotic therapy ; the seminal contributions for societal benefit, especially for Armed Forces defending our nation. His laboratory is engaged in Machine-Learning Platform development for pharmacogenomics based personalized medicine. His research work found special importance during this pandemic since the COVID-19 virus triggers hypoxemia induced inflammatory cytokines that activates coagulation, the very mechanism was proposed by their team (PNAS, 2017) for blood clotting under hypoxia at attitudes. As a consequence, the therapeutic strategies like Low molecular weight heparin (LMWH) is now widely recommended. The anti-inflammatory properties further make LMWH, a preferred choice in mitigating cytokine storm in COVID-19 patients.

Prof. Ashraf is a bright, confident person with good leadership qualities who has focused his research career in an area of societal relevance. He has clearly exhibited his exceptional research capabilities through consistent performance over the years. As is evident, Prof. Ashraf will be able to take on the challenges of pursuing important problems in depth with enthusiasm and self believe.

In my opinion, his translational work on High altitude induced Thrombosis has added new dimensions to the field as evident by the number and the quality of work being cited.

I strongly recommend Prof Ashraf for the Prestigious Sun Pharma Award



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