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A Precision Medicine Approach to Sickle Cell Disease by Targeting the Adhesion Interactome

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Abstract : Sickle cell disease disproportionately affects sub-Saharan Africa and certain tribal populaces in India and has consequently drawn little intertest from Pharma. In sickle cell patients, adhesion of erythrocytes or reticulocytes to one another and the vessel wall results in painful ischemic episodes with few, if any, effective treatments for vaso-occlusive crises. Identification of disease-associated adhesion markers on erythrocytes or reticulocytes might inform the use of more effective therapies against vaso-occlusive crises. Increased expression of one or more of bcam, itga4, cd44, cd47, rap1a, vcam1, or icam4 has been reported in sickle cell subjects. Using the miRNet ontology knowledgebase, peripheral blood interactomes were generated by seeding various combinations of the afore-referenced mRNA. These interactomes yielded an array of miR targets. As examples, targeting hsa-miR-155-5p can potentially neutralize the rap1a-bcam-cd44-itga4-vcam1 erythrocyte/reticulocyte adhesion interactome whereas targeting hsa-miRs-103a-3p or 107 can potentially neutralize adhesion in cells overexpressing icam4-cd47-bcam-itga4-cd36. AM3380 (MIRacle™) is an off-the shelf hsa-miR-155-5p agomiR that can potentially neutralize the rap1a-bcam-cd44-itga4-vcam1 signaling axis. Phlebotomy coupled with transcriptomics represents a potentially feasible and effective precision medicine strategy to mitigate vaso-occlusive crises in sickle cell patients.

Keywords : adhesion, interactome, precision, medicine
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