

VWF-ADAMTS13 axis dysfunction in children with sickle cell disease treated with hydroxycarbamide compared to blood transfusion – biological mechanisms and clinical significance.

Helen Fogarty^{1, 2, 3}, Azaz Ahmad¹, Ferdows Atiq¹, Dearbhla Doherty¹, Soracha Ward¹, Ellie Karampini¹, Aisling Rehill¹, Gemma Leon¹, Rosena Geoghegan², Helena Conroy², Mary Byrne⁴, Ulrich Budde⁵, Sonja Schneppenheim⁵, Ciara Sheehan⁶, Noel Ngwenya⁶, Ross I. Baker,^{7, 8} Roger J.S. Preston^{1, 3}, Emma Tuohy⁶, Corrina McMahon^{2, 3} and James S. O'Donnell^{1, 3, 4, 8}

¹ Irish Centre for Vascular Biology, School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland, Dublin 2, Ireland.

² Department of Haematology, Children's Health Ireland (CHI) at Crumlin, Dublin, Ireland.

³ National Children's Research Centre, Children's Health Ireland (CHI) at Crumlin, Dublin, Ireland.

⁴ National Coagulation Centre, St James's Hospital, Dublin, Ireland

⁵ Medilys Laborgesellschaft mbH, Department of Hämostaseology, Hamburg, Germany

⁶ Department of Haematology, St James's Hospital, Dublin, Ireland

⁷ Western Australia Centre for Thrombosis and Haemostasis, Perth Blood Institute, Murdoch University, Perth, WA, Australia.

⁸ Irish-Australian Blood Collaborative (IABC) Network.

SUPPLEMENTAL MATERIALS

Supplementary Legends

Supplementary Figure 1: Flow cytometry gating strategy for measuring phosphatidylserine exposure on red blood cells.

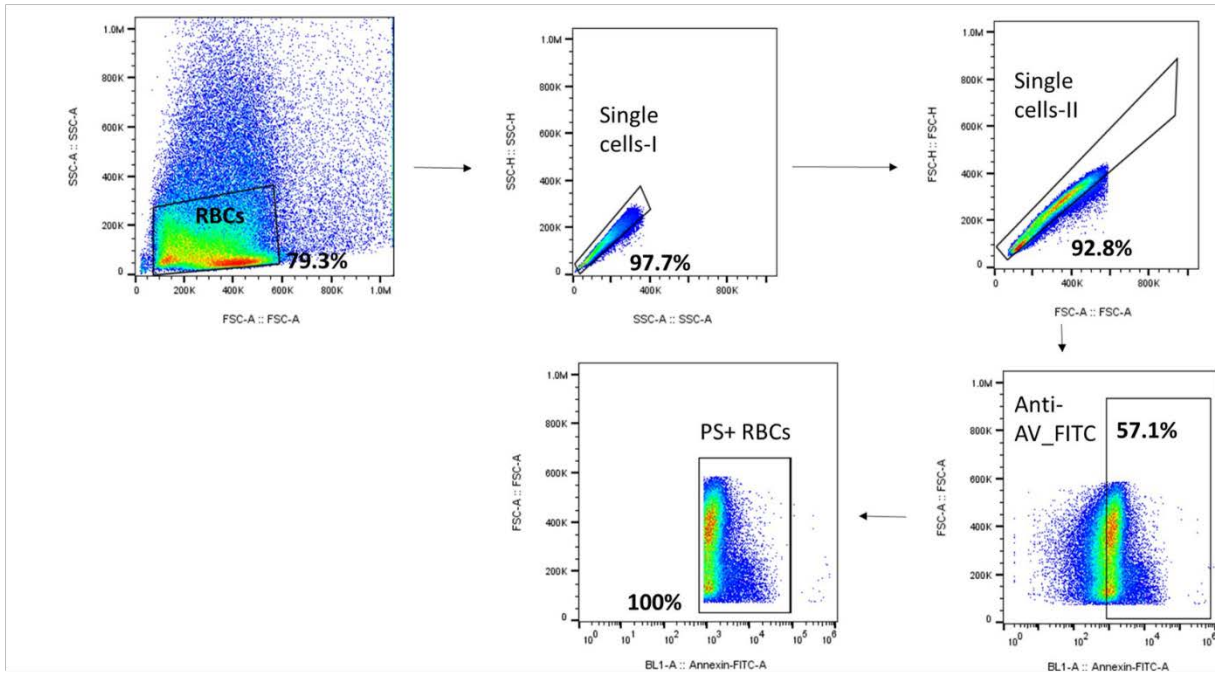
Supplementary Figure 2: Flow cytometry gating strategy for measuring recombinant VWF binding to red blood cells.

Supplementary Figure 3: HC children (n=96) were divided according to Hb F quartiles and levels of VWF:Ag **A)** and VWF:CB **B)** were compared. HbF quartile 1 is <12.1%, Quartile 2 is 12.1%-16.1%, Quartile 3 is 16.2%-20.8% and Quartile 4 is >20.8% BT treated children (n=84) were divided according to Hb S quartiles and levels of VWF:Ag **C)** and VWF:CB **D)** were compared. HbS quartile 1 is <14.1%, Quartile 2 is 14.1%-19.7%, Quartile 3 is 19.7%-27.4% and Quartile 4 is >27.4%. Comparison between first and fourth quartiles was performed with independent sample *t*-test. (**p*<0.05).

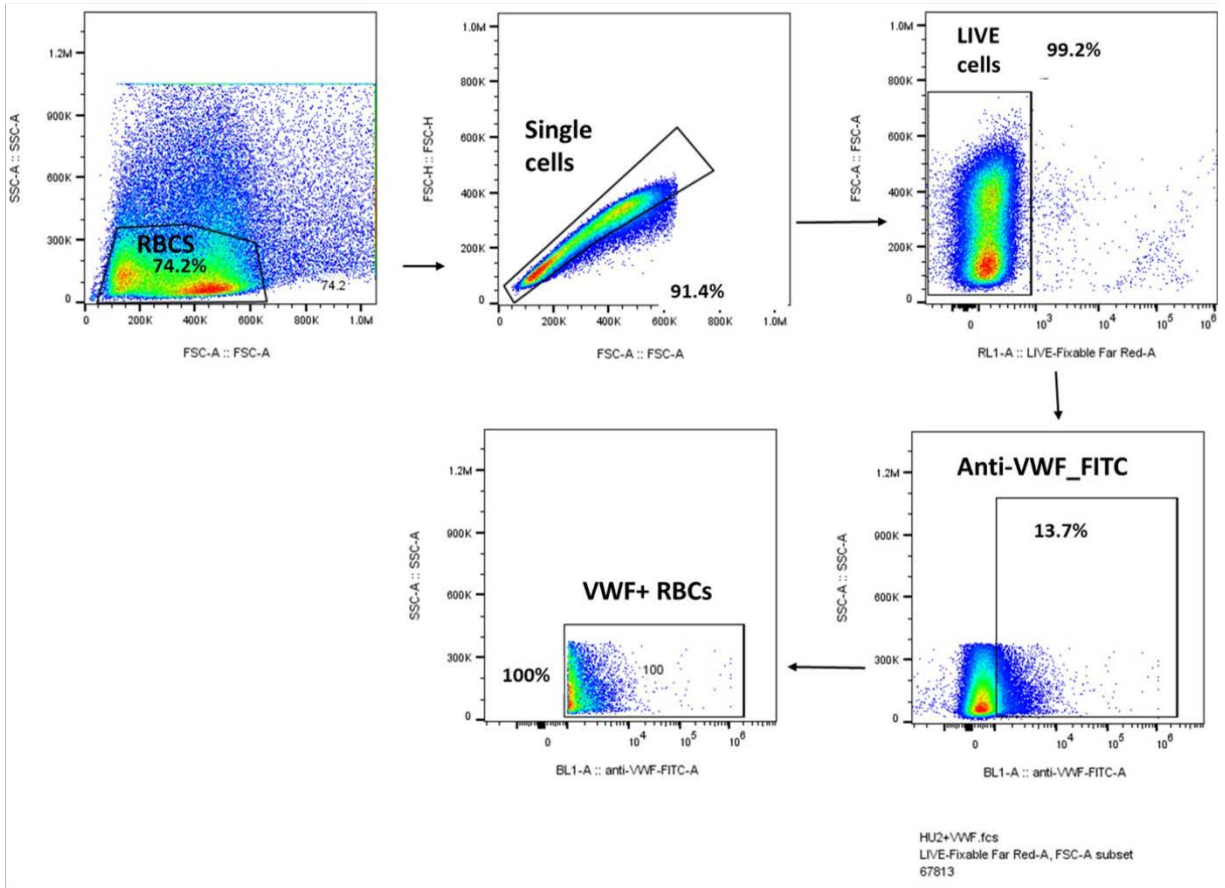
Supplementary Figure 4: Comparisons between Group O and Non O ABO blood group are shown for plasma VWF:CB (n=119 Group O, n=76 Non O) **A)** and VWFpp (n=72 Group O, n=51 Non-O) **B)** levels.

Supplementary Figure 5: Association between plasma free haem and ADAMTS13 activity is shown **A)**. ADAMTS13 activity is shown according to free haem quartiles comparing the highest and lowest quartiles for the HC **B)** and BT **C)** cohorts. Comparison between first and fourth quartile was performed with independent sample *t*-test. (ns= not significant).

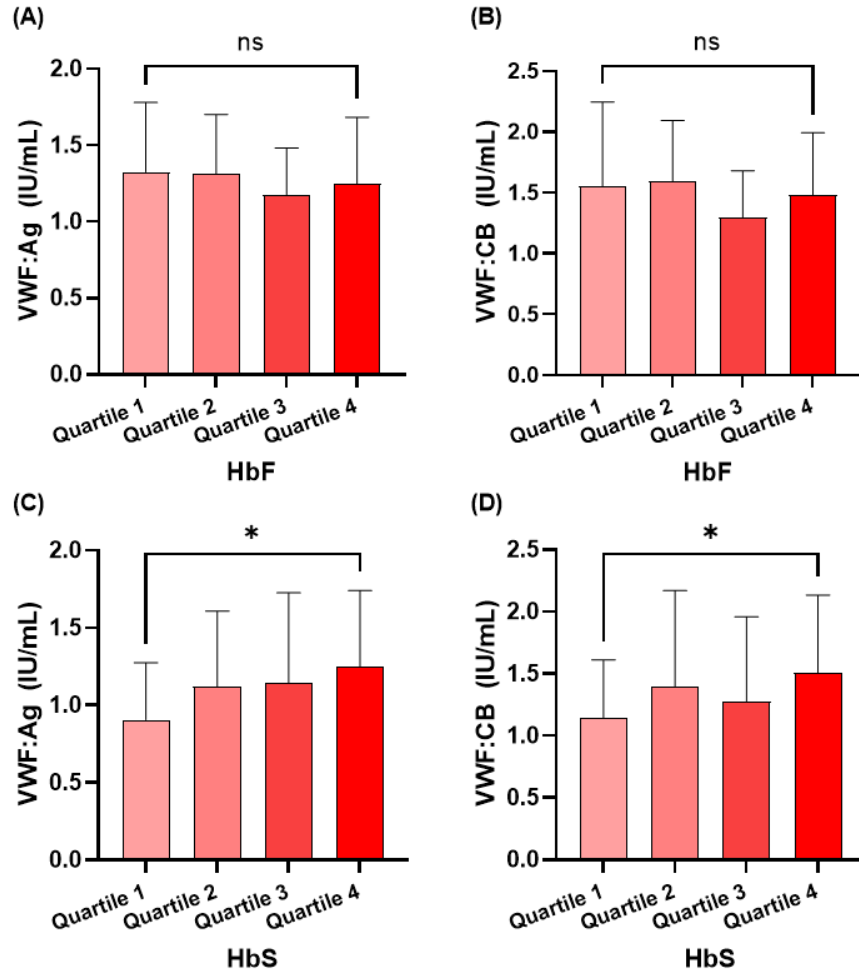
Supplementary Figure 1



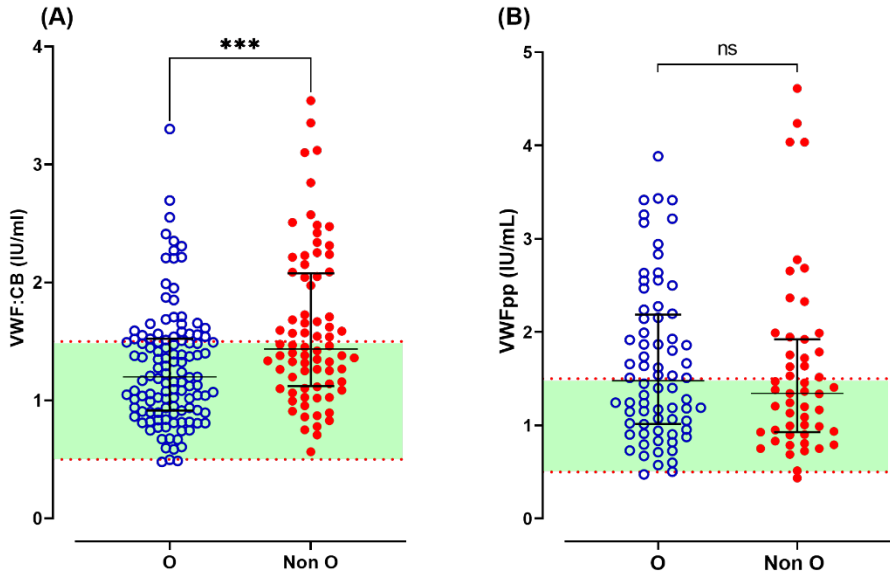
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5

