Methods: UFH (20 U/kg) alone or UFH (20 U/kg) plus AB053 (5 mg/kg) were given intravenously to juvenile baboons. Fifteen to 30 minutes later, Terumo CAPIOX RX5 baby oxygenators were deployed for 60 minutes into high flow chronic femoral arteriovenous shunts. Thrombogenesis was monitored using a gamma camera and quantified by measuring radiolabeled platelet and fibrin deposition in the oxygenators. Prothrombin time, bleeding time and volume were used to assess hemostasis.

Results: Using heparin only for anticoagulation during perfusion of the device, platelet accumulation rate averaged 1.2 billion/min, with 60 minutes end-point deposition of 52±11 billion platelets and 45±22 mg fibrin in the oxygenator (n=4). When compared to heparin, the combination of heparin with AB053 reduced average platelet accumulation rate to 0.6 billion/min, 60 minutes end-point platelet deposition to 24±5 billion, and fibrin deposition to 15±9 mg (n=3), without affecting hemostasis markers.

Conclusions: Our data suggest that supplementing heparin anticoagulation with selective pharmacological inhibition of contact activation reduces thrombogenesis in membrane oxygenators during perfusion. Therefore, this approach may allow for the reduction of the heparin dose and improve the hemostatic safety of temporal extracorporeal organ support.

PB367 | Effects of SERPINC1, PROC, PROS1 and EPCR Polymorphisms on the Risk of Venous Thromboembolism and Myocardial Infarction in Young Individuals

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Background: Antithrombin (AT), protein C (PC) and protein S (PS) are natural anticoagulants and EPCR plays a role in PC activation. Controversial data concerning the effect of their polymorphisms on the risk of venous thromboembolism (VTE) and myocardial infarction (MI) have been published, so far.

Aims: Our aim was to investigate the effects of 12 SNPs (PROC rs1799809, rs1799808, rs1799810, rs2069928, rs1401296, PROCR rs867186, rs6088735, rs8119351, SERPINC1 rs222758, rs121909548, PROS1 rs8178649 and rs121918472) on the risk of VTE and MI in young individuals.

Methods: A multiplex PCR-primer extension assay was used to detect the SNPs simultaneously in 144 VTE (median age 40; range 19-49) and in 78 MI (median age 36; range 24-40) patients and in their matched controls (n=277 for VTE and n=72 for MI). AT activity was measured by FXa-based assays, PC activity and free PS concentration were measured by chromogenic assay and latex-immunoturbidimetry, respectively.

Results: The ratio of individuals with positive thrombotic family history and with FV Leiden was higher in the VTE group as compared to controls (P<0.001 for both parameters). The ratio of smokers and patients with hyperlipidemia was higher in the MI group as compared to its control group (P<0.001 for both). AT Cambridge (rs121909548) was absent in our population and rs2227589 had no effect on the risk of VTE and MI. PS Heerlen (rs121918472) decreased free PS markedly (104 vs. 64%, P<0.001), while rs8178649 was without effect on PS levels and on the risk of thrombosis. PC activity was independently increased by PROCR rs8119351 (P=0.004) and decreased by rs6088735 (P=0.005). The PROC rs1401296 increased the risk of VTE by 2.5-fold (P=0.009), while PROCR rs867186 was protective against VTE in FV Leiden negative patients (OR 0.24, P=0.026) and against MI (OR 0.13, P=0.044).

Conclusions: Our observations suggest that some PROC and PROCR SNPs may play a role not only in venous but also in arterial thrombosis, which is worthy of further investigations.

PB368 | Structural and Functional Study of Naringin Octasulfate (NOS) on Human Antithrombin and Probing its Role in Thrombus Reduction using Rat Model

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Background: Thrombotic disorders are major contributors to the global disease burden. In such pathologies anticoagulants are the first line of defense, however due to complications the demand is growing for development of safer anticoagulants. Animal models are fundamental in accomplishing new approaches of antithrombotics. The search for novel anticoagulants with better understanding of anticoagulant pharmacology, dosing and toxicity remains a major subject of research.

Aims: To design novel naringin octasulfate (NOS) and evaluate its *in vivo* antithrombotic potential using rat model.

Methods: Synthesis of NOS was done using triethylamine-sulfur trioxide and purified by HPLC. Structural modifications were confirmed by FTIR, NMR and Mass spectrometry. The clotting assays APTT, PT and TT were performed to test *in vitro* efficacy of NOS. Antithrombotic potential of NOS was analyzed using *in vivo* venous thrombosis model which involves thrombus induction *via* ligation of inferior vena cava in rats. The *ex vivo* APTT, PT and various coagulation variables like clot rate (CT), activated clotting time (ACT) and platelet function were measured from NOS treated thrombotic rats. Molecular Docking of NOS with antithrombin (AT) was done using Auto-dock 4.0. To check secondary and tertiary structural changes on binding of NOS to AT, Far-UV CD and florescence spectroscopy were performed.